

Advances in Precision Medicine

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Advances in Precision Medicine

Focus and Scope

Advances in Precision Medicine (APM) brings together all aspects of the rapidly growing field of personalized/precision medicine. Biomarkers are a key focus of APM's scope. In particular, papers on stratification biomarkers and companion diagnostics enabling personalized medicine are highly welcome. Other categories of biomarkers accepted for consideration include pharmacodynamic biomarkers demonstrating target engagement which are potentially useful for dose finding, safety biomarkers to exclude patients with high risk for side effects or to detect induction of adverse effects early, and disease biomarkers which can be used for diagnosis, as surrogate endpoints, or to determine early response to therapy.

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Mechanism and Clinical Translation of Probiotic Preparations in the Prevention and Treatment of Periodontal Diseases

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Abstract: Periodontitis is a chronic infectious disease associated with oral microbial dysbiosis and characterized by excessive activation of host immune inflammation. It can lead to gingival inflammation, periodontal pocket formation, alveolar bone resorption, and even tooth loss, and is closely associated with systemic conditions such as diabetes and cardiovascular disease. Probiotics, as active microorganisms capable of regulating host microecology and immune function, demonstrate significant potential in the prevention and treatment of periodontal diseases. They exert protective effects by antagonizing pathogenic bacteria, restoring oral microbial homeostasis, inhibiting inflammatory responses, alleviating oxidative stress-induced damage, and promoting the repair of periodontal soft and hard tissues. The Nrf2-Keap1-ARE signaling pathway, a key regulator of antioxidant and anti-inflammatory responses in the body, is involved in the modulation of the periodontal microenvironment by probiotics and plays a crucial mediating role in inhibiting oxidative stress, resolving inflammation, and promoting osteogenic differentiation. Biomaterial carriers, represented by hydrogels, can enhance the retention and bioavailability of probiotics in the periodontal region, providing critical support for the clinical translation of probiotic preparations. This article systematically reviews the mechanisms of probiotics in periodontal diseases, elucidates the regulatory functions of the Nrf2-Keap1-ARE pathway, compares the application characteristics of different types of hydrogel carriers, and summarizes the current clinical applications, translational bottlenecks, and future directions of probiotic preparations, offering a theoretical basis for microecological regulation therapy and the development of novel formulations for periodontal diseases.

Keywords: Probiotics; Periodontitis; Oxidative stress; Nrf2-Keap1-ARE pathway; Hydrogel

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1. Introduction

Periodontal diseases are common conditions that endanger both oral and systemic health in humans. Their onset and progression are not solely caused by pathogenic bacterial infections but result from a combination of microbial community imbalance, host immune-inflammatory responses, oxidative stress damage, and tissue metabolic abnormalities^[1,2]. During the pathological process of periodontitis, biofilms formed by pathogenic bacteria such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* continuously stimulate host tissues, triggering the accumulation of reactive oxygen species (ROS) and excessive release of inflammatory cytokines, further exacerbating tissue

destruction and bone resorption, and forming a vicious cycle of “infection—oxidative stress—inflammation—tissue damage.” Systemic metabolic abnormalities such as diabetes significantly worsen periodontal lesions and reduce the effectiveness of conventional treatments, posing greater challenges for the prevention and treatment of periodontitis ^[3]. Traditional periodontal therapies can effectively remove plaque and calculus, but struggle to fundamentally restore oral microecological balance. Prolonged use of antimicrobial agents may also disrupt normal microbial flora structure and induce the emergence of drug-resistant strains. In recent years, microecological regulation therapy has gradually become a hot topic in periodontal disease research. Probiotics, due to their high safety, minimal side effects, and dual functions of ecological and immune regulation, have been widely applied in adjuvant treatment studies for periodontitis. With advancements in biomaterial technology, injectable, photocurable, and responsive hydrogels provide stable carriers for the local delivery of probiotics, effectively addressing issues such as probiotics being easily washed away by saliva, short survival times, and insufficient concentrations at lesion sites ^[4]. Meanwhile, the crucial roles of the Nrf2-Keap1-ARE signaling pathway in antioxidant, anti-inflammatory, and osteogenic processes have been gradually revealed, offering important theoretical support for elucidating the molecular mechanisms of probiotics in preventing and treating periodontitis.

2. Core mechanisms

The protective effects of probiotics on periodontal tissues are not achieved through a single pathway but are based on microecological regulation, synergistically acting at multiple levels, including pathogenic bacterial antagonism, immune-inflammatory regulation, oxidative stress alleviation, and tissue regeneration promotion, to form a systematic protective effect.

2.1. Oral microecological imbalance

In a healthy oral cavity, commensal and pathogenic bacteria coexist in a dynamic balance. When external stimuli or reduced host resistance occur, pathogenic bacteria overproliferate and form pathogenic biofilms, initiating subsequent tissue damage processes. Probiotics can inhibit the adhesion and proliferation of pathogenic bacteria through nutrient competition, spatial occupation, and antibacterial effects of metabolic products. Substances such as organic acids, hydrogen peroxide, and bacteriocins produced by probiotics can lower the local microenvironmental pH, disrupt the survival conditions of pathogenic bacteria, and simultaneously promote the proliferation of beneficial bacteria such as streptococci and actinomycetes, re-establishing a stable oral microbial flora structure and blocking the onset and progression of periodontitis at its source ^[5].

2.2. Overactivation of the immune-inflammatory

Responses Pathogen-associated molecular patterns can activate host signaling pathways such as TLR4/NF- κ B, leading to the massive release of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6, which trigger the degradation of gingival connective tissue and alveolar bone resorption ^[6]. Probiotics can bidirectionally regulate host immune responses, inhibiting the excessive activation of pro-inflammatory signaling pathways and reducing the synthesis and release of inflammatory cytokines on the one hand, and promoting the secretion of anti-inflammatory cytokines such as IL-10 and TGF- β , guiding macrophage polarization toward the M2 phenotype, facilitating inflammation resolution and tissue repair, while enhancing the barrier function of the periodontal epithelium and reducing the risk of pathogenic bacterial invasion and dissemination on the other hand ^[7,8].

2.3. Oxidative stress

Under infectious and inflammatory conditions, host cells produce large amounts of ROS, exceeding the body's antioxidant system's clearance capacity, causing cellular lipid peroxidation, protein damage, and DNA destruction, further amplifying

inflammatory signals and inhibiting osteogenic differentiation^[9]. Probiotics can alleviate oxidative stress damage by enhancing the body's antioxidant capacity, scavenging ROS, and increasing antioxidant enzyme activity, with their regulatory effects largely dependent on the mediation of the Nrf2-Keap1-ARE signaling pathway. Under normal physiological conditions, Nrf2 binds to Keap1 and remains in the cytoplasm, where it is easily ubiquitinated and degraded^[10]; when oxidative stress occurs, Nrf2 dissociates from Keap1 and translocates into the nucleus, binding to antioxidant response elements (ARE) to initiate the expression of antioxidant proteins such as HO-1, NQO1, and SOD, thereby inhibiting oxidative stress, reducing inflammation levels, promoting the expression of osteogenic-related genes, and achieving the protection and repair of periodontal tissues.

2.4. Periodontal tissue regeneration and alveolar bone reconstruction

Probiotics can positively regulate bone metabolism by inhibiting RANKL expression, increasing OPG levels, reducing osteoclast differentiation and bone resorption, while promoting the expression of osteogenic marker genes such as Runx2 and OCN, enhancing osteoblast activity. They can also promote the proliferation of periodontal ligament cells and collagen synthesis, accelerating soft tissue repair and providing support for the structural and functional recovery of periodontal tissues^[11].

2.5. Schematic diagram of the regulatory mechanism of the Nrf2-Keap1-ARE pathway

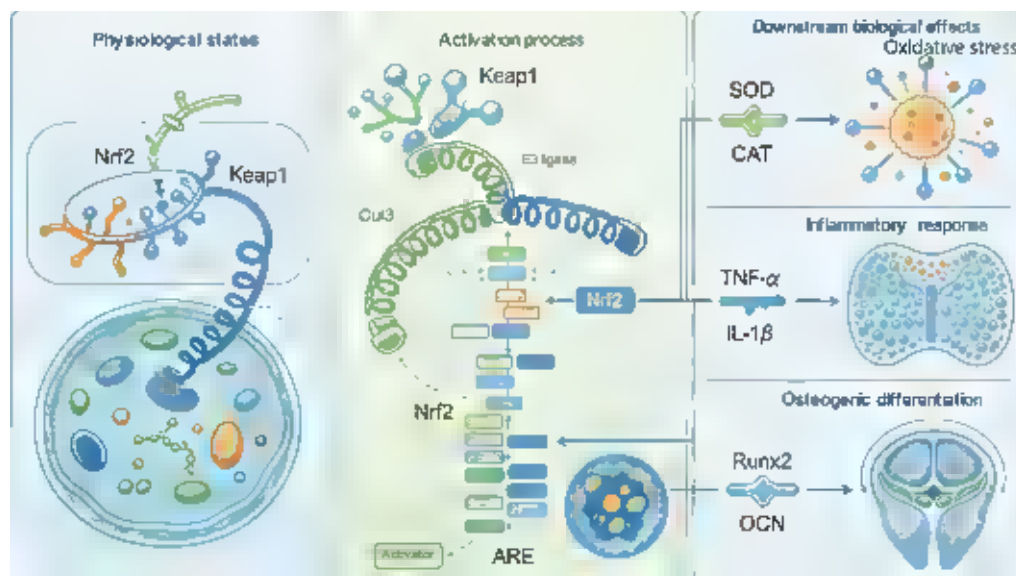


Figure 1. Mechanism of the Nrf2-Keap1-ARE pathway in regulating oxidative stress, inflammatory responses, and osteogenic differentiation.

This schematic diagram (**Figure 1**) systematically illustrates the physiological state, activation process, and downstream biological effects of this pathway. Under physiological resting conditions (left column), the transcription factor Nrf2 binds to the negative regulatory protein Keap1 in the cytoplasm, maintaining low levels of Nrf2 through ubiquitination-mediated degradation, with the pathway in an inhibited state^[12]. When cells are stimulated by oxidative stress or other factors, the conformation of Keap1 changes, leading to the dissociation of Nrf2, which then translocates into the nucleus and binds to antioxidant response elements (ARE), initiating the transcription of downstream target genes^[13].

Upon activation of Nrf2-ARE, it regulates cellular functions through multiple pathways:

- (1) It upregulates the expression of antioxidant enzymes such as SOD and CAT, scavenging reactive oxygen species (ROS) and exerting antioxidant effects^[14];
- (2) It inhibits the release of pro-inflammatory cytokines such as TNF- α and IL-1 β , regulating inflammatory responses;

- (3) It participates in the regulation of bone differentiation and metabolism through molecules such as Runx2 and OCN^[15].

This pathway serves as a core mechanism for cellular defense against oxidative stress, regulation of inflammation, and maintenance of tissue homeostasis, holding significant research value in fields such as tumors, bone metabolic diseases, and inflammatory diseases.

3. Comparison of hydrogel material properties for probiotic delivery

In local periodontal applications, hydrogels represent one of the most ideal carriers for probiotics, enhancing retention time, maintaining activity, and enabling controlled-release delivery^[16]. Different types of hydrogels exhibit significant differences in origin, properties, drug-loading methods, and response characteristics. This directly affects the delivery efficacy of probiotics and their clinical applicability.

Table 1. Comparison of properties of different types of hydrogels in local probiotic delivery

Material Type	Typical Materials	Drug Loading Type	Responsive Mechanism	Advantages	Disadvantages
Natural Hydrogel	Chitosan, sodium alginate, gelatin, hyaluronic acid, collagen	Live probiotics, anti-inflammatory proteins, growth factors	Passive release, pH-responsive, ion-responsive ^[17]	Excellent biocompatibility, biodegradable, good adhesion, high oral environment compatibility, easy to mold	Low mechanical strength, fast degradation rate, moderate stability, batch-to-batch variability
Synthetic Hydrogel	PEG, PLGA, PVA, photocurable acrylate hydrogels	Probiotics, small molecule drugs, antimicrobial peptides, and enzyme preparations	Light-responsive, pH-responsive, temperature-responsive, enzyme-responsive	High mechanical strength, stable structure, controllable degradation rate, injectable/photocurable, and precise drug release	Slightly lower biocompatibility than natural materials, relatively complex preparation process, degradation products of some materials require attention ^[18]

4. Clinical application and translation status of probiotic preparations

The clinical application of probiotics in periodontal diseases has gradually transitioned from basic research to clinical practice, with application methods primarily including local delivery and systemic intake. Both methods have demonstrated favorable outcomes in the adjunctive treatment of diseases, such as gingivitis, chronic periodontitis, and diabetic periodontitis.

4.1. Local delivery

Local application is the preferred method for periodontal probiotic therapy, as it enables direct action on the lesion site, increases local drug concentration, and reduces the risk of systemic exposure^[19]. Common clinical dosage forms include probiotic gels, solutions, films, periodontal packs, and injectable hydrogel preparations, which are typically used after periodontal basic treatment. These formulations significantly reduce periodontal probing depth, decrease probing bleeding, and improve clinical attachment levels. Long-term use helps maintain microbial stability and reduce disease recurrence rates^[20]. For patients with diabetes complicated by periodontitis, local probiotic preparations can alleviate oxidative stress and inflammatory responses exacerbated by hyperglycemia, enhancing the efficacy of conventional periodontal treatment.

4.2. Systemic intake

Systemic application primarily involves oral probiotic powders, capsules, and emulsions, which indirectly influence oral microbiota and host immune function by regulating intestinal microecology. This approach is suitable for patients with poor systemic conditions, recurrent disease, or those unable to undergo frequent local treatments. Multiple clinical studies have shown that continuous administration of preparations containing *Lactobacillus reuteri* and *Lactobacillus rhamnosus* effectively improves gingivitis symptoms, reduces the pathogenic bacterial load in the oral cavity of periodontitis patients, and positively regulates systemic inflammatory markers ^[21,22].

In clinical treatment protocols, probiotics are often used as adjunctive agents in combination with periodontal basic therapy, forming a comprehensive treatment model of “debridement + antibacterial + anti-inflammatory + repair.” Compared to monotherapy, this approach more effectively controls infection, alleviates inflammation, and promotes tissue repair, particularly in patients with moderate-to-severe periodontitis or periodontitis complicated by systemic conditions ^[23].

Despite the promising clinical application prospects of probiotic preparations, their clinical translation faces several bottlenecks. Probiotic strains exhibit high specificity, with significant variations in efficacy among different strains, and there is currently a lack of unified screening and evaluation criteria. The complex oral environment, including salivary flushing, chewing movements, and microbial competition, makes it difficult for probiotics to colonize and survive long-term, affecting treatment durability ^[24]. Live probiotic preparations have stringent storage and transportation requirements, making them prone to inactivation and limiting clinical adoption. Additionally, large-scale, long-term, multicenter clinical studies remain relatively insufficient, and standardized protocols for dosing, treatment duration, and patient eligibility have yet to be established.

5. Development directions for clinical translation of probiotic preparations

With advancements in microecological medicine, biomaterials, and molecular biology technologies, the clinical translation of probiotic preparations for periodontal diseases will progress toward precision, intelligence, and efficiency. Precision strain screening and engineering modification represent a critical future direction. By selecting probiotic strains with strong targeting and high stability based on oral microecological characteristics and host disease types, and enhancing their antibacterial, colonization, and tolerance capabilities through gene editing technologies, treatment efficacy can be significantly improved ^[25].

Optimization of biomaterial carriers will drive upgrades in probiotic delivery systems. Photocurable, injectable, and multi-responsive hydrogels enable stable retention and controlled release of probiotics in periodontal tissues. Combined delivery with Nrf2 pathway activators, anti-inflammatory drugs, or osteogenic factors can produce synergistic therapeutic effects, particularly in complex cases such as diabetic periodontitis.

Clinical research and standardized system construction are key supports for clinical translation. Conducting more large-sample, long-term follow-up, multicenter randomized controlled trials to clarify the scope of application, optimal protocols, and safety of probiotic preparations, and establishing full-process standards for strain selection, preparation, clinical application, and efficacy evaluation, will accelerate their transition from laboratory to clinical practice.

Individualized microecological regulation represents an important future trend in precision periodontal therapy. By customizing personalized probiotic formulations and treatment plans based on oral microbiota sequencing results, targeted interventions can maximize treatment efficacy and drive the transition of periodontal disease treatment from traditional symptomatic models to precision microecological regulation models.

6. Conclusion

Probiotic preparations hold significant application value in the prevention and treatment of periodontal diseases, exerting protective effects through multiple mechanisms, including regulating oral microecological balance, antagonizing pathogens, inhibiting excessive immune inflammation, alleviating oxidative stress damage, and promoting periodontal

tissue regeneration. The Nrf2-Keap1-ARE signaling pathway plays a key regulatory role in their antioxidant, anti-inflammatory, and osteogenic processes. Hydrogel carrier materials effectively enhance the delivery efficiency and bioactivity of probiotics in periodontal tissues, with natural and synthetic hydrogels offering distinct advantages that can be selected based on clinical needs. Currently, probiotic preparations have been preliminarily applied in clinical practice, demonstrating significant efficacy in the adjunctive treatment of periodontitis. However, challenges remain in strain standardization, colonization survival, preparation stability, and insufficient clinical evidence. Future efforts should focus on precision strain development, intelligent delivery system construction, clinical standard refinement, and individualized treatment exploration to promote the safe, efficient, and standardized clinical application of probiotic preparations for periodontal diseases, providing new therapeutic strategies for chronic periodontitis, diabetic periodontitis, and other conditions.

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The authors declare no conflict of interest.

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Application and Feasibility Study of High-Pressure CO₂ Sterilization Technology in Chinese Medicinal Materials Sterilization

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Abstract: Aiming at the risks of excessive microorganisms and irradiation sterilization residues in the direct use of raw powder of Chinese medicinal materials, this paper took the production line of a Chinese patent medicine enterprise as the engineering research object to study the engineering application of high-pressure CO₂ sterilization technology. With the designed sterilization conditions of pressure 30–60 MPa and temperature 35°C–65°C, the raw powder sterilization of medicinal materials with different medicinal parts was completed, and a technical parameter system for industrial application was established. During the project implementation, key technical problems, such as equipment pressure-bearing design, process energy consumption control and multi-round sterilization capacity improvement, were solved. The sterilization effect meets the pharmacopoeia standards, realizing the industrial application goal, and providing a green and safe technical alternative for the sterilization of raw powder of Chinese medicinal materials.

Keywords: High-pressure CO₂ sterilization; Raw powder of Chinese medicinal materials; Engineering application

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1. Introduction

The direct use of raw powder of Chinese medicinal materials is a common method in the production of Chinese patent medicines. Raw powder raw materials generally contain a large number of microorganisms and pathogenic flora. Traditionally, ⁶⁰Co irradiation technology is used for sterilization. Although irradiation sterilization has strong penetrability and large processing capacity, it has potential safety hazards of nuclear ray irradiation residues, and high-energy rays may affect the active components of some heat-sensitive medicinal materials. With the continuous improvement of drug safety requirements, the development of new, environmentally friendly, safe and cost-effective sterilization technologies has become a major demand in the field of Chinese patent medicine production. As a low-temperature physical treatment method, high-pressure CO₂ extraction technology exhibits good mass transfer performance and biological activity inhibition effect in the supercritical state. Starting from engineering application, this paper selected the raw powder medication process involved in the key products of a Chinese patent medicine enterprise, deeply analyzed the technical feasibility of high-pressure CO₂ sterilization technology in industrial scenarios, and formed an overall technical scheme including process parameter design, equipment selection and configuration, and on-site implementation improvement,

providing practical basis for the upgrading of sterilization technology for raw powder of Chinese medicinal materials.

2. Engineering overview and technical basis analysis

2.1. Process characteristics and sterilization requirements of the production line

A Chinese patent medicine enterprise located at the foot of the Qinling Mountains has an advanced production line and a fully intelligent integrated production workshop. The core products of the enterprise adopt the raw powder medication process of Chinese medicinal materials, covering four major categories of medicinal materials: roots and rhizomes, flowers, leaves, and fruits and seeds, involving key medicinal materials such as *Salvia miltiorrhiza*, *Bupleurum chinense*, *Schisandra chinensis*, *Lonicera japonica*, *Isatis indigotica* leaves and *Ligustrum lucidum* fruit ^[1]. According to the microbial limit specifications of Table 3 “Non-sterile pharmaceutical raw materials and excipients” in the *Chinese Pharmacopoeia*, the total number of aerobic bacteria in pills shall not exceed 30,000 colony-forming units per gram (CFU·g⁻¹), and the total number of molds and yeasts shall not exceed 10² colony-forming units per gram (the maximum acceptable number of bacteria is 200).

2.2. Technical principle and applicability demonstration of high-pressure CO₂ sterilization

High-pressure CO₂ sterilization technology relies on the strong diffusivity and low viscosity of supercritical CO₂ fluid, and destroys the microbial cell membrane structure through the combined action of pressure and temperature. When CO₂ is in a supercritical state with pressure exceeding 7.38 MPa and temperature exceeding 31.1°C, its density is close to that of liquid and its diffusion coefficient is close to that of gas, which can penetrate the tiny pores inside the medicinal material powder ^[2]. In the high-pressure CO₂ environment, microbial cells suffer from physiological inhibition, such as the extraction of cell wall lipids, a decrease in internal pH value and inactivation of important enzyme systems. For the treatment of raw powder of Chinese medicinal materials, this technology can achieve a sterilization effect in the temperature range of 35°C–65°C, avoiding the color change of medicinal materials and loss of volatile oil components caused by high temperature in the traditional dry heat sterilization method, and also solving the hydrolysis damage of active components of medicinal materials caused by the moist heat sterilization method. The technical applicability evaluation shows that this process has good applicability to the raw powder of Chinese medicinal materials with low water content (such as less than 12%), and can well adapt to the material characteristics of different medicinal parts, such as rhizomes, leaves and flowers.

Table 1. Microbial background value and sterilization target of medicinal raw materials in the project

Sample Name	Total aerobic bacteria (cfu/g)
Mixed coarse powder of <i>Salvia miltiorrhiza</i> / <i>Schisandra chinensis</i>	Uncountable
Mixed coarse powder of <i>Salvia miltiorrhiza</i> / <i>Schisandra chinensis</i> (1st round sterilization)	7000
Mixed coarse powder of <i>Salvia miltiorrhiza</i> / <i>Schisandra chinensis</i> (2nd round sterilization)	1000
<i>Ligustrum lucidum</i> fruit	12000
<i>Ligustrum lucidum</i> fruit (1st round sterilization)	1200
<i>Isatis indigotica</i> leaves	53000
<i>Isatis indigotica</i> leaves (1st round sterilization)	21000
<i>Lonicera japonica</i>	18000
<i>Lonicera japonica</i> (1st round sterilization)	2000
<i>Bupleurum chinense</i>	Not studied

3. Design of engineering application scheme for high-pressure CO₂ sterilization

3.1. Sterilization process route and pressure parameter configuration

The project adopted the batch-type high-pressure autoclave sterilization method, equipped with two vertical high-pressure sterilization autoclaves with a capacity of 1000 liters. The working pressure was designed to be 60 MPa and the temperature was 70°C. Each autoclave can load 800 kg of coarse medicinal material powder, and the powder particle size is kept in the range of 40 to 60 meshes to enhance the penetration effect of CO₂ fluid^[3]. The process pressure parameters are set in an adjustable range of 30 MPa to 60 MPa and adjusted according to different types of medicinal materials: a higher pressure condition of 55 MPa is used for roots and rhizomes, a medium pressure condition of 40 MPa for flowers and leaves, and a medium-high pressure condition of 50 MPa for fruits and seeds. The sterilization cycle is 3 hours per round, including 30 minutes of pressure rise, 150 minutes of pressure holding for sterilization and 30 minutes of pressure relief and exhaust. The multi-round sterilization scheme is adjusted according to the microbial detection results, and the basic scheme is two rounds of treatment.

3.2. Design of CO₂ fluid circulation and temperature control system

The system is equipped with a CO₂ circulation and recovery device to control the operation cost, adopting a closed circulation mode of compressor pressurization and condenser liquefaction. The capacity of the CO₂ storage tank is set to 5 cubic meters, the storage pressure is kept at about 6 MPa, and the storage temperature is normal room temperature^[4]. The pressurization system uses a three-stage piston compressor to compress liquid CO₂ to the process pressure and send it to the sterilization autoclave. Temperature regulation is completed by the jacketed heat exchanger of the autoclave body, with a 60°C hot water circulation system as the heat source and a 5°C-ethylene glycol solution circulation system as the cold source. Hot CO₂ fluid at 60°C is introduced during the pressure rise stage, so that the temperature in the autoclave reaches the target sterilization temperature of 35°C–65°C within 15 minutes. During the pressure holding stage, the temperature fluctuation range is controlled within $\pm 2^\circ\text{C}$ by a proportional regulating valve to ensure the stability of the sterilization process.

3.3. Design of equipment, material and sealing structure

The main material of the high-pressure sterilization autoclave is S30408 austenitic stainless steel; the inner diameter of the cylinder is 800 mm, and the wall thickness is set to 45 mm according to the strength requirements. The head of the autoclave body adopts a standard elliptical head with a major-minor axis ratio of 2:1 and the same thickness as the cylinder. The sealing method adopts a double wedge ring self-sealing structure, and the sealing material is polytetrafluoroethylene composite material, which can bear a pressure range of 0 to 70 MPa^[5]. The design life of the equipment is about 15 years, and the corrosion allowance is about 1.5 mm. Three layers of perforated clapboards are arranged in the autoclave, and the loading height of each layer is not more than about 200 mm to ensure the uniformity of the longitudinal flow of CO₂ fluid. The pressure relief pipeline is equipped with a muffler and a CO₂ recovery interface, and the pressure relief rate is controlled at no more than about 2 MPa per minute to avoid powder entrainment with the air flow.

4. Analysis of technical difficulties in project implementation

4.1. Fluctuation of multi-batch sterilization efficiency

During the commissioning stage of the project, the detection results of the total number of aerobic bacteria in the mixed powder of *Salvia miltiorrhiza* and *Schisandra chinensis* showed obvious differences between batches, with 7000 CFU per gram measured in a certain batch after the first round of sterilization. The analysis found that the uneven bulk density of the coarse medicinal material powder in the autoclave led to poor flow of CO₂ fluid and channeling in some areas, resulting in incomplete sterilization. The bulk density measurement results showed that the value varied from 0.35 to 0.42 liters per kilogram, which was different from the uniform accumulation expected in the equipment design. Similarly, the

water content of medicinal materials harvested in different seasons varied from 8% to 15%, and the increase in water content caused the change of CO₂ fluid solubility, thus interfering with the lipid extraction effect of cell membranes^[6]. The temperature field distribution detection found that the temperature difference between the upper and lower parts of the autoclave body reached 5°C in some cases, exceeding the temperature stability requirements for microbial sterilization kinetics. The experimental data on the sterilization effect of coarse *Bupleurum chinense* powder showed that its initial microbial content was 4000 colony-forming units per gram. After one process of high-pressure CO₂ sterilization, the microbial content decreased to 100 colony-forming units per gram, a reduction of 97.5% in the number of microorganisms^[7]. After the second process of sterilization, the microbial content further decreased to less than 10 colony-forming units per gram, with an overall reduction ratio of more than 99.75%, meeting the limit standard of not more than 100 colony-forming units per gram specified in the *Chinese Pharmacopoeia*^[8]. This indicates that the high-pressure CO₂ sterilization process has a significant microbial killing effect on medicinal materials containing volatile oil components such as *Bupleurum chinense*, and can meet the relevant compliance requirements of the pharmacopoeia after two rounds of treatment. At the same time, this process can avoid the damage of heat-sensitive active components caused by the traditional high-temperature sterilization method, which reflects the technical advantages of this process in ensuring the quality and safety of medicinal materials.

4.2. Hidden danger of fatigue cracks in equipment pressure-bearing components

After three months of project operation, fine cracks were found in the weld-adjacent area of the sealing surface of the quick-opening blind plate during the tank opening inspection of the sterilization autoclave. Nondestructive testing confirmed that the cracks were stress corrosion cracks, caused by the combined action of water in the high-pressure CO₂ environment and residual stress on the equipment surface. The material of the main cylinder met the strength requirements, but frequent pressure cycle loading led to fatigue cracks in local stress concentration areas. The polytetrafluoroethylene composite material of the sealing structure showed a cold flow phenomenon in the high-pressure environment, and needed to be replaced when the service life was only about 60% of the design life. The wear rate of the piston ring in the high-pressure stage of the compressor exceeded the expectation, and the fine powder particles carried by CO₂ caused abrasive wear during the compression process, reducing the volumetric capacity to about 85% of the design value.

5. Project optimization and technical solutions

5.1. Powder fluidized loading and multi-round process optimization

Aiming at the problem of unstable sterilization capacity, the technical transformation of powder fluidized uniform loading was carried out. A vibrating feeder and a distributor were equipped at the feeding port of the autoclave body, so that materials such as coarse *Bupleurum chinense* powder were evenly filled in a layered accumulation mode, and the thickness of single-layer loading was controlled at 180 mm with stainless steel wire mesh support laid between layers. A differentiated sterilization scheme based on the initial colony count was established: when the initial total number of molds and yeasts of medicinal materials such as *Bupleurum chinense* exceeds 4000 CFU per gram, a four-round sterilization process is adopted with a pressure of about 55 MPa, a temperature of 60°C, a pressure holding time of about 2.5 hours and a total processing time of no more than 12 hours^[9]. For relatively clean plant medicinal materials such as *Lonicera japonica* in the initial state, two rounds of sterilization are carried out with a pressure of 40 MPa, a temperature of 45°C and a pressure holding time of 3 hours. The online rapid microbial detection technology is adopted to shorten the culture detection time from 48 hours to 8 hours, realizing flexible adjustment of the number of sterilization rounds and avoiding over-treatment.

The calculation formula and process verification are as follows. The calculation formula of sterilization efficiency η is:

$$\eta = \frac{N_0 - N_t}{N_0} \times 100\%$$

where N_0 represents the initial colony number and N_t represents the colony number after sterilization treatment. Taking the second round of sterilization of coarse *Bupleurum chinense* powder as an example, the initial number of molds and yeasts N_0 is 4000 CFU per gram, and the number after sterilization treatment N_t is 10 CFU per gram. Substitute the values into the formula for calculation:

$$\eta = \frac{4000 - 10}{4000} \times 100\% = 99.75\%$$

The calculation results show that two rounds of high-pressure CO₂ treatment can inactivate a large number of microorganisms, meeting the requirements specified in the pharmacopoeia.

5.2. Equipment structure strengthening and material upgrading scheme

Aiming at the fatigue crack problem of pressure-bearing components, the material and structure of the equipment were improved: the material of the quick-opening blind plate was changed from S30408 to S31603, a polytetrafluoroethylene anti-corrosion coating with a thickness of about 2 mm was added to reduce the corrosion rate of CO₂ aqueous solution; the sealing groove structure was redesigned, adopting a combined sealing form of O-ring and wedge ring to improve the anti-cold flow capacity of the sealing part under high pressure; more flow guide devices were added inside the cylinder to make the CO₂ fluid distribution more uniform and reduce the wear of the vessel wall caused by local turbulence; a life evaluation model based on the number of pressure cycles was established and an annual maintenance plan was formulated, adopting a combination of magnetic particle testing and ultrasonic testing for integrity evaluation; the compressor system was equipped with an inlet filter and a buffer tank with a filtration accuracy of 5 microns to prevent medicinal material dust from entering the compression chamber.

5.3. Optimization of process parameter boundary and efficacy protection strategy

A balanced control method of sterilization intensity and component preservation was established, and the pressure-time critical values of various medicinal materials were determined by single-factor experiments. For medicinal materials containing volatile oil components such as *Bupleurum chinense*, the sterilization pressure was reduced from 55 MPa to 45 MPa, the temperature was kept at 40°C, and the pressure holding time was extended to 4 hours to make up for the sterilization intensity^[10]. CO₂ fluid saturation control technology was adopted, and a CO₂ mixed fluid containing saturated water vapor was introduced in the pressure rise stage to weaken the dissolution and extraction effect on fat-soluble components. For fruits and seeds, the pressure difference cycle process was adopted, with a pressure change of about 0.5 MPa every half hour during the pressure holding stage to enhance the penetration effect of CO₂ fluid on cell membranes, achieving the same sterilization effect at a lower pressure, and the retention rate of active components was increased to more than 98%. A medicinal material classification and coding system was formulated, and the most suitable combination of process parameters was selected according to the medicinal parts and component characteristics.

6. Conclusion

Taking the production line of raw powder preparation of a Chinese patent medicine enterprise as an engineering example, this paper studied the engineering application approach of high-pressure CO₂ sterilization technology, designed the sterilization conditions with a pressure range of 30 to 60 MPa and a temperature range of 35°C to 65°C, and solved the technical problem of replacing irradiation residues in raw powder of Chinese medicinal materials. During the project implementation, relying on the transformation of powder fluidized loading, improvement of equipment materials, optimization of process parameter range and configuration of heat energy recovery system, the main technical

problems, such as unstable sterilization capacity, equipment wear and cracks, loss of active components and high energy consumption, were solved. Practice shows that this technology has universal application value for medicinal materials of roots and rhizomes, flowers and leaves, and fruits and seeds, and can meet the microbial limit standards of the *Chinese Pharmacopoeia* after process improvement. With the characteristics of low-temperature treatment, advantages of no chemical residues and recyclable operation, high-pressure CO₂ sterilization technology provides an environmentally friendly and safe technical scheme for the sterilization of raw powder of Chinese medicinal materials, and has the potential for large-scale industrial application.

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The Application of Checklist Management in the Risk Management of Clinical Teaching for Chronic Wound Care in Burn and Plastic Surgery

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Abstract: *Objective:* To explore the application effect of checklist management in the clinical teaching risk management of chronic wound care in the burn and plastic surgery department. *Methods:* 80 nursing students who interned in our department from January 2022 to December 2023 were divided into the control group (40 students, using the traditional teaching mode) and the observation group (40 students, implementing the checklist management teaching mode) according to the teaching time sequence. The theoretical knowledge and operational skills assessment scores, the incidence of nursing risk events, and the teaching satisfaction of the two groups were compared respectively. *Results:* The theoretical knowledge score (91.3 ± 5.2 points) and operational skills score (90.5 ± 4.8 points) of the observation group were both higher than those of the control group (82.4 ± 6.3 points and 78.6 ± 7.1 points), and the differences were statistically significant ($P < 0.05$); the incidence of nursing risk events in the observation group (5.0%) was lower than that in the control group (20.0%), and the difference was statistically significant ($P < 0.05$); the teaching satisfaction rate of the observation group (97.5%) was higher than that of the control group (75.0%), and the difference was statistically significant ($P < 0.05$). *Conclusion:* The application of checklist management in the clinical teaching of chronic wound care in the burn and plastic surgery department can effectively improve the comprehensive skills of nursing students, reduce the incidence of nursing risk events, and enhance teaching satisfaction, which is worthy of clinical promotion.

Keywords: Checklist management; Burn and plastic surgery department; Chronic wound; Clinical teaching; Risk management

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1. Introduction

The management of chronic wounds in burn and plastic surgery is a complex task involving dressing changes, infection control, and local anatomical identification, which has always been a key and challenging area in clinical nursing education. Tang et al. (2025) found that the traditional single teaching method in burn and plastic surgery nursing education is no longer sufficient to meet the needs of comprehensive ability training for intern nurses ^[1]. Common problems among intern nurses include weak awareness of operational norms and insufficient risk identification ability. Given the characteristics of the specialty, such as the variable state of wounds, the vulnerability of patients, and the high risk of wound infection, intern nurses are more prone to assessment omissions, operational deviations, and even nursing

risk events during independent operations, and the stability of teaching quality needs to be improved.

2. Materials and methods

Checklist management originated from the fields of aviation and surgical safety. By standardizing complex procedures into checklists that can be verified item by item, it effectively reduces the safety risks caused by human omissions. Zeng et al. (2015) pointed out that checklist management has broad application prospects in nursing and can standardize nursing behaviors and reduce nursing defects^[2]. Foreign studies have also shown that introducing systematic teaching tools in clinical nursing education can significantly improve interns' mastery of clinical skills and reduce operational errors^[3]. In terms of risk management education, Padash et al. (2023) confirmed that clinical risk management training for nursing students can effectively enhance their patient safety competence, and structured intervention is an important means to improve teaching effectiveness^[4]. In addition, Yang et al. (2024) combined checklist-based teaching management with a two-way evaluation system and achieved positive results in clinical nursing teaching practice^[5]; Liu et al. (2023) also systematically reviewed the research progress of checklist-based teaching methods in undergraduate nursing education and concluded that this method has obvious advantages in improving teaching quality^[6]. Based on the above background, this study takes chronic wound care in burn and plastic surgery as the entry point and introduces checklist management into the clinical teaching risk management system, aiming to explore a new path for specialized nursing teaching that is both practical and safe.

2.1. General information

A total of 80 nursing students who participated in clinical internships in the burn and plastic surgery department of our hospital from January 2022 to December 2023 were selected and divided into a control group ($n = 40$) and an observation group ($n = 40$) based on the order of their internships. Inclusion criteria: full-time undergraduate or junior college students majoring in nursing; first-time internship in this department; voluntary participation in this study. Exclusion criteria: those who withdrew from the internship halfway; those with severe communication disorders. There were no statistically significant differences in general data such as age, gender, education level, and teaching duration between the two groups ($P > 0.05$, see **Table 1**), making them comparable.

Table 1. Comparison of general data of intern nurses in the two groups

Item control	Group ($n = 40$)	Observation group ($n = 40$)	χ^2/t	P Value
Age (years, mean $\pm$ SD)	21.3 $\pm$ 1.2	21.5 $\pm$ 1.1	0.79	0.432
Gender (male/female, n)	12/28	13/27	0.05	0.819
Education (junior college/undergraduate, n)	18/22	17/23	0.05	0.819
Teaching Duration (months, mean $\pm$ SD)	3.1 $\pm$ 0.4	3.0 $\pm$ 0.5	1.01	0.316

2.2. Teaching methods

The control group adopted the traditional teaching mode, where the teaching instructor arranged operational demonstrations, on-the-job observations, and exit examinations according to the department's routine. The teaching content was mainly oral instruction and experience sharing, without a unified operational procedure standard.

The observation group implemented a teaching mode based on checklist management, based on the control group, with the following specific measures:

- (1) Construction of a specialized nursing teaching checklist system. The head nurse of the department, in collaboration with associate chief nurses, wound care specialists, and senior teaching nurses, developed the "Teaching Checklist for Chronic Wound Care in the Burn and Plastic Surgery Department" (hereinafter referred to as the "Teaching Checklist") after repeated discussions. The checklist covers six major modules: wound assessment, aseptic technique,

dressing change norms, secretion sampling, instrument handling, and risk prevention, with a total of 32 verification items. Each item is presented in a “yes/no” format, accompanied by notes and risk warnings, requiring nursing students to check each item before and after each operation.

- (2) The teaching checklist is implemented in three phases over 12 weeks. In the first phase (weeks 1–4), the teaching nurse demonstrates the procedures, and the nursing students observe and learn by referring to the checklist. In the second phase (weeks 5–8), the students perform the operations independently under the supervision of the teaching nurse, who explains the risk items before each operation, and the students self-assess and fill out the checklist after each operation. In the third phase (weeks 9–12), the students operate independently, and the teaching nurse conducts a two-way evaluation based on the checklist, providing targeted reinforcement training for weak items.
- (3) A dynamic risk early warning mechanism is established. The teaching nurse summarizes the checklist verification records weekly, identifies high-frequency error items, and provides feedback at the morning meeting. Real cases are used to organize case discussions, guiding the nursing students to internalize the checklist thinking into operational habits. When there are signs of nursing risk events, the department’s special review process is immediately triggered, and the teaching nurse provides one-on-one guidance to the relevant nursing students.

2.3. Observation indicators

- (1) Assessment Scores: This includes the theoretical knowledge test (out of 100 points, covering wound anatomy, dressing change principles, infection control, etc.) and the operation skills assessment (out of 100 points, scored based on the items on the teaching checklist) before leaving the department.
- (2) Nursing Risk Incidents: The number of risk incidents, such as dressing change errors, insufficient infection control, and missed reporting of patient conditions, during the internship period will be counted.
- (3) Teaching Satisfaction: A self-made questionnaire by the department will be used to assess the satisfaction of the interns before leaving the department, with three levels: very satisfied, satisfied, and dissatisfied. The satisfaction rate is calculated as (very satisfied + satisfied) / total number of people $\times$ 100%.

2.4. Statistical methods

SPSS 26.0 software was used to process the data. Measurement data were expressed as mean $\pm$ standard deviation (SD), and the independent sample *t*-test was used for comparison between groups; count data were described by frequency and percentage, and the χ^2 test was used for comparison between groups. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of assessment scores between the two groups of nursing students

The theoretical knowledge score (91.3 ± 5.2 points) and operation skills score (90.5 ± 4.8 points) of the observation group were both higher than those of the control group (82.4 ± 6.3 points and 78.6 ± 7.1 points, respectively), and the differences were statistically significant ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of assessment scores of interns in the two groups (Points, mean $\pm$ SD)

Group	n	Theoretical Knowledge (Points, mean $\pm$ SD)	Operation Skills (Points, mean $\pm$ SD)
Control Group	40	82.4 ± 6.3	78.6 ± 7.1
Observation Group	40	91.3 ± 5.2	90.5 ± 4.8
<i>t</i>		8.74	9.52
<i>P</i> value		< 0.05	< 0.05

3.2. Comparison of the occurrence of nursing risk incidents between the two groups

The incidence of nursing risk incidents in the observation group (5.0%) was significantly lower than that in the control group (20.0%), and the difference was statistically significant ($\chi^2 = 4.114$, $P = 0.043$), as shown in **Table 3**.

Table 3. Comparison of occurrence of nursing risk incidents in the two groups [n(%)]

Group	n	Medication change operation error	Insufficient infection control in the hospital	Omission in reporting of patient condition observation	Total number of risk events	Occurrence rate (%)
Control Group	40	4	3	1	8	20.00
Observation Group	40	1	1	0	2	5.00
χ^2	—	—	—	—	4.114	—
<i>P</i> value	—	—	—	—	0.043	—

3.3. Comparison of teaching satisfaction between the two groups

The teaching satisfaction rate of the observation group (97.5%) was higher than that of the control group (75.0%), and the difference was statistically significant ($P = 0.003$), as shown in **Table 4**.

Table 4. Comparison of teaching satisfaction in the two groups [n(%)]

Group	n	Very Satisfied	Satisfied	Not Satisfied	Satisfaction Rate (%)	<i>P</i> value
Control Group	40	16 (40.0)	14 (35.0)	10 (25.0)	75.00	0.003
Observation Group	40	27 (67.5)	12 (30.0)	1 (2.5)	97.50	

4. Discussion

The care of chronic wounds in burn and plastic surgery departments is a weak link in the specialized skills training of nursing students due to the numerous operation steps and scattered risk factors. The results of this study show that the theoretical knowledge and operation skills scores of the observation group were significantly higher than those of the control group before leaving the department, confirming the positive value of checklist management in the training of nursing students' skills. The reason for this is that the teaching checklist solidifies the key technical nodes scattered in each operation process in a list form, providing a basis for each practical operation of the nursing students and effectively shortening the transition period from theory to practice. Alizadeh-Taghiabad et al. (2023) proposed in their study on the standard for the frequency of dressing changes for burn wounds that establishing clear and quantifiable operational standards is a key prerequisite for shortening the learning curve and improving the quality of operations, which is highly consistent with the functional positioning of the checklist items in this study^[7]. Additionally, Gillespie et al. (2023) confirmed through a prospective study that nurse-led wound care education without structured content support will show significant fluctuations in educational outcomes with changes in the operational scenarios; using a checklist as a framework can effectively ensure the consistency and completeness of educational content^[8].

In this study, the incidence of nursing risk events in the observation group (5.0%) decreased by 75% compared to the control group (20.0%), and the difference was statistically significant. The checklist management fundamentally shifts the risk prevention and control to the front end - before each dressing change, nursing students must confirm each item on the checklist, including the establishment of a sterile barrier, the completeness of wound assessment records, and the proper disposal of operational waste. Any omissions will be intercepted by the checklist mechanism. Purabdollah et al. (2023) pointed out in their scoping review that the cultivation of clinical competence among nursing students not only depends on knowledge accumulation but also on the continuous reinforcement of safe behaviors in real clinical environments, and structured operation checklists are an effective carrier for this reinforcement process^[9]. Padash et al. (2023) also found that

systematically embedding risk management concepts into nursing student training can improve their ability to identify and respond to patient safety situations, which is consistent with the design concept of the dynamic risk warning mechanism in this study. For risk management in specialized nursing teaching to shift from passive response to active prevention and control, checklist-based and process-oriented teaching tools are indispensable.

The improvement in the teaching satisfaction of nursing students reflects the positive role of checklist management in the teaching relationship. When the assessment dimensions are clear and the expected goals are visible, the learning anxiety of nursing students decreases; when teaching instructors evaluate according to a unified checklist standard, it also reduces the inconsistency of subjective scoring, making nursing students more accepting of the assessment results. Onarici et al. (2021) confirmed through a randomized controlled trial that introducing a structured intervention model in the teaching of burn patient care plans improved the skill mastery and subjective satisfaction of nursing students, which is consistent with the conclusion of this study^[10]. Bobbink et al. (2022) also found in the evaluation of a blended learning project for wound care among undergraduate nursing students that when students can obtain clear operational path guidance, their self-efficacy and course satisfaction significantly increase^[11]. Parker et al. (2022) further suggested that an integrated multi-professional perspective framework for wound care education helps nursing students establish a more complete clinical thinking, which provides a direction for the iterative optimization of checklist content in the future^[12].

5. Conclusion

In conclusion, introducing checklist management into the risk management system for clinical teaching in chronic wound care in burn and plastic surgery is not only a beneficial supplement to the traditional teaching model but also a practical path for ensuring the quality of specialized nursing education. Future studies can appropriately expand the research scale to further verify the long-term effects and application boundaries of checklist management.

Disclosure statement

The authors declare no conflict of interest.

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Effect Analysis of Multidisciplinary Team (MDT) Concept in the Teaching of Medical Oncology

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Abstract: To address the disconnection between oncology nursing education and clinical multidisciplinary collaboration, the MDT concept was integrated into the nursing education system. The framework was constructed through theoretical integration, modularized teaching content, multidisciplinary collaborative instruction, and practical pathways, with evaluations conducted from dimensions such as comprehensive professional competencies, quantitative and qualitative indicators, and application outcomes. Results demonstrated that this model enhanced nursing students' specialized knowledge, teamwork skills, and clinical thinking, aligned teaching more closely with clinical practice, and effectively improved the quality of talent cultivation. The study provides references for reforming oncology nursing education and promotes the development of specialized nursing professionals toward comprehensive and collaborative capabilities.

Keywords: Multidisciplinary collaboration; MDT; Medical oncology; Nursing education; Teaching effectiveness

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1. Introduction

In the oncology nursing department, dealing with patients who have complex conditions, multiple comorbidities, and diverse needs requires highly specialized skills and a strong interdisciplinary nature. This demands a comprehensive assessment of nursing staff, cross-departmental communication, emergency response, and humanistic care capabilities. Traditional nursing education mainly focuses on teaching single-discipline knowledge and skills training, with relatively independent teaching content and a lack of systematic training in multi-disciplinary collaboration and realistic clinical scenarios, resulting in nursing students' difficulty in quickly integrating into the MDT diagnosis and treatment team and insufficient overall nursing and collaborative work capabilities. Integrating the MDT concept into oncology nursing education helps break disciplinary boundaries, restructure teaching content and practice models, and strengthen students' teamwork awareness and full-cycle care capabilities. This paper conducts research from the aspects of theoretical integration, teaching system construction, and effect evaluation, exploring scientific and feasible teaching reform paths to improve the quality of oncology nursing education and cultivate specialized nursing talents that meet modern clinical needs.

2. Theoretical integration of the MDT concept and oncology nursing education

2.1. Core goals and competency requirements of oncology nursing education

The core goal of oncology nursing education is to cultivate specialized nursing talents with professional care capabilities, humanistic care qualities, and clinical adaptability to meet the comprehensive care needs of complex tumor patients. The teaching process should not only solidify the theoretical foundation of oncology disease care, medication observation, and complication prevention, but also highlight the combination of clinical thinking and practical operation, enabling nursing staff to accurately identify changes in the condition and standardly implement diagnostic and therapeutic cooperation measures. With the continuous development of tumor diagnosis and treatment models, nursing work is no longer limited to basic operations but extends to psychological counseling, nutritional support, rehabilitation guidance, and hospice care, placing higher standards on the comprehensive qualities of nursing staff. In terms of competency requirements, systematic professional knowledge, proficient operational skills, fluent communication and expression, and decisive emergency response are all indispensable, and a strong sense of responsibility and humanistic care spirit are also required. The traditional teaching model often focuses on knowledge imparting, neglecting cross-scenario collaboration and multi-dimensional care capabilities training, leading to students' difficulty in quickly adapting to the team collaboration model upon entering the clinical setting. Defining the core goals and competency requirements can help position the integration of the MDT concept, making the teaching reform more targeted, promoting the transformation of teaching from skill imparting to comprehensive ability cultivation, and laying the foundation for the construction of a modern oncology nursing education system ^[1].

2.2. Interpretation of the MDT model and adaptability of the nursing profession

MDT, or multi-disciplinary collaboration model, is centered on integrating resources and advantages from different professional fields to form a collaborative diagnosis and treatment system for patients' needs. It has become the mainstream practice model in tumor diagnosis and treatment. MDT emphasizes breaking disciplinary boundaries and, through the joint efforts of doctors, nurses, pharmacists, nutritionists, psychologists, etc., form individualized and full-cycle treatment and care plans for patients. Its core value lies in improving treatment effects, optimizing service processes, and enhancing patients' medical experience. From the perspective of the nursing profession, the MDT model and oncology nursing have a high degree of compatibility. Nursing staff, as the key role accompanying patients throughout the process, are the link and executor of the multi-disciplinary team, responsible for information transmission, condition monitoring, implementation of care measures, and communication and coordination. Integrating the MDT concept with the nursing profession can highlight the dominant position of nursing work in multi-disciplinary collaboration, transforming the role of nursing staff from a single executor to an active participant in team discussions and plan formulation. This adaptability is not only reflected in the complementary nature of the work content but also aligns with the patient-centered service concept of nursing work, helping nursing staff establish an overall care mindset and enhance problem-solving abilities. At the same time, it also makes nursing teaching more closely related to clinical practice, providing theoretical support for cultivating specialized nursing talents who are adaptable to the modern oncology medical environment.

2.3. The integration logic of the MDT concept and the nursing teaching system

The integration of the MDT concept with the oncology nursing teaching system follows the internal logic of clinical demand orientation, ability-based core, and interdisciplinary collaboration development. It is an inevitable choice for the teaching model to adapt to the changes in clinical practice. Traditional nursing teaching divides content based on disciplines, with relatively independent knowledge structures, lacking cross-disciplinary linkage design, and being disconnected from real clinical work scenarios. The integration of the MDT concept essentially reconfigures teaching content and organization, integrating multi-disciplinary collaboration thinking throughout the process of theoretical teaching, practical operation, and clinical internship, enabling students to establish teamwork awareness during the learning stage. The integration process adheres to the nursing profession as the main body, while also moderately permeating

knowledge from other related disciplines. It does not blindly expand the teaching scope but focuses on the responsibilities and ability requirements of the nursing position in the MDT team, optimizing teaching modules and practical links. At the same time, the integration logic emphasizes the consistency between teaching and clinical practice. Through forms such as simulated MDT consultations and interdisciplinary case discussions, students understand the key points of cooperation between nursing work and other disciplines, and improve their collaborative work ability. This integration respects the inherent laws of nursing teaching while absorbing the advantages of the MDT model, achieving seamless connection between theoretical teaching and clinical practice, promoting the transformation of nursing teaching from a traditional one-way transmission to interactive and collaborative methods, and providing a clear path for building a scientific and complete innovative teaching model for oncology nursing ^[2].

3. Construction of the nursing teaching system for oncology internal medicine under the MDT concept

3.1. Modular design of nursing teaching content based on MDT

The nursing teaching content for oncology internal medicine, based on the MDT concept, is oriented towards real clinical diagnosis and treatment scenarios, breaking through the limitations of traditional single-nursing knowledge. It is modularly integrated according to the needs of multidisciplinary collaboration, forming a complete knowledge system covering assessment, intervention, communication, and management. The teaching content breaks the boundaries of disciplines and integrates oncology, internal medicine, nursing, surgical intervention, radiotherapy, pharmacology, nutritional support, psychological counseling, and palliative care, allowing nursing learners to systematically master the role positioning and collaboration points of different disciplines in oncology diagnosis and treatment. The module setting takes into account both theory and clinical application, highlighting the core role of nursing in the MDT team, and focusing on key contents such as condition observation, medication safety, complication prevention, and cross-disciplinary information transmission.

The modular design follows the principle of progressive learning, transitioning from basic oncology nursing knowledge to cross-disciplinary collaborative handling of complex cases. Each module clearly indicates the connection points with other disciplines. The teaching content is closely combined with clinical guidelines and team collaboration norms, strengthening the awareness of precise nursing, humanistic care, and team cooperation, enabling learners to not only possess solid specialized nursing skills but also establish a holistic care mindset. Through structured and systematic content arrangement, the MDT collaboration concept can be naturally integrated into the entire knowledge learning process, laying a solid theoretical foundation for subsequent clinical practice ^[3].

3.2. Organizational form of multi-disciplinary collaborative nursing teaching

The organizational form of multi-disciplinary collaborative teaching changes the traditional single teaching mode dominated by nursing teachers, and builds a teaching team composed of multiple professionals from disciplines such as nursing, oncology, internal medicine, radiotherapy, imaging, pharmacy, nutrition, and psychology. The teaching organization focuses on collaborative co-education, using joint teaching, joint lesson preparation, and synchronous teaching methods. Different discipline teachers interpret oncology cases from professional perspectives, allowing nursing learners to intuitively experience the operation mode and collaboration process of the MDT team. The classroom organization is flexible and diverse, balancing theoretical lectures and interactive exchanges, highlighting cross-disciplinary dialogue and thinking collisions, and enhancing the authenticity and practicality of teaching.

The teaching organization emphasizes scenario-based and immersive experiences. Through multi-disciplinary joint ward rounds simulation, group discussions, cross-disciplinary mutual evaluation, etc., the communication skills and cooperation awareness of nursing personnel in the team are strengthened. The teaching weight of each discipline is reasonably allocated, highlighting the dominant position of the nursing discipline while also considering the complementarity of other disciplines' knowledge. This organizational form can effectively eliminate disciplinary barriers,

allowing learners to adapt to the multi-disciplinary collaboration model during the learning stage, understanding the value of different disciplines in oncology diagnosis and treatment, and gradually forming an overall care concept centered on the patient, laying a good foundation for rapid integration into the MDT team after entering clinical practice.

3.3. Implementation path of nursing practice teaching integrated with the MDT concept

The nursing practice teaching integrated with the MDT concept is carried out with real clinical cases as the carrier, constructing a progressive implementation path from simulation training to clinical internship. The practice teaching is based on the MDT team collaboration process as a framework, organizing nursing learners to participate in case discussions, condition assessment, nursing plan formulation, cross-disciplinary communication and coordination, etc., throughout the entire process of practice. It focuses on training nursing operations, condition monitoring, and emergency response capabilities in a multi-disciplinary collaboration model. The practice process strictly follows clinical diagnosis and treatment norms, reproducing real team collaboration scenarios, allowing learners to understand the connection points between nursing work and other disciplines in the process of practice.

The implementation of practice teaching emphasizes hierarchical progression and ability improvement. It starts with basic collaborative training in simulated wards and then enters the clinical environment to participate in real MDT consultations and nursing implementation. The teaching process is guided by multiple discipline teachers, correcting non-standard communication methods and nursing behaviors promptly, strengthening team collaboration awareness and responsibility awareness. Through a systematic practice approach, learners can transform theoretical knowledge into practical working abilities, enhance their comprehensive nursing literacy and interdisciplinary collaboration skills, and ensure that they can efficiently cooperate with the team in future clinical work, providing continuous, comprehensive and high-quality holistic nursing services for cancer patients ^[4].

4. Evaluation of the effect of integrating the MDT concept into oncology internal medicine nursing teaching

4.1. Evaluation dimensions of comprehensive professional competence of nursing students

The effectiveness of the MDT concept integration in oncology internal medicine nursing teaching is mainly reflected in the improvement of students' comprehensive professional competence. The evaluation dimensions focus on professional cognition, practical operation, communication, collaboration, and clinical thinking. The professional cognition dimension mainly examines students' mastery of the multidisciplinary diagnosis and treatment process, key points of nursing assessment, and specialized knowledge, to determine whether they can establish a systematic oncology nursing knowledge framework and break away from the limitations of a single discipline. The practical operation dimension focuses on oncology-specific nursing skills, such as intravenous therapy, symptom care, psychological intervention, and hospice care, to assess the students' operational standardization and problem-solving ability in various scenarios ^[5].

The communication, collaboration and clinical thinking are particularly crucial evaluation contents under the MDT model. The communication collaboration dimension mainly observes the students' communication efficiency with physicians, pharmacists, nutritionists, patients, and their families, measuring their awareness and coordination ability in the team. The clinical thinking dimension focuses on evaluating whether students can make comprehensive judgments based on multidisciplinary information and develop individualized nursing plans for complex cases, possessing overall and forward-looking nursing thinking. Through multi-dimensional comprehensive evaluation, it can objectively reflect the growth extent of students under the MDT teaching model, clarify the key directions for teaching optimization, and provide precise references for the cultivation of oncology internal medicine specialized nursing talents ^[6].

4.2. Quantitative and qualitative evaluation index system for teaching effect

Constructing a scientific, quantitative and qualitative evaluation index system is an important guarantee for accurately

measuring the effect of integrating the MDT concept into nursing teaching. Quantitative evaluation is centered on objective data, including theoretical assessment scores, practical operation scores, team collaboration task completion degree, and case analysis accuracy rates, etc. By comparing the data changes before and after teaching, it can directly reflect improvement in knowledge and skills. At the same time, process indicators such as classroom participation, group discussion contribution, and case report completion quality are set to comprehensively record students' performance in teaching activities, ensuring that the evaluation results are objective and comparable.

Qualitative evaluation focuses on exploring students' internal growth and teaching experience. Through interviews, reflective diaries, and group feedback, subjective feelings of students towards the MDT teaching model are collected. The focus is on students' understanding of interdisciplinary collaboration, the transformation process of clinical thinking, the enhancement of professional identity, and the changes in their perception of their own nursing capabilities. The qualitative indicators also include teacher evaluation and peer evaluation, analyzing the feasibility and applicability of the MDT teaching model from the perspectives of teaching implementers and professional observers. The combined quantitative and qualitative evaluation system ensures the accuracy of evaluation results while providing a multi-level and all-round reference basis for model optimization ^[7].

4.3. Comprehensive analysis of the application effect of the MDT teaching model

Comprehensive analysis of the application effect of the MDT concept integration into oncology internal medicine nursing teaching can systematically summarize the advantages and improvement spaces of the model. From the results of teaching implementation, this model effectively breaks through disciplinary boundaries, enabling students to be closer to the clinical real work scenarios, significantly improving the integration degree of theoretical knowledge and practical skills, and fully exercising teamwork, communication and expression ability. Compared with the traditional teaching model, students receiving MDT teaching perform better in complex case nursing decision-making and emergency handling, and their professional competence improvement is obvious ^[8].

At the same time, comprehensive analysis can also identify problems in teaching implementation, such as the difficulty in coordinating multi-disciplinary teachers, the need for further optimization of teaching time allocation, and the slow establishment of interdisciplinary thinking among some students. Through a comprehensive review of advantages and disadvantages, the optimization direction of the MDT nursing teaching model can be clarified, providing support for the subsequent improvement of teaching content, innovation of teaching methods, and integration of teaching resources. The comprehensive analysis results can also provide a reference for introducing the MDT concept into other specialized nursing teaching, promoting the development of nursing teaching towards a direction that is more in line with clinical needs and pays more attention to comprehensive ability cultivation, and helping to build a high-quality specialized nursing talent team.

5. Conclusion

This paper integrates the MDT concept into the oncology internal medicine nursing teaching, systematically constructing a theoretical integration mechanism, a modular teaching system, and a multi-dimensional effect evaluation model. The research shows that MDT teaching can effectively break through disciplinary barriers, strengthen nursing students' clinical thinking, communication, collaboration and comprehensive care abilities, making the teaching more in line with the real clinical diagnosis and treatment scenarios, and significantly improving the quality of talent cultivation in oncology internal medicine nursing. At the same time, it is found that there is still room for optimization in aspects such as the coordination of multi-disciplinary teachers and the design of teaching rhythms. In the future, further integration of teaching resources can be deepened, the practical teaching path can be improved, and the MDT concept can be continuously integrated into the entire process of nursing teaching. This can provide more solid support for cultivating high-quality oncology specialized nursing talents and improving the clinical nursing service level.

Disclosure statement

The authors declare no conflict of interest.

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Analysis of the Effect of Specialized Rehabilitation Nursing Combined with Family Support on Cardiac Function and Quality of Life in Patients with Coronary Heart Disease

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Abstract: *Objective:* To explore the actual effectiveness of professional rehabilitation nursing combined with family support in the care of patients with coronary heart disease, and to clarify its specific impact on patients' cardiac function and quality of life. *Methods:* 80 patients with coronary heart disease admitted to our hospital from January 2024 to December 2025 were selected as the research subjects, and divided into a routine nursing group and a combined nursing group using the random number table method, with 40 patients in each group. The routine nursing group adopted routine nursing intervention methods for coronary heart disease, while the combined nursing group used specialized rehabilitation nursing combined with a family support model under the premise of routine nursing. The cardiac function indicators and quality of life scores of the two groups of patients were compared before and after care. *Results:* Before the intervention, the cardiac function indicators and quality of life scores of the two groups were similar ($P > 0.05$); after the intervention, the improvement degree of cardiac function indicators in the combined nursing group was significantly better than that of the routine nursing group, and the total score of CQQC quality of life was significantly higher than that of the routine nursing group ($P < 0.05$). *Conclusion:* Professional rehabilitation nursing combined with family support can effectively improve the cardiac functional status of coronary heart disease patients, significantly improve the quality of life of patients, and has high clinical application value.

Keywords: Coronary heart disease; Specialized rehabilitation nursing; Family support; Cardiac function; Quality of life

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1. Introduction

Coronary heart disease is a very common cardiovascular disease in clinical practice. The onset of the disease is mostly related to the narrowing of the vascular lumen and insufficient blood supply to the myocardium caused by coronary atherosclerosis. Patients often experience symptoms such as chest tightness, chest pain, and shortness of breath after the disease. When the disease is severe, it can also induce secondary diseases such as heart rhythm disorders and heart failure, posing a great threat to the patient's health and life safety^[1]. People's living habits are constantly changing, and the aging of the population continues to deepen. The incidence rate of coronary heart disease is increasing year by year, and the

diseased population is gradually becoming younger, which also brings greater challenges to clinical nursing work^[2]. The current clinical nursing care for patients with coronary heart disease is mostly based on the conventional nursing model. The nursing content is mostly focused on basic items such as disease observation and medication explanation. There is a lack of targeted rehabilitation interventions and family-level assistance and cooperation. As a result, the rehabilitation effect for patients after discharge is suboptimal, the recovery of cardiac function is slow, and quality of life cannot be effectively improved^[3]. Reasonable and standardized rehabilitation care can optimize the myocardial blood supply of patients with coronary heart disease and accelerate the recovery of heart function. Family support is important for patients during their recovery, which can improve their cooperation with care and strengthen their belief in recovery. Based on the above situation, this study selected coronary heart disease patients treated in the hospital as a research sample to analyze the effectiveness of professional rehabilitation nursing combined with family support.

2. Materials and methods

2.1. General information

80 patients with coronary heart disease admitted to our hospital from January 2024 to December 2025 were selected as cases and divided into two groups using the random number table method. Forty patients were selected in the joint nursing group, including 22 men and 18 men, aged 55 to 78 (66.25 ± 5.32) years old. There were 40 patients selected in the routine care group, including 21 men and 19 men, aged 56 to 79 (66.78 ± 5.29) years old. There was no statistical significance in the comparison of general data between the two groups, $P > 0.05$. Inclusion criteria (1) Meet the clinical diagnostic standards for coronary heart disease and be confirmed by electrocardiogram, coronary angiography and other examinations; (2) Have clear consciousness and be able to cooperate in completing nursing and follow-up work; (3) No other serious diseases such as severe liver and kidney insufficiency, malignant tumors. Exclusion criteria: (1) Complicated with severe arrhythmia, heart failure and other complications; (2) Cognitive dysfunction and mental illness, unable to cooperate with care; (3) Dropping out of the study midway or losing contact during follow-up.

2.2. Method

The routine nursing team implements routine nursing interventions for patients with coronary heart disease. The nursing content includes real-time observation of the patient's vital signs, such as heart rate, blood pressure, and breathing, and paying attention to the changes in the patient's chest tightness, chest pain, and other symptoms. According to the doctor's instructions, the patient is provided with antiplatelet, blood lipid regulation, myocardial blood supply and other drug treatments, together with guidance on medication use. The patient is explained to the patient the basic content of the disease and matters that need attention, guides the patient to eat scientifically, work regularly, and promptly informs the doctor when abnormal conditions occur.

The joint nursing team carries out specialized rehabilitation care and family support intervention on the premise of routine care. The specific measures are as follows:

- (1) Professional rehabilitation assessment. The nursing staff formulates an exclusive rehabilitation care plan for each patient based on the patient's age, severity of illness, cardiac function classification, and body status, and determines the rehabilitation goals, recovery process, and precautions. The patient's recovery status is assessed every week, and the rehabilitation plan is adjusted on time based on the assessment results to ensure that the rehabilitation care is targeted and effective.
- (2) Full-time disease monitoring, arrange specialized personnel to be responsible for the patient's condition monitoring, in addition to routine monitoring of vital signs, focus on observing the patient's electrocardiogram changes, myocardial enzyme spectrum related indicators, carefully check whether the patient has angina pectoris attacks, arrhythmias and other abnormal conditions, completely record the monitoring data, and immediately take intervention measures once abnormalities are discovered to prevent the condition from continuing to worsen. At the same time, the monitoring

results are notified to the doctor on time to provide a reference for adjustment of the treatment plan.

- (3) Professional rehabilitation training. A progressive rehabilitation training program is developed based on the patient's cardiac function status. In the early stage, the patient is mainly bed-rested and guided to carry out simple physical activities, such as fisting, leg raising, etc. The duration of a single activity is controlled to 5 to 10 minutes, and is carried out 2 to 3 times a day to prevent excessive activities from increasing the cardiac load; until the patient's cardiac function. After improvement is achieved, the intensity of the activity is gradually increased, and the patient is instructed to carry out soothing exercises such as walking and Tai Chi. The duration of a single activity is controlled to 15 to 30 minutes and is carried out 1 to 2 times a day. During the exercise, pay close attention to the patient's physical reaction. If symptoms such as chest tightness, shortness of breath, palpitation, etc. occur, stop exercising immediately and rest to ensure the smooth progress of rehabilitation training.
- (4) Professional diet and medication guidance, combined with the characteristics of coronary heart disease, develop exclusive diet plans for patients, guide patients to eat low-salt, low-fat, low-sugar and high-fiber foods, reduce the consumption of spicy, greasy and other irritating foods, control the daily salt intake within 5 g, eliminate excessive eating, and maintain regular meals; at the same time, strengthen medication guidance, fully inform patients of the usage, dosage, duration of medication, and precautions, highlight the necessity of taking medication according to the doctor's instructions, prevent patients from adjusting the dosage or stopping medication without authorization, regularly understand the patient's physical reaction after medication, and promptly deal with discomfort symptoms that occur after medication.
- (5) Family support intervention: nursing staff strengthen communication with patients' families, popularize knowledge about coronary heart disease, rehabilitation care priorities, and the important role of family support to family members, and guide family members to assist nursing staff in implementing rehabilitation care work, such as urging patients to take medications on time, eat scientifically, and work regularly. After completing rehabilitation training, provide more care and encouragement to patients to avoid negative emotions such as anxiety and depression, and build a comfortable and harmonious family rehabilitation environment for patients. At the same time, they answer questions raised by family members, improve the level of care and cooperation of family members, and build a care model in which caregivers and family members collaborate.

2.3. Observation indicators

- (1) To compare the cardiac function indicators of the two groups of patients before and after nursing, three indicators, including left ventricular ejection fraction, left ventricular end-diastolic diameter, and stroke volume, were selected, all of which were obtained through cardiac ultrasound examination. They were tested before the nursing intervention and three months after the intervention.
- (2) Compare the quality of life of the two groups of patients before and after nursing, using the Chinese Quality of Life Questionnaire for Cardiovascular Patients (CQQC). The questionnaire has a total score of 0 to 154 points. The higher the score, the better the quality of life of the patient. It was evaluated before the nursing intervention and three months after the intervention.

2.4. Statistical methods

SPSS 24.0 was used to analyze the data. Measurement data that conformed to the normal distribution were expressed as mean plus or minus standard deviation and a t-test was performed; count data were expressed as percentages and χ^2 test was performed. $P < 0.05$ represents a significant difference.

3. Results

3.1. Comparison of cardiac function indicators between the two groups before and after care

After the intervention, the left ventricular ejection fraction and stroke volume of the combined nursing group were significantly higher than those of the routine nursing group, and the left ventricular end-diastolic diameter was significantly smaller than that of the routine nursing group ($P < 0.05$). See **Table 1** for details.

Table 1. Comparison of cardiac function indicators between the two groups before and after nursing (mean $\pm$ SD)

Group	Left ventricular ejection fraction (%)		Left ventricular end diastolic diameter (mm)		Stroke volume	
	Before nursing	After nursing	Before nursing	After nursing	Before nursing	After nursing
Routine nursing group (n = 40)	52.36 $\pm$ 4.12	56.78 $\pm$ 4.25	58.65 $\pm$ 3.42	55.42 $\pm$ 3.31	58.25 $\pm$ 5.36	62.34 $\pm$ 5.42
Combined nursing group (n = 40)	52.45 $\pm$ 4.08	63.56 $\pm$ 4.31	58.72 $\pm$ 3.38	49.87 $\pm$ 3.26	58.32 $\pm$ 5.31	70.65 $\pm$ 5.38
<i>t</i>	0.098	7.084	0.092	7.555	0.059	6.882
<i>P</i>	0.922	0.000	0.927	0.000	0.953	0.000

3.2. Comparison of quality of life scores between the two groups before and after nursing

After the intervention, the total score of cqqc in the combined nursing group was significantly higher than that in the conventional nursing group ($P < 0.05$), see **Table 2** for details.

Table 2. Comparison of quality of life scores between the two groups before and after nursing (mean $\pm$ SD, points)

Group	Before intervention	After intervention
Routine nursing group (n = 40)	78.56 $\pm$ 8.42	89.65 $\pm$ 8.38
Combined nursing group (n = 40)	78.62 $\pm$ 8.39	108.72 $\pm$ 8.45
<i>t</i>	0.032	10.135
<i>P</i>	0.975	0.000

4. Discussion

Coronary heart disease is a chronic progressive cardiovascular disease. The core of its treatment is not only to alleviate clinical symptoms and control the development of disease, but also to improve the patient's cardiac function, improve the quality of life, and help the patient return to normal living conditions^[4]. Impaired cardiac function is one of the main pathological characteristics of patients with coronary heart disease. Left ventricular ejection fraction, left ventricular end diastolic diameter and stroke volume are important indicators for evaluating cardiac function. Their level changes can directly reflect the patient's myocardial blood supply and cardiac systolic and diastolic function, and the quality of life can comprehensively reflect the patient's physical, psychological and social adaptation, which is an important reference for evaluating the nursing effect. Under the conventional nursing mode, the nursing work is mainly focused on basic condition monitoring and medication guidance, lacking targeted rehabilitation intervention and family-level support, which can not meet the rehabilitation needs of patients with coronary heart disease, resulting in slow recovery of cardiac function and no obvious improvement of quality of life. Full-time rehabilitation nursing combines family support mode, combines full-time rehabilitation intervention with family support, and provides comprehensive and personalized nursing services for patients

from the perspective of individual needs of patients, can effectively improve patients' cardiac function and quality of life.

The results of this study showed that after the intervention, the left ventricular ejection fraction and stroke volume in the combined nursing group were significantly higher than those in the conventional nursing group, while the left ventricular end diastolic diameter was significantly smaller than that in the conventional nursing group, indicating that professional rehabilitation nursing combined with family support can effectively improve the cardiac function of patients with coronary heart disease. The reasons were analyzed. In full-time rehabilitation nursing, the nursing staff formulated an exclusive rehabilitation nursing plan for the patients. Through the full-time condition monitoring, the changes of the patients' cardiac function and the development of the disease could be grasped in time, and the rehabilitation plan and nursing measures could be adjusted in time to prevent the aggravation of the disease. Professional rehabilitation training follows the principle of gradual progress, and appropriate exercise programs are formulated according to the patient's cardiac function. In the early stage, simple limb activities are mainly used and the amount of activity is gradually increased. Mild exercise can promote the patient's systemic blood circulation, improve myocardial blood and oxygen supply, and enhance myocardial contractility, thereby improving left ventricular ejection fraction and stroke output, while promoting the recovery of left ventricular diastolic function and reducing left ventricular end diastolic diameter ^[5]. In addition, professional diet and medication guidance also provide an important guarantee for the recovery of cardiac function. A low salt, low fat and low sugar diet can reduce the cardiac load, and avoid further aggravation of coronary atherosclerosis due to improper diet, which leads to increased blood lipids and blood pressure fluctuations; Standardized medication guidance can ensure that patients take medicine according to the doctor's advice, effectively control the disease and improve myocardial blood supply, laying the foundation for the recovery of cardiac function. The participation of family support can improve the compliance of patients' rehabilitation training and medication. The supervision and encouragement of family members can make patients more actively cooperate with rehabilitation nursing work, and avoid the effect of unauthorized interruption of training or withdrawal of drugs on the recovery of cardiac function. At the same time, the care and support of family members can relieve the psychological pressure of patients, reduce the impact of adverse emotions on cardiac function, and promote better recovery of cardiac function ^[6].

The improvement of quality of life in this study is also an important goal of rehabilitation nursing for patients with coronary heart disease. After the intervention, the total score of cqqc in the combined nursing group was significantly higher than that in the conventional nursing group, indicating that professional rehabilitation nursing combined with family support can effectively improve the quality of life of patients with coronary heart disease. Patients with coronary heart disease are troubled by symptoms for a long time. They often have chest distress, chest pain and other discomfort and worry about the aggravation of the disease. They are prone to anxiety, depression and other negative emotions. These factors will seriously affect the quality of life of patients. In the process of full-time rehabilitation nursing, nursing staff not only pay attention to the physical rehabilitation of patients, but also pay attention to the psychological state of patients. Through communication with patients, they can timely understand their psychological needs, give psychological counseling and support, help patients relieve bad emotions and enhance their rehabilitation confidence. Personalized diet and rehabilitation training programs can effectively reduce the clinical symptoms of patients, reduce the impact of discomfort on life, gradually restore the normal diet and activities of patients, and improve physical comfort ^[7]. Family support plays an obvious role in improving the quality of life of patients. The company and care of family members can make patients feel warm care and reduce loneliness. At the same time, family members can help nurses do well in patients' daily nursing and rehabilitation training, and help patients better adapt to the disease and restore the normal rhythm of life. In addition, professional rehabilitation nursing can help patients master disease-related knowledge and self-care skills, so that patients can also effectively self-care after discharge, reduce disease recurrence and further improve the quality of life. The core reason is that it can fully combine the disease characteristics and rehabilitation needs of patients with coronary heart disease, and realize the pertinence of nursing. As an important extension of nursing work, family support can make up for the shortage of hospital nursing, enable patients to obtain continuous nursing and support after discharge, form a good model of hospital family collaborative nursing, and effectively improve the continuity of nursing ^[8].

5. Conclusion

In a word, professional rehabilitation nursing combined with family support can effectively improve cardiac function of patients with coronary heart disease and significantly improve quality of life of patients. This nursing model meets the rehabilitation needs of patients with coronary heart disease, is scientific and feasible, and has high clinical promotion value. It can provide effective reference for the nursing work of patients with coronary heart disease, and help more patients with coronary heart disease recover to health and return to normal life.

Disclosure statement

The author declares no conflict of interest.

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SOX10 in Neurodevelopment and Disease: Molecular Mechanisms, Pathological Models and Therapeutic Prospects

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Abstract: SOX10 is a neural crest transcription factor that preserves lineage competence and guides differentiation. Because it functions in enteric progenitors, Schwann cells, melanocytes, and auditory-supporting cells, reduced activity can produce multisystem disease. This review links SOX10-centered regulation to Waardenburg syndrome, Hirschsprung disease, deafness, and glial dysfunction, and highlights models that support mechanism-based therapy design.

Keywords: Neural crest; Neurocristopathy; Hirschsprung disease; Waardenburg syndrome; Schwann cell biology; Inner-ear homeostasis; Precision medicine

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1. Introduction

SOX10 should not be treated only as a marker used to identify neural crest derivatives. After neural crest induction at the neural border, it helps maintain migratory neural crest cells and later contributes to enteric, glial, melanocytic, and auditory-supporting lineages ^[1-4]. In this sense, the main developmental task of SOX10 is to keep cells competent while allowing differentiation to occur at the appropriate stage and tissue site ^[1,4,5].

This developmental role explains why pathogenic SOX10 variants rarely produce a single isolated phenotype. Since the first association between SOX10 mutations and Waardenburg-Hirschsprung syndrome, subsequent work has described combined defects in tissues that share neural crest ancestry ^[6-8]. The following sections. Therefore, focus on three connected issues: the regulatory circuits involving SOX10, the multisystem pathology that follows SOX10 disruption, and the model systems that may support intervention guided by mechanism rather than by phenotype alone.

2. Molecular architecture and regulatory logic of SOX10

SOX10 is a SOXE-family factor whose HMG domain bends DNA and shapes transcriptional responses ^[1]. Induced downstream of WNT, BMP, and FGF signals, it stabilizes a neural crest program that remains plastic but lineage-committed ^[2,3]. SOX10 thus links transient border signaling to durable developmental identity ^[1-3].

The specificity of SOX10 action depends strongly on its transcriptional partners. In pigment cells, it participates in MITF-centered networks; in enteric progenitors, it is linked to RET-associated modules; and in glial lineages, it converges with EGR2/KROX20-related myelination circuits ^[9-14]. Disease may therefore reflect reduced dosage or failed enhancer engagement in a given lineage, explaining overlapping but non-identical combinations of aganglionosis, deafness, pigmentation defects, and glial dysfunction ^[6,10-12,7].

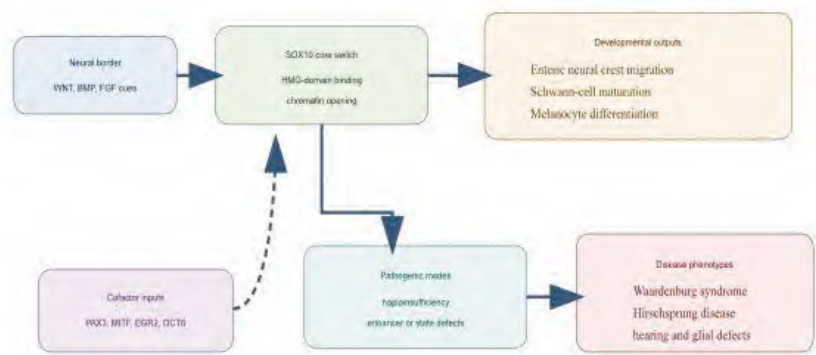


Figure 1. SOX10-centered regulatory logic linking neural crest developmental programs with representative disease phenotypes ^[1-5,6,15,9,20,7,16].

3. SOX10 in neural crest and neuroglial lineage allocation

3.1. Multipotency, migration, and enteric colonization

SOX10 preserves neural crest multipotency while limiting premature neuronal differentiation, allowing progenitors to migrate and remain competent ^[4]. In enteric lineages, even partial disruption can impair colonization enough to produce distal aganglionosis ^[5,17,12,16].

The enteric nervous system is a strong model of dosage-sensitive SOX10 biology. Mouse and single-cell studies show that Sox10 insufficiency alters progenitor allocation and lineage trajectory, not just cell number ^[17,16]. SOX10-associated Hirschsprung disease, therefore, likely reflects mixed survival, enhancer, timing, and modifier effects rather than one mechanism ^[6,12,7,16,8].

Table 1. Core developmental modules controlled or interpreted by SOX10

Developmental context	Principal regulatory logic	Representative consequence of perturbation	Key references
Neural border to premigratory neural crest	SOX10 consolidates border-derived competence after WNT/BMP/FGF induction and stabilizes a migratory neural crest program.	Reduced lineage competence or unstable specification before widespread dispersal.	[1-3]
Multipotent migratory and enteric progenitors	SOX10 preserves progenitor identity, restrains premature neuronal differentiation, and supports RET-linked enteric programs.	Distal gut colonization failure and Hirschsprung-associated trajectory defects.	[4,17,12,16]

Developmental context	Principal regulatory logic	Representative consequence of perturbation	Key references
Schwann-cell lineage	SOX10 cooperates with stage-specific glial regulators and later with myelination circuitry such as EGR2/KROX20.	Arrest before mature Schwann-cell identity or impaired myelin-gene deployment.	[18,15,9,19]
Melanocyte lineage	SOX10 activates MITF-centered transcriptional hierarchies and pigment-cell differentiation modules.	Hypopigmentation, patchy melanocyte loss, or lineage instability.	[10-14]
Inner ear homeostasis and cochlear glia	SOX10 intersects with auditory-supporting and glial programs that maintain ionic balance and glial plasticity.	Sensorineural hearing loss and compromised reparative potential.	[20-22]

3.2. Schwann-lineage specification and myelination

In the Schwann lineage, SOX10 is required for identity and progression through precursor, immature, and myelinating states [18,15,9]. Loss-of-function studies place it at the center of maturation beyond the immature Schwann-cell stage [15]. Its activity is integrated with NRG1 signaling and partner exchange during myelination [18,9].

This function also matters in nerve repair, where Schwann cells transiently dedifferentiate and then remyelinate [18]. SOX10 thus influences both congenital glial disease and adult recovery. Engineering studies further show that SOX10 plus immobilized NRG1 can improve production of Schwann-like cells for regenerative use [19].

3.3. Melanocyte and inner-ear lineages

The melanocyte lineage clearly demonstrates context-dependent SOX10 partnership. By cooperating with PAX3 and MITF, SOX10 supports melanoblast commitment, survival, and melanogenic gene expression [10-14]. This explains why pigmentary changes in Waardenburg syndrome are developmentally central and why severity can vary by variant class [10-11,13-14,7].

Auditory phenotypes also reflect lineage-specific SOX10 dysfunction. In the cochlea, SOX10 works with SOX9 to support fluid homeostasis and hearing-related support functions [20]. Cochlear SOX10-positive glia retain plasticity in three-dimensional culture, and new AAV studies suggest targeted intervention in relevant nonsensory compartments may become feasible [20-21,8].

4. Disease mechanisms across the SOX10 spectrum

4.1. Waardenburg-Shah syndrome and Hirschsprung disease

Waardenburg-Shah syndrome is the clearest SOX10 disorder because it combines pigmentary, enteric, and auditory defects within one developmental framework. Haploinsufficiency matters, but phenotype also depends on variant type, residual activity, lineage context, and modifier background [6-7]. The syndrome is embryologically coherent yet mechanistically variable [6-8].

SOX10-associated Hirschsprung disease shows how distal aganglionosis can arise from layered developmental defects. Mouse and single-cell studies support dosage sensitivity, altered cell-state allocation, and interaction with RET/PAX3-related regulatory logic [17,12,16,8]. Precision classification will likely need lineage-level biomarkers, not variant names alone [16,8].

4.2. Auditory phenotypes, glial vulnerability, and variable expressivity

The hearing phenotype in SOX10 disease is more than generic sensorineural loss. Because SOX10 contributes to auditory-supporting neural crest derivatives and cooperates with SOX9 in inner-ear homeostasis, variants can disrupt the microenvironment needed for normal hearing [20,7]. This also helps explain coexistence with pigmentary and broader neuroglial features [20,7-8].

Variable expressivity is therefore not simply clinical noise. Small changes in remaining SOX10 activity, partner availability, or enhancer compensation may shift developmental outcomes differently in each tissue [6-8]. Therapeutic research will need assays that resolve lineage and dosage effects, rather than endpoints that combine multiple phenotypes into broad diagnostic labels.

5. Pathological Models and Precision-Medicine Platforms

Current SOX10 research depends on a wider set of experimental platforms than earlier genetic studies. Mouse models remain indispensable for examining developmental timing, tissue architecture, and whole-organ effects, particularly in enteric and glial systems [17,15,16]. But they cannot capture the full allelic diversity seen in human sequencing or subtle variant effects across human lineages [17,15,16,8].

Human pluripotent stem-cell systems help fill this gap by allowing isogenic comparison, reporter-based tracking, and controlled differentiation toward neural crest-derived lineages. SOX10 reporter iPSCs, genome editing, single-cell analysis, cochlear glial culture, and Schwann-cell engineering now provide practical tools for stratifying mechanisms and testing lineage-specific hypotheses [23,19,21].

Table 2. Model systems currently informing SOX10 pathology and translational design

Model platform	Major strength	Best-suited question	Key references
Dominant megacolon and related mouse models	Whole-organism timing and tissue architecture	How SOX10 insufficiency distorts enteric colonization and lineage allocation in vivo	[17,16]
Schwann-lineage genetic models	Direct access to stage-specific glial maturation defects	Which transcriptional transitions fail when Sox10-dependent progression is blocked	[18,15,9]
SOX10 knock-in reporter human iPSCs	Live tracking of SOX10-positive human trajectories	How human neural crest derivatives emerge, bifurcate, and respond to engineered perturbation	[23]
SOX10 plus NRG1 Schwann-engineering systems	Regenerative manufacturing relevance	How to generate functional Schwann-like cells for repair-oriented applications	[19]
Cochlear Sox10-positive glial 3D cultures	Auditory microenvironment and plasticity	Whether glial-to-neuronal conversion or rescue can be modelled in vitro	[21]
Integrated clinical-genetic neurocristopathy frameworks	Patient stratification across syndromes	How genotype, lineage, and phenotype should be grouped for precision medicine	[7-8]

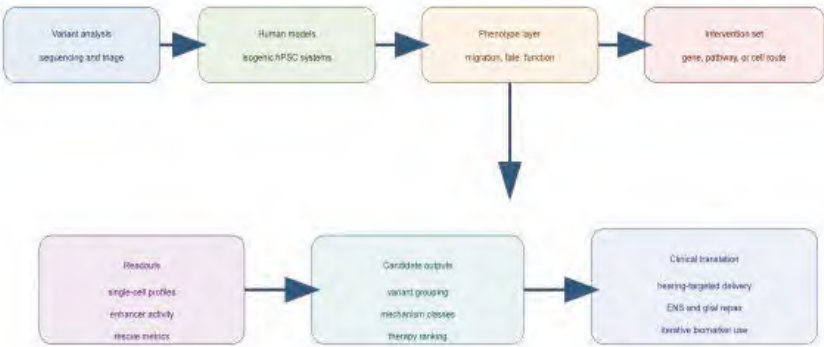


Figure 2. Mechanism-stratified precision-medicine workflow for SOX10-associated disorders, spanning variant interpretation, human modeling and therapeutic prioritization [7,16,23,19,21,8,22,24].

6. Therapeutic prospects and translational constraints

SOX10 is an attractive but difficult therapeutic target. Restoring an upstream lineage regulator could rescue multiple downstream programs, yet uncontrolled overexpression may distort fate balance or developmental timing^[7-8]. Near-term gene therapy is most plausible where delivery and dosage can be locally constrained^[20,7,22].

A second strategy is lineage engineering and cell replacement. SOX10 with immobilized NRG1 can guide neural crest-like cells toward Schwann-cell identity^[19]. Cochlear SOX10-positive glia may also support in situ or ex vivo regenerative strategies if fate control is precise^[21].

A third approach is to modulate downstream pathways rather than replace SOX10 directly. Small molecules, biologics, or restricted SOX10 delivery could stabilize selected programs while reducing the risk of broad fate perturbation. Exosome-mediated Sox10 loading in demyelination models provides proof of concept for SOX10-centered cargo delivery^[24]. Treatment will likely require lineage-specific, mechanism-stratified strategies rather than a universal SOX10 therapy^[7,19,21,8,22,24].

Table 3. Emerging intervention concepts for SOX10-associated disease

Intervention concept	Rationale	Current status	Major caveat	Key references
Local gene augmentation or editing	Could restore upstream lineage control in accessible tissues.	Conceptually attractive; delivery feasibility improving in the auditory field.	Narrow therapeutic window and lineage-specific dosage risk.	[7-8,22]
Pathway-guided rescue without full SOX10 replacement	May stabilize downstream programs while avoiding global fate perturbation.	Mechanistically plausible but not yet standardized clinically.	Requires precise knowledge of variant- and lineage-specific failure points.	[12,7-8]
SOX10-guided Schwann-cell engineering	Recreates developmental logic for peripheral nerve repair.	Supported by recent differentiation studies.	Cell identity, durability, and manufacturing reproducibility remain unresolved.	[19]
Auditory glial plasticity or local regenerative conversion	Targets Sox10-positive cochlear support populations with reparative intent.	Early-stage experimental evidence in 3D systems and delivery studies.	Functional integration in vivo remains unproven.	[21-22]
Restricted SOX10 cargo delivery (e.g., exosomal)	Allows transient or compartmentalized restoration of SOX10-related activity.	Proof-of-concept in demyelination models.	Disease-context transferability and off-target biology remain concerns.	[24]

7. Conclusion

SOX10 integrates embryonic signaling, enhancer logic, lineage competence, and tissue maturation across neural crest-derived populations^[1-4,8,15,9-14,20]. Waardenburg syndrome, Hirschsprung disease, auditory dysfunction, and glial vulnerability are different outputs of one developmental control problem^[6,20,7,16,8]. Precision medicine will depend on lineage-resolved, dosage-aware intervention.

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Disclosure statement

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Mechanism of RIPK1-RIPK3-MLKL Axis-Mediated Necroptosis in Alzheimer's Disease

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Abstract: To address the unclear mechanism of neuronal loss and the lack of therapeutic targets in Alzheimer's disease (AD), Western blot, real-time PCR, and immunohistochemistry were used to examine brain tissues from 32 AD patients and 20 controls. MTT assay, PI staining, Morris water maze, and Nissl staining were performed to investigate the effects of phosphorylated tau on HT22 cells and the intervention of Nec-1s in APP/PS1 mice. Results showed that mRNA levels of RIPK1, RIPK3, and MLKL in AD brains were increased by 2.86-, 2.43-, and 2.17-fold, respectively, and p-MLKL was positively correlated with CDR scores. 1.0 $\mu\text{mol/L}$ phosphorylated tau reduced cell viability to 52.3%, while Nec-1 increased viability by 56.0%. Nec-1s shortened the escape latency by 28.5% and increased CA1 neurons by 42.6% in model mice. These findings suggest that RIPK1-RIPK3-MLKL axis-mediated necroptosis is involved in AD pathogenesis, and targeting RIPK1 can alleviate pathological damage in AD.

Keywords: Alzheimer's disease; RIPK1-RIPK3-MLKL axis; Necroptosis; Phosphorylated tau protein

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1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder primarily characterized by cognitive dysfunction and neuronal loss, with its pathogenesis not yet fully understood ^[1]. Necroptosis, a regulated form of cell death mediated by the RIPK1-RIPK3-MLKL axis, has recently been found to play a significant role in the neuronal loss observed in AD ^[2]. This study investigates the molecular mechanism of RIPK1-RIPK3-MLKL axis-mediated necroptosis in AD by examining brain tissue from AD patients, as well as cellular and animal models. It also evaluates the interventional effects of targeting RIPK1, aiming to provide new strategies for AD treatment.

2. Materials and methods

2.1. General information

Brain tissue samples and clinical data were collected from patients with Alzheimer's disease (AD) admitted to the Department of Neurology of our hospital from January 2020 to December 2025. The AD group comprised 32 patients with pathologically confirmed AD, including 18 males and 14 females, aged 65–88 years old, with a mean age of $76.5 \pm$

6.8 years old. The control group included brain tissue samples from 20 volunteer donors who died of non-neurological diseases during the same period, including 11 males and 9 females, aged 66–85 years old, with a mean age of 75.2 ± 7.1 years old. There were no statistically significant differences in age, sex, or other general information between the two groups ($P > 0.05$), ensuring comparability.

Animal experiments: Male APP/PS1 transgenic AD model mice ($n = 30$) and age-matched wild-type C57BL/6J mice ($n = 30$), aged 8 months, weighing 25–30 g, were used. AD model mice were randomly divided into a model group (AD group) and an intervention group (RIPK1 inhibitor group), with 15 mice per group.

Cell experiments: The mouse hippocampal neuronal cell line HT22 was provided by the Institute of Neuroscience of our hospital.

2.2. Diagnostic criteria

AD was diagnosed according to the criteria established by the National Institute on Aging-Alzheimer's Association (NIA-AA):

- (1) Core clinical criteria: Meeting the diagnostic criteria for dementia syndrome, with insidious onset, a clear history of cognitive decline, and early and most prominent cognitive deficits being either amnesic or non-amnesic (language, visuospatial, or executive dysfunction);
- (2) Exclusion criteria: Excluding other neurological disorders causing cognitive impairment, active cerebrovascular disease, toxic or metabolic abnormalities;
- (3) Biomarker evidence: Decreased A β 42 levels and/or increased total tau or phosphorylated tau levels in cerebrospinal fluid, or positive A β deposition on PET imaging.

2.3. Inclusion and exclusion criteria

Inclusion criteria: (1) Meeting the above AD diagnostic criteria; (2) Age ≥ 60 years old; (3) Well-preserved brain tissue samples with qualified RNA and protein quality; (4) Complete clinical data.

Exclusion criteria: (1) Comorbid with other neurodegenerative diseases such as Parkinson's disease or frontotemporal dementia; (2) Comorbid with cerebrovascular disease or brain tumors; (3) Recent use of immunosuppressants or cytoprotective agents; (4) Obvious autolysis or contamination of samples.

2.4. Methods

2.4.1. Treatment methods

- (1) Animal intervention: The intervention group received daily intraperitoneal injections of the specific RIPK1 inhibitor Nec-1s (1.0 mg/kg) for 8 consecutive weeks; the model group and wild-type group received equal volumes of saline. Behavioral tests and brain tissue sampling were performed after the intervention period.
- (2) Cell intervention: HT22 cells were treated with different concentrations (0, 0.1, 0.5, 1.0, 2.0 $\mu\text{mol/L}$) of phosphorylated tau protein (pTau) for 24 h; in some experiments, cells were pre-incubated with the RIPK1 inhibitor Nec-1 (10 $\mu\text{mol/L}$) or the RIPK3 inhibitor GSK'872 (1 $\mu\text{mol/L}$) for 1 h before pTau treatment.

2.4.2. Outcome measures

- (1) Human brain tissue samples: Western blot was used to detect the protein expression levels of RIPK1, p-RIPK1, RIPK3, MLKL, and p-MLKL in the hippocampus and cortex; immunohistochemical staining was used to observe the localization and expression distribution of these proteins; real-time PCR was used to detect mRNA levels.
- (2) Cell experiments: Cell viability (MTT assay), lactate dehydrogenase (LDH) release rate, and cell death morphology (PI staining) were measured; expression and phosphorylation levels of RIPK1/RIPK3/MLKL were detected; co-immunoprecipitation was used to detect RIPK1-RIPK3 complex formation.

- (3) Animal experiments: The Morris water maze test was used to assess learning and memory abilities (escape latency, time spent in the target quadrant, number of platform crossings); Nissl staining was used to observe the number of surviving neurons in the hippocampal CA1 region; immunofluorescence was used to detect the colocalization of p-MLKL with the neuronal marker NeuN; ELISA was used to measure the levels of inflammatory factors TNF- α , IL-1 β , and IL-6 in hippocampal tissue.

2.4.3. Criteria for therapeutic efficacy

- (1) Molecular level: RIPK1 kinase activity inhibition rate $\geq 50\%$ was defined as effective inhibition; p-MLKL level reduced to below 60% of the model group was considered significant blockade of necroptosis.
- (2) Cellular level: Cell viability increased by $\geq 30\%$ compared to the model group, which was considered protective.
- (3) Animal level: Escape latency in the water maze shortened by $\geq 20\%$ or time spent in the target quadrant prolonged by $\geq 25\%$ compared to the model group was considered significant cognitive improvement; the number of surviving neurons increased by $\geq 30\%$ compared to the model group was considered significant neuroprotection.

2.4.4. Statistical methods

SPSS 26.0 statistical software was used for data analysis. Measurement data were expressed as mean $\pm$ standard deviation (SD). Comparison between the two groups was performed using an independent samples t-test. Comparison among multiple groups was performed using one-way ANOVA, followed by the LSD-t test for pairwise comparisons. Correlation analysis was performed using Pearson correlation. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Expression changes of RIPK1/RIPK3/MLKL in brain tissue of AD patients

Compared to the control group, RIPK1, RIPK3, and MLKL mRNA levels in the AD group were increased by 2.86, 2.43, and 2.17 times, respectively ($P < 0.001$); the p-RIPK1/RIPK1 and p-MLKL/MLKL ratios were increased by 3.24 and 3.28 times, respectively. RIPK1-positive and p-MLKL-positive neurons were increased by 2.46 and 6.10 times, respectively. p-MLKL levels were positively correlated with CDR scores ($r = 0.672$, $P < 0.01$). See **Table 1**.

Table 1. Comparison of RIPK1/RIPK3/MLKL expression in brain tissue between AD patients and control group (mean $\pm$ SD)

Indicator	Control Group (n = 20)	AD Group (n=32)	t value	P value
RIPK1 mRNA	1.00 $\pm$ 0.12	2.86 $\pm$ 0.35	22.64	< 0.001
RIPK3 mRNA	1.00 $\pm$ 0.15	2.43 $\pm$ 0.41	18.92	< 0.001
MLKL mRNA	1.00 $\pm$ 0.11	2.17 $\pm$ 0.38	16.35	< 0.001
p-RIPK1/RIPK1	0.21 $\pm$ 0.04	0.68 $\pm$ 0.09	21.76	< 0.001
p-MLKL/MLKL	0.18 $\pm$ 0.03	0.59 $\pm$ 0.08	20.14	< 0.001
RIPK1+ Neurons (cells/mm ²)	45.3 $\pm$ 8.7	156.8 $\pm$ 21.4	22.03	< 0.001
p-MLKL+ Neurons (cells/mm ²)	12.6 $\pm$ 3.5	89.4 $\pm$ 15.2	21.87	< 0.001

3.2. pTau induces neuronal necroptosis via the RIPK1-RIPK3-MLKL axis

After treatment with 1.0 $\mu\text{mol/L}$ pTau for 24 h, cell viability decreased to 52.3% of the control group, and the LDH release rate increased by 3.8 times; the p-MLKL/MLKL ratio increased by 4.73 times, and RIPK1-RIPK3 binding increased by 4.21 times. Nec-1 intervention increased viability by 56.0%, decreased LDH by 56.0%, and decreased p-MLKL/MLKL by 56.3%; GSK'872 intervention increased viability by 50.9%, decreased LDH by 51.8%, and decreased p-MLKL/MLKL by 63.4% (**Table 2**).

Table 2. pTau-Induced Necroptosis in HT22 Cells and the Effect of Inhibitor Intervention (mean $\pm$ SD, n = 6)

Group	Cell Viability (%)	LDH Release Rate (U/L)	p-MLKL/MLKL	RIPK1-RIPK3 Binding
Control	100.0 $\pm$ 5.3	85.4 $\pm$ 9.2	0.15 $\pm$ 0.03	1.00 $\pm$ 0.11
pTau 0.1 μ M	89.6 $\pm$ 6.2*	112.3 $\pm$ 12.5*	0.28 $\pm$ 0.05*	1.56 $\pm$ 0.18*
pTau 0.5 μ M	71.4 $\pm$ 5.8**	198.7 $\pm$ 18.6**	0.49 $\pm$ 0.06**	2.84 $\pm$ 0.26**
pTau 1.0 μ M	52.3 $\pm$ 4.9**	324.5 $\pm$ 25.3**	0.71 $\pm$ 0.08**	4.21 $\pm$ 0.35**
pTau + Nec-1	81.6 $\pm$ 5.7###	142.8 $\pm$ 15.4###	0.31 $\pm$ 0.04###	1.92 $\pm$ 0.21###
pTau + GSK'872	78.9 $\pm$ 6.1###	156.3 $\pm$ 16.7###	0.26 $\pm$ 0.04###	3.98 $\pm$ 0.33###

Note: Compared with the control group, * P < 0.05, ** P < 0.01; compared with pTau 1.0 μ M group, ### P < 0.01.

3.3. Ameliorative effects of inhibiting RIPK1 kinase activity in AD model mice

Nec-1s treatment significantly improved cognitive function in APP/PS1 mice: escape latency was shortened by 28.5% (58.3 $\rightarrow$ 41.7 s), time spent in the target quadrant was increased by 45.5% (18.9 $\rightarrow$ 27.5 s), and the number of platform crossings was increased by 65.5% (2.9 $\rightarrow$ 4.8 times) (all P < 0.01). Regarding molecular pathology, p-RIPK1/RIPK1 was reduced by 51.4%, p-MLKL/MLKL was reduced by 55.4%, and TNF- α , IL-1 β , and IL-6 were reduced by 44.4%, 46.4%, and 43.5%, respectively. Surviving neurons in the CA1 region increased by 42.6%, and the p-MLKL+NeuN colocalization rate decreased by 60.8% (Table 3).

Table 3. Effects of Nec-1s on Cognitive Function and Neuropathology in APP/PS1 Mice (mean $\pm$ SD, n = 15)

Indicator	Wild-type Control	AD Model Group	AD + Nec-1s Group	F value	P value
Escape Latency (s)	28.6 $\pm$ 4.2	58.3 $\pm$ 6.5**	41.7 $\pm$ 5.4###	45.32	< 0.001
Time in Target Quadrant (s)	35.8 $\pm$ 4.1	18.9 $\pm$ 3.6**	27.5 $\pm$ 4.2###	38.76	< 0.001
Platform Crossings	6.8 $\pm$ 1.2	2.9 $\pm$ 0.8**	4.8 $\pm$ 1.1###	32.18	< 0.001
p-RIPK1/RIPK1	0.19 $\pm$ 0.04	0.72 $\pm$ 0.09**	0.35 $\pm$ 0.06###	58.43	< 0.001
p-MLKL/MLKL	0.16 $\pm$ 0.03	0.65 $\pm$ 0.08**	0.29 $\pm$ 0.05###	52.67	< 0.001
TNF- α (pg/mg)	12.4 $\pm$ 2.3	38.7 $\pm$ 5.2**	21.5 $\pm$ 3.6###	46.21	< 0.001
IL-1 β (pg/mg)	8.6 $\pm$ 1.8	29.5 $\pm$ 4.1**	15.8 $\pm$ 2.9###	41.85	< 0.001
CA1 Neurons (cells/mm)	185.6 $\pm$ 15.3	92.4 $\pm$ 11.7**	131.8 $\pm$ 13.5###	48.76	< 0.001

Note: Compared with the wild-type group, ** P < 0.01; compared with the AD model group, ### P < 0.01.

4. Discussion

4.1. Necroptosis as a key link between AD pathological features and neuronal loss

This study shows significantly elevated expression of RIPK1, RIPK3, and p-MLKL in the brain tissue of AD patients, positively correlated with the degree of cognitive impairment, indicating abnormal activation of the necroptosis pathway in the AD brain, consistent with previous studies^[3].

Analysis of the reasons:

- (1) A β oligomers can activate microglia via TNF- α signaling, triggering RIPK1/RIPK3/MLKL activation, which is then transmitted to neurons;
- (2) This study confirms that phosphorylated tau protein can directly induce neuronal necroptosis, promoting RIPK1-RIPK3 complex formation and MLKL phosphorylation in a concentration-dependent manner. Therefore, necroptosis constitutes a key link between core AD pathologies and neuronal loss.

4.2. Potential of RIPK1 as a therapeutic target in AD and current intervention strategies

RIPK1 is a critical node regulating cell death and inflammation. The use of Nec-1s in this study significantly improved cognitive function in APP/PS1 mice, reduced hippocampal neuronal loss by 42.6%, and decreased inflammatory factor levels, confirming the therapeutic potential of targeting RIPK1.

Analysis of the reasons:

- (1) Inhibiting RIPK1 kinase activity directly blocks the execution of necroptosis;
- (2) Reducing the release of DAMPs indirectly mitigates neuroinflammation.

Recent research by the Yuan Junying team found ^[4]:

- (1) INPP5D, as a microglial homeostasis regulator, directly binds to RIPK1 via its SH2 domain, inhibiting its excessive activation;
- (2) INPP5D deficiency leads to aberrant RIPK1 activation and expression of AD risk genes;
- (3) Inhibiting RIPK1 kinase activity alleviates neuroinflammation. The brain-penetrant RIPK1 inhibitor SIR9900 has shown a good safety profile in Phase I clinical trials ^[5], offering a new strategy for AD treatment.

4.3. Limitations of this study and future research directions

Limitations: (1) Relatively small human sample size and cross-sectional design; (2) Only the APP/PS1 model was used, not encompassing tau pathology models; (3) Long-term safety and optimal intervention timing require further exploration.

Future directions: (1) Develop highly brain-penetrant RIPK1 inhibitors and promote clinical translation; (2) Explore the value of biomarkers like p-MLKL in early AD diagnosis; (3) In-depth study of the microglial INPP5D-RIPK1 axis; (4) Explore the crosstalk between necroptosis and other forms of cell death and comprehensive intervention strategies.

4. Conclusion

This study confirms that RIPK1-RIPK3-MLKL axis-mediated necroptosis plays a crucial role in neuronal loss in Alzheimer's disease, with phosphorylated tau protein acting as a direct activator of this pathway. Targeting RIPK1 significantly improves cognitive function, reduces neuroinflammation, and attenuates neuronal loss in AD model mice. With the revelation of the INPP5D-RIPK1 regulatory axis and the clinical advancement of brain-penetrant RIPK1 inhibitors, targeting necroptosis holds promise as a new therapeutic strategy for AD.

Disclosure statement

The author declares no conflict of interest.

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Effect of Cognitive Rehabilitation Nursing on Cognitive Function of Patients with Schizophrenia

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Abstract: *Objective:* To explore the impact of cognitive rehabilitation nursing on the cognitive function of patients with schizophrenia. *Methods:* Patients with schizophrenia in our hospital from 2023.1 to 2026.1 were collected. The total sample size included was 58 cases. They were divided into groups using the ball-touching method and carried out different nursing methods. There were 29 cases in both the control group and the observation group. The corresponding nursing plans were routine nursing and cognitive rehabilitation nursing. *Results:* The difference in cognitive function between groups was small at the time of enrollment, and the MCCB score after nursing was higher in the observation group than in the control group, $P < 0.05$. The social function score value of the observation group was lower than that of the control group, $P < 0.05$. *Conclusion:* Patients with schizophrenia receiving cognitive rehabilitation care have significant value in promoting the improvement of patients' cognitive functions and enhancing their social functions.

Keywords: Schizophrenia; Cognitive rehabilitation nursing; Cognitive function; Social function

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1. Introduction

The main symptoms of schizophrenia include not only positive symptoms, such as hallucinations and delusions, but also negative symptoms such as apathy and loss of will. Patients are generally accompanied by cognitive impairment, so it is a complex, severe mental disorder ^[1]. Cognitive impairment in schizophrenia involves many fields such as attention, memory, executive function, and social cognition. It is a key factor that causes patients to become disabled in social functions and find it difficult to return to normal life and work. Although traditional drug treatment and routine care can effectively control psychotic symptoms, they have a limited effect on improving the core disorder of cognitive function ^[2]. Cognitive deficits will continue to hinder patients from achieving true functional recovery. Relevant studies have shown that non-drug intervention methods that directly target cognitive function, that is, cognitive rehabilitation care, are effective intervention programs for mental rehabilitation. Structured intervention models with skill training as the core can systematically train to compensate for or compensate for cognitive deficits ^[3]. Based on this, this article includes 58 patients to conduct a comparative analysis of the value of cognitive rehabilitation care for patients with schizophrenia in promoting the improvement of patients' cognitive functions and enhancing their social functions.

2. Materials and methods

2.1. General information

58 schizophrenia patients treated in our hospital from 2023.1 to 2026.1 were divided into a control group and an observation group using the ball-touching method. Among the 29 patients in the control group, there were 15 males and 14 females; the age range was 22 to 58 years old, with an average age of (39.72 ± 8.15) years old; the disease duration ranged from 1 to 15 years, with an average disease duration of (7.24 ± 3.86) years; the years of education ranged from 9 to 16 years, and the average years of education were (12.03 ± 2.14) years. Among the 29 patients in the observation group, there were 16 males and 13 females; the age range was 24 to 60 years old, with an average age of (40.31 ± 8.64) years; the disease duration ranged from 2 to 16 years, with an average disease duration of (7.89 ± 4.02) years; the years of education ranged from 8 to 17 years, and the average years of education were (11.76 ± 2.37) years. The baseline data of the two groups were balanced, $P > 0.05$.

Inclusion criteria: Meet the diagnostic criteria for schizophrenia in the “Chinese Expert Consensus on the Surgical Treatment of Psychiatric Diseases”^[4]; be in the stable stage of the disease; be between 18 and 65 years old; have more than 6 years of education, and have basic reading comprehension and communication skills; and provide informed consent.

Exclusion criteria: severe vision or hearing impairment; combined with serious organic diseases; history of alcohol or drug abuse and dependence in the past 3 months; fluctuating condition or severe uncooperation.

2.2. Method

2.2.1. Control group

Patients in the control group received basic clinical routine nursing services. The nursing staff followed the doctor's orders and urged the patients to take medicines on time and in the right amount, track physical reactions after taking the medicines, record abnormal manifestations promptly, and do a good job in medication safety control; ensure that the patients' basic life needs are met during hospitalization, do a good job in ward environment organization and safety protection, and maintain a stable and orderly rest environment; carry out basic disease knowledge education, answer simple questions of patients and their families, mainly passively implement medical orders and daily life management, and do not carry out any special intervention and training for cognitive deficiencies.

2.2.2. Observation team

This group of patients received cognitive rehabilitation care as follows.

2.2.2.1. Develop an individualized rehabilitation plan

After the patient's condition stabilizes after admission, the nursing staff uses standardized cognitive assessment tools to check the status of the patient's core cognitive areas, such as attention, memory, and executive functions, and distinguish areas of advantageous cognition from areas of deficiency. The nursing team joins hands with the supervisor's physician and rehabilitation therapist to formulate a three-month exclusive rehabilitation plan based on the patient's cognitive impairment characteristics, cultural level, and personal preferences. Abandoning general goals, the overall cognitive improvement goal is broken down into specific tasks that can be implemented and measured every week, so that each intervention fits the patient's actual situation and ensures that nursing intervention is accurate and executable.

2.2.2.2. Structured cognitive special training

Layered training is carried out for different cognitive deficiencies. Attention training takes the form of deletion tasks and listening to number retellings, etc., to gradually strengthen the patient's ability to continuously focus and directionally filter information. Memory training combines story retelling, object classification recall and associative memory skills to simultaneously improve patients' working memory and long-term memory levels. Executive function training exercises

patients' thinking flexibility and independent decision-making ability through card sorting, planning, problem scenario simulation and other methods. Information processing speed is gradually improved with the help of simple response tests and rapid naming exercises. The training follows a rhythm from easy to difficult and is carried out one-on-one or in groups. When patients make progress, they are given positive encouragement in a timely manner to enhance rehabilitation compliance.

2.2.2.3. Social function adaptive training

Special guidance is carried out around social adaptability, and emotional pictures and video materials are used to help patients identify the emotional states conveyed by different expressions and tones, and improve their emotional perception and discrimination abilities. Situation interpretation and role-playing exercises are carried out in combination with real social situations, so that patients can learn to capture social cues, understand other people's thoughts and make appropriate responses. Nursing staff combine the skills learned through cognitive training with daily hospitalization scenarios, guide patients to apply the training results in life, promote the transformation of cognitive abilities into social functions, reduce the occurrence of abnormal behaviors, and help patients gradually adapt to social and life rhythms.

2.2.2.4. Family collaborative support intervention

Regularly organize family members to participate in health education activities, explain in detail the core logic of rehabilitation related to cognitive impairment and the practical skills of family care, guide family members to accompany the patient in an encouraging way, and help the patient use cognitive strategies to deal with daily affairs in life. When the patient is about to be discharged from the hospital, the nursing staff once again comprehensively assesses the patient's cognitive and social functional status, works with the patient and family members to plan home rehabilitation content after discharge, clarifies follow-up arrangements and phased rehabilitation goals, builds a coherent rehabilitation support system inside and outside the hospital, and consolidates the effect of early intervention.

2.3. Observation indicators

- (1) Cognitive function: The Schizophrenia Cognitive Function Battery Consensus Version (MCCB) is used to evaluate the condition. The higher the score, the better the cognitive function of the patient.
- (2) Social function: evaluated using the Inpatient Psychiatric Rehabilitation Outcomes Rating Scale (IPROS). The higher the score, the more serious the social function deficit.

2.4. Statistical methods

The calculation software used for relevant data is SPSS 25.0. Cognitive function and social function scores are measurement data, described in mean $\pm$ standard deviation (SD), and t-value test. $P < 0.05$ is statistically significant.

3. Results

3.1. Compare the cognitive functions of the two groups of patients before and after treatment

The difference between the groups in cognitive function was small at the time of enrollment, and the MCCB score after nursing was higher in the observation group than in the control group, $P < 0.05$. See **Table 1** for details.

Table 1. Comparison of MCCB scores between the two groups before and after treatment (mean $\pm$ SD)

Group		Information processing speed	Attention/alertness	Working memory	Language learning	Visual learning	Problem solving	Social cognition
Control group (n = 29)	Before care	38.22 $\pm$ 8.14	33.61 $\pm$ 4.75	37.99 $\pm$ 4.31	37.57 $\pm$ 5.14	38.76 $\pm$ 7.15	39.74 $\pm$ 7.53	44.26 $\pm$ 6.55
	After care	47.31 $\pm$ 5.54	42.20 $\pm$ 5.15	43.12 $\pm$ 5.34	47.70 $\pm$ 5.52	49.01 $\pm$ 5.56	45.03 $\pm$ 5.10	47.52 $\pm$ 5.31
Observation group (n = 29)	Before care	37.55 $\pm$ 8.33	32.85 $\pm$ 5.64	37.28 $\pm$ 6.64	36.94 $\pm$ 7.20	38.77 $\pm$ 7.86	38.90 $\pm$ 6.51	43.54 $\pm$ 6.89
	After care	50.69 $\pm$ 5.85	45.93 $\pm$ 5.70	46.31 $\pm$ 5.74	51.38 $\pm$ 6.40	52.09 $\pm$ 4.57	47.93 $\pm$ 3.15	50.82 $\pm$ 5.17
t Comparison within the control group		4.971	6.603	4.026	7.233	6.094	3.132	2.082
P Comparison within the control group		0.000	0.000	0.000	0.000	0.000	0.003	0.042
t Comparison within the observation group		6.952	8.784	5.540	8.072	7.889	6.724	4.551
P Comparison within the observation group		0.000	0.000	0.000	0.000	0.000	0.000	0.000
t Comparison between groups before nursing		0.310	0.555	0.483	0.384	0.005	0.454	0.408
P Comparison between groups before nursing		0.758	0.581	0.631	0.703	0.996	0.651	0.685
t Comparison between groups after nursing		2.259	2.615	2.191	2.345	2.305	2.605	2.398
P Comparison between groups after nursing		0.028	0.012	0.033	0.023	0.025	0.012	0.020

3.2. Compare the social function scores of the two groups

The social function score value of the observation group was lower than that of the control group, $P < 0.05$. See **Table 2** for details

Table 2. Comparison of social function scores between the two groups (mean $\pm$ SD)

Group	n	Industrial and medical conditions	Living ability	Social skills	Pay attention to hygiene ability	Concern and interest	Total score
Control group	29	15.32 $\pm$ 2.57	14.13 $\pm$ 2.51	11.18 $\pm$ 2.69	9.48 $\pm$ 1.15	13.64 $\pm$ 2.38	63.75 $\pm$ 7.52
Observation group	29	13.45 $\pm$ 2.52	12.41 $\pm$ 2.38	9.02 $\pm$ 2.75	9.17 $\pm$ 1.38	12.48 $\pm$ 1.35	56.53 $\pm$ 7.76
t	--	2.798	2.678	3.024	0.929	2.283	3.598
P	--	0.007	0.010	0.004	0.357	0.026	0.001

4. Discussion

Schizophrenia is a severe mental illness that is chronic and has a high risk of disability. Compared with symptom control, patients' deeper rehabilitation needs lie in comprehensive functional recovery, that is, through continuous intervention, helping patients gradually repair and improve their independent life, carry out social interactions, participate in professional activities and other core social functions, which is also the key to ensuring patients' return to family and society ^[5].

Cognitive rehabilitation nursing is based on the theory of neuroplasticity and is a structured psychosocial intervention. The core is to use repeated, highly targeted special training, combined with scientific strategic learning guidance, to target improve or compensate for patients' cognitive deficiencies in dimensions such as attention, memory, logical thinking, and social information processing. The entire intervention process always adheres to the principle of assessment first, formulates exclusive plans based on individual differences, strictly refers to each patient's cognitive function impairment map, and tailors training tasks and intervention content that are realistic^[6,7]. Compared with the traditional nursing model, cognitive rehabilitation nursing has outstanding initiative and skill-oriented advantages, completely breaking the limitations of passive care in conventional nursing, allowing nursing staff to transform from mere caregivers into organizers, guides and supervisors of rehabilitation training^[8].

The results showed that the difference between the groups in cognitive function was small at the time of enrollment, and the MCCB score after care was higher in the observation group than in the control group, $P < 0.05$. The social function score value of the observation group was lower than that of the control group, $P < 0.05$. The reason is that systematic sub-module training at the cognitive level, such as attention scheduling, memory strategy application, and executive function problem-solving simulation, provides targeted and repeated activation and practice opportunities for patients' damaged neurocognitive circuits, and promotes compensatory reorganization or efficiency improvement of related brain area functions, which is measured as a general improvement in the scores of all dimensions of MCCB^[9]. Cognitive abilities improved at the level of social functions are the basis for improving social functions. Through emotion recognition and social situation role-playing training, patients' social cognitive abilities are directly exercised, making them more able to accurately interpret the intentions and emotions of others. The improvement of working memory and executive functions allows patients to better maintain dialogue clues in complex and changeable social interactions. Combining cognitive strategies with hospital life scenarios accelerates the transformation process from laboratory training to real-world applications^[10].

5. Conclusion

In summary, cognitive rehabilitation care for patients with schizophrenia has significant value in promoting the improvement of patients' cognitive functions and enhancing their social functions.

Disclosure statement

The author declares no conflict of interest.

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Construction of a Collaborative Model of Community Pharmacy Services and Family Doctor Contracting System and Evaluation of Its Application Effects

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Abstract: *Objective:* To analyze the specific content of the collaborative model of community pharmacy services and family doctor contracting system, and explore the application effect of this plan. *Methods:* This article selects the research subjects who visited our hospital as the research object. After grouping by the odd-even number grouping method, 40 cases each. After investigation, all patients were admitted during the same time period, namely: January 2024 to December 2025; during the treatment phase, routine management was used for the control group, and the collaborative model of community pharmacy services and family doctor contracting system was used for the experimental group. The blood pressure, blood sugar, health knowledge mastery, self-management ability and satisfaction were compared between the two groups. *Results:* (1) Before clinical intervention, there was no difference in blood pressure and blood sugar levels between the two groups of research subjects, $P > 0.05$; after intervention, the above indicators were significantly improved, and the experimental group was at a lower level, $P < 0.05$; (2) Health knowledge mastery and self-management After ability statistics, the experimental group scored higher than the control group, $P < 0.05$; (3) In terms of satisfaction, 77.50% (31/40) of the research subjects in the control group and 95.00% (38/40) of the experimental group. The comparison results showed that the experimental group was higher, $P < 0.05$. *Conclusion:* In the clinical treatment stage, the collaborative model of community pharmacy services and the family doctor contracting system is more effective. For the research subjects, it can significantly improve blood pressure and blood sugar levels, improve health knowledge, self-management ability, and ensure patient satisfaction. It is worthy of widespread implementation.

Keywords: Community pharmacy services; Family doctor contracting system; Collaborative model; Application effects; Satisfaction analysis

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1. Introduction

Chronic diseases are a global public health problem. According to epidemiological surveys, the incidence of such diseases has shown an increasing trend year by year, and the degree of harm is high ^[1]. In specific classifications, typical manifestations of chronic diseases include: hypertension, diabetes, etc. The causes are: family inheritance, long-term mental stress, unhealthy eating habits, lack of regular exercise, etc. Once the disease occurs, it will cause a serious decline

in the patient's quality of life and pose a greater threat to the patient's health^[2]. In the field of clinical treatment, research subjects rely on drug regimens. Although the effects are obvious, during long-term intervention, patients are prone to irritability, depression, and rejection behaviors, which in turn lead to poor prognosis. Therefore, it is necessary to actively analyze, explore, and introduce effective management models in clinical practice to better meet the various needs of research subjects^[3]. In this study, with reference to the analysis of research subjects admitted to the hospital from January 2024 to December 2025, after grouping them, the application effect of the collaborative model of routine management, community pharmacy services and family doctor contracting system was explored. The specific report is as follows.

2. Clinical data and methods

2.1. General information

This study was carried out after approval by the hospital's ethics department. There were 80 reference subjects, all of whom were admitted to our hospital. The selection time started in January 2025 and ended in February 2026. After grouping by the odd-even number grouping method, the details are as follows. Control group: 40 cases. After counting male and female patients, the ratio was 22:18. In terms of age, the upper and lower limits were 78 and 55 years old, and the average was (66.59 ± 1.24) years old. Experimental group: 40 cases. After counting male and female patients, the ratio was 21 and 19. In terms of age, the upper and lower limits were 77 and 57 years old, and the average was (67.01 ± 1.03) years old. There is no difference in the above information (gender, age), this study is feasible, $P > 0.05$.

2.2. Method

Control group: Provide routine management. During the treatment phase of the research subjects, clinical indications need to be continuously monitored, including: blood pressure, blood sugar change trends, disease symptoms, etc. Patients are supervised to take medications correctly and drug reactions are recorded; symptomatic intervention is provided if discomfort occurs.

Experimental group: Provide a collaborative model of community pharmacy services and family doctor contracting system. The main contents are:

- (1) Creating a team. Led by the person in charge of the community health center, community pharmacists, family doctors, nurses, and health managers are selected to form a working group. Secondly, professional training is arranged. The core content includes: information related to common chronic diseases, typical characteristics of such patients, pharmaceutical service content, and family doctor contract service content. After the training, an assessment link can be added, and those who pass the assessment can clarify their responsibilities and formally take up the post.
- (2) Personalized service. After the research subject signs the contract, team members need to actively evaluate various information, including: age, education level, past medical history, current medical history, medication status, living habits and physiological indicators, etc. After fully understanding the patient's condition, community pharmacists and family doctors need to work together to review relevant literature or develop targeted management strategies based on clinical guidelines and their own experience.
- (3) Follow-up. In the current social stage, when research subjects are treated at home, clinical follow-up is usually carried out by telephone and WeChat. During this process, family doctors need to take the initiative to understand and make detailed records of the patient's medication use, whether symptoms have improved, and their living habits. At the same time, family doctors still need to actively ask and record the problems and adverse drug reactions encountered in the patient's life. Community pharmacists need to analyze the above issues, determine the root cause of the patient's adverse drug reactions, adjust the medication plan, and enter them in detail into the patient's electronic information system to achieve resource sharing.
- (4) Medication management. Among the research subjects, drug treatment is the main method. Therefore, community pharmacists also need to provide timely targeted introductions, including: the efficacy, principle of action, common

adverse reactions, etc. of the drugs used by patients, and understand the patient's medication compliance through family doctors; for patients with poor compliance, the specific plan can be simplified and a medication reminder alarm can be set.

- (5) Knowledge mission. It can be carried out through online and offline channels, such as WeChat public accounts, WeChat group education, and offline health lectures. During the activities, community pharmacists and family doctors need to patiently introduce information about the types of common chronic diseases, their hazards, and how to prevent them, and they need to carefully answer patients' questions and correct misconceptions.
- (6) Summarize improvements. During the drug treatment phase of the research subjects, the working group needs to hold a summary meeting once a month. Internal members will report on the management of the corresponding patients, sort out specific problems and launch brainstorming to determine solutions. In addition, team members need to provide targeted dietary plans and exercise suggestions based on the actual conditions of the research subjects to ensure that relevant measures are more in line with the patients' needs, thereby ensuring the overall service quality.

2.3. Evaluation indicators

- (1) Among the research subjects, compare the blood pressure levels of the two groups before and after the intervention, including: diastolic blood pressure and systolic blood pressure;
- (2) Compare blood sugar levels, including: fasting blood sugar and 2h postprandial blood sugar;
- (3) Compare clinical indicators: health knowledge mastery and self-management ability scores.
- (4) Comparative satisfaction, the specific levels set among the research objects are: satisfied, average, and dissatisfied.

2.4. Statistical analysis

The measurement data and counting data obtained in this study were analyzed and processed by SPSS 25.0 software. Among the research subjects, blood pressure levels, blood sugar levels, and clinical indicators were tested by the *t*-test, and satisfaction was tested by the chi-square test. All information was represented in the form of mean $\pm$ standard deviation (SD), (%), $P < 0.05$.

3. Results

3.1. Blood pressure level

In the statistical results of the blood pressure levels of the research subjects, there was no difference before the intervention, $P > 0.05$; after the intervention, the experimental group was at a lower level, $P < 0.05$ (**Table 1**).

Table 1. Comparison of blood pressure levels between the control group and the experimental group (mean $\pm$ SD)

Specific group	Diastolic blood pressure (mmHg)		Systolic blood pressure (mmHg)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 40 cases)	92.55 $\pm$ 5.98	89.23 $\pm$ 4.11	144.38 $\pm$ 6.75	138.46 $\pm$ 5.42
Experimental group (n = 40 cases)	92.47 $\pm$ 5.91	83.65 $\pm$ 4.19	144.41 $\pm$ 6.69	131.97 $\pm$ 4.88
<i>t</i>	0.060	6.013	0.020	5.628
<i>P</i>	0.952	0.000	0.984	0.000

3.2. Blood sugar level

Comparing fasting blood glucose and 2h postprandial blood glucose, there was no difference between the two groups before the intervention, $P > 0.05$; after the intervention, the experimental group had a lower value, $P < 0.05$ (**Table 2**).

Table 2. Comparison of blood glucose levels between the control group and the experimental group (mean $\pm$ SD)

Specific group	Fasting blood glucose (mmol/L)		Blood glucose 2 hours after meal (mmol/L)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 40 cases)	8.09 $\pm$ 1.26	7.42 $\pm$ 1.01	10.08 $\pm$ 5.43	8.74 $\pm$ 1.19
Experimental group (n = 40 cases)	8.11 $\pm$ 1.34	6.69 $\pm$ 0.93	10.11 $\pm$ 5.37	7.02 $\pm$ 1.48
<i>t</i>	0.069	3.363	0.025	5.728
<i>P</i>	0.945	0.001	0.980	0.000

3.3. Clinical indicators

Comparing the health knowledge mastery and self-management ability of the research subjects, the experimental group scored higher, $P < 0.05$ (Table 3).

Table 3. Comparison of clinical indicators between the control group and the experimental group (mean $\pm$ SD)

Specific group	Health knowledge mastery (points)	Self-management ability (points)
Control group (n = 40 cases)	83.46 $\pm$ 2.57	81.59 $\pm$ 2.11
Experimental group (n = 40 cases)	92.97 $\pm$ 2.06	93.05 $\pm$ 1.62
<i>t</i>	18.261	27.246
<i>P</i>	0.000	0.000

3.4. Satisfaction

In terms of satisfaction, the subjects in the experimental group were higher than those in the control group, $P < 0.05$ (Table 4).

Table 4. Comparison of satisfaction between control group and experimental group (%)

Specific group	Very satisfied	Satisfied	Not satisfied	Total satisfaction (%)
Control group (n = 40 cases)	17 (42.50)	14 (35.00)	9 (22.50)	31 (77.50)
Experimental group (n = 40 cases)	22 (55.00)	16 (40.00)	2 (5.00)	38 (95.00)
χ^2	-	-	-	5.165
<i>P</i>	-	-	-	0.023

4. Discussions

Chronic diseases have a high clinical incidence and are generally characterized by long cycles, strong recurrence, and difficulty in curing. For such patients, in the early stages of disease onset, the subjective symptoms are not obvious, and in the continuous progression stage, some cardiovascular and cerebrovascular complications will occur, which are more harmful^[4].

The results of this study show: (1) The research subjects were investigated and compared with blood pressure and blood sugar levels before intervention. There was no difference between the two groups, $P > 0.05$; after clinical intervention, the above indicators in both groups improved, and the experimental group was lower than the control group, $P < 0.05$; (2) Health knowledge mastery and self-management ability In terms of strength, the comparison results between the control group and the experimental group were significantly different, and the experimental group was higher, $P < 0.05$; (3) After different modes of intervention, the satisfaction of the research subjects was 77.50% (31/40), 95.00% (38/40). The comparison results showed that the experimental group was higher, $P < 0.05$. The specific analysis is as follows: The application of the collaborative model of community pharmacy services and family doctor contracting system

is highly standardized and coherent, which can fully highlight the “patient-centered” management concept. In clinical practice, creating working groups and strengthening training measures can improve the professionalism and collaboration skills of team members and ensure the efficiency of follow-up services^[5]; in terms of research subjects, after the contract is completed, community pharmacists and family doctors need to jointly analyze and evaluate the patient’s condition and develop a personalized management plan for them. During the home medication process, family doctors can proactively inquire about various indications of research subjects through phone calls and WeChat channels and make detailed records to provide patients with guidance. Community pharmacists will then analyze and judge the rationality of drug use, and dynamically adjust specific plans based on adverse reactions to improve patient treatment safety^[6]. After analyzing the above collaborative management model, it can demonstrate the close collaborative relationship between family doctors and community pharmacists, and provide relatively complete services to the research subjects. Moreover, knowledge education measures through collaboration between parties can help correct misconceptions of research subjects and improve medication compliance. At the same time, this measure can help patients actively adjust their lifestyle and improve their self-management abilities^[7]. In addition, the integration of summary and improvement links can help members of the working group discover problems on time, and the process can be continuously optimized through collective discussion to better make up for the shortcomings of traditional management. For research subjects, it can reduce disease symptoms, optimize self-experience, and ensure the best prognosis level^[8,9].

5. Conclusion

In summary, the development of a collaborative model of community pharmacy services and family doctor contracting systems is of great clinical significance and can improve the health knowledge and self-management abilities of research subjects. At the same time, the application of this program can also reduce patients’ blood pressure and blood sugar levels, relieve disease symptoms, improve curative effects, and better ensure patient satisfaction, which has significant promotional value.

Disclosure statement

The author declares no conflict of interest.

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Analysis of the Effectiveness of Physical Rehabilitation in Treating Patients with Neck, Shoulder, Waist and Leg Pain

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Abstract: *Objective:* To explore the application value of physical rehabilitation programs in the treatment of patients with neck, shoulder, waist and leg pain. *Methods:* 80 patients were studied, all diagnosed with neck, shoulder, waist and leg pain after admission. After being divided into groups according to the odd-even number method, 40 cases were assigned to each group. The selection time of the two groups started in January 2025 and ended in December 2025. During the treatment phase, conventional Western medicine was used in the control group and a physical rehabilitation program was used in the experimental group. The final effect was evaluated and compared, including: VAS score (visual analogue scale for pain), clinical efficacy and quality of life in patients with neck, shoulder, waist and leg pain. *Results:* (1) After statistics of VAS scores of patients with neck, shoulder, waist and leg pain, the difference before treatment was small, $P > 0.05$; after treatment, both groups improved, and the experimental group (3.18 ± 0.47 points) was at a lower level, $P < 0.05$; (2) In terms of total effective rate, conventional Western medicine treatment, The statistical data of physical rehabilitation treatment were: 80.00% (32/40), 95.00% (38/40). The comparison results showed that the experimental group was higher, $P < 0.05$; (3) In the quality of life scores, the patients with neck, shoulder, waist and leg pain in the experimental group were higher, $P < 0.05$. *Conclusion:* In the clinical treatment stage, the physical rehabilitation program is effective. For patients with neck, shoulder, waist and leg pain, it can significantly improve pain symptoms and other disease symptoms, and promote an improvement in the total effectiveness. At the same time, this program can also better protect the best quality of life for patients, and has significant promotional value.

Keywords: Patients with neck, shoulder, waist and leg pain; Physical rehabilitation treatment; VAS score; Total effective rate; Quality of life score

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1. Introduction

Neck, shoulder, waist and leg pain have a high clinical incidence. The most common groups are: middle-aged patients and elderly patients. After a comprehensive analysis, it is found that the typical symptoms of this group include: pain, swelling, limited activity in the neck and shoulders, upper limbs, lower back and lower limbs. In the continuous progression stage, the patient's various discomforts will further worsen, which will seriously affect the patient's quality of life and physical and mental health ^[1]. During the treatment process, with the continuous development of national medical technology,

there are relatively many suitable solutions for patients with neck, shoulder, waist and leg pain. Among them, although drug intervention can effectively alleviate the pain, patients are prone to dependence and adverse reactions, and its safety factor is low^[2]; while physical rehabilitation therapy can effectively stimulate the patient's affected parts through physical factors, thereby improving blood circulation and promoting recovery^[3]. In view of this, this article will analyze the patients with neck, shoulder, waist and leg pain who visited our hospital from January 2025 to December 2025, and explore the application value of conventional treatment (control group) and physical rehabilitation treatment (experimental group) after random grouping, as follows.

2. Clinical data and methods

2.1. General information

After approval by the hospital's ethics department, this activity was launched. After the investigation, the research time was January 2025 to December 2025. The specific composition of the reference objects: patients with neck, shoulder, waist and leg pain. During the clinical treatment stage, all patients ($n = 80$ cases) need to be grouped in time. The details are as follows. Control group: 40 cases in total. After counting the number of men and women, the proportion is 20:20. In terms of age, the upper and lower limits are 78 and 51 years old, and the average value is (64.55 ± 1.39) years old. After counting the course of the disease, the shortest and longest times are 0.5 and 1.7 years, and the average time is (1.08 ± 0.23) years; Experimental group: 40 cases in total. After counting the number of men and women, the proportion was 22 cases: 18 cases. In terms of age, the upper and lower limits were 76 and 52 years old, and the average value was (64.08 ± 1.51) years old. After counting the course of the disease, the shortest and longest times were 0.8 and 1.6 years, and the average time was (1.17 ± 0.13) years. The above research information (gender, age, disease duration) is balanced and comparable. This study has high feasibility, $P > 0.05$.

Inclusion criteria: (1) The in-hospital examination results of the patients were analyzed, and all patients were diagnosed with "neck, shoulder, waist and leg pain", and the personal information was relatively complete; (2) After drug treatment, the patients with neck, shoulder, waist and leg pain had no allergies; (3) After professionals introduced the research purpose and content popularly, the patients and their families expressed full understanding, high recognition of the internal regulations, and voluntarily signed relevant agreements.

Exclusion criteria: (1) Patients with neck, shoulder, waist, and leg pain who have short-term or long-term mental illnesses and have lost basic communication skills; (2) Patients with malignant tumor disease; (3) Patients with neck, shoulder, waist, and leg pain who have serious organic lesions in the examination results of important organs; (4) Patients with poor mental status and severe resistance to various examinations and treatments; (5) Patients with neck, shoulder, waist, and leg pain who dropped out of the participation midway after considering the influence of multiple factors.

2.2. Method

Control group: Provide conventional Western medicine treatment. The specific type is mainly ibuprofen sustained-release capsules. For patients with neck, shoulder, waist and leg pain, the oral route can be used for administration. The single dosage is 1 capsule, twice a day. The observation time is: 14 days. The drug information is: Ibuprofen sustained-release capsules, produced by Sino-US Tianjin SmithKline Pharmaceutical Co., Ltd., national drug approval number H10900089, product specifications: $0.3 \text{ g} \times 20$ capsules.

Experimental group: Provide a physical rehabilitation treatment plan, the main contents are: (1) Medium frequency electrotherapy. In clinical practice, the instrument involved is a computerized medium-frequency electrotherapy instrument, model: CM2000A, and the pulse current is adjusted to 1000–10000Hz; during specific operations, the patient can be adjusted to a comfortable position. Secondly, the electrode pads of the instrument are correctly pasted on the pain points and surrounding acupoints to treat the patient, 20 minutes/time, once/day; (2) Acupuncture treatment. For the analysis of patients with neck, shoulder, waist and leg pain, the acupuncture points selected for clinical intervention are: Neck Jiaji,

Jianjing, Shenshu, Yaoyangguan, Huantiao, Weizhong, and Zusanli. Secondly, staff need to disinfect them correctly and use disposable sterile acupuncture. Insert the needle, and then perform acupuncture treatment. During this process, the main method is to strengthen and relieve the pain. The patient is asked about his or her feelings on time. The needle is retained when there is soreness, numbness, swelling, and pain. The specific time is: 20 minutes, once a day; (3) Traditional Chinese medicine fumigation. After analyzing the indications of patients with neck, shoulder, waist and leg pain, the specific types of traditional Chinese medicine were determined, including: 20 g each of safflower, kudzu root, and *Ligusticum chuanxiong*; 15 g each of papaya, angelica, Qianghuo, Bupleurum, and Duhuo; 10 g each of Fangfeng, Aracenia, and *Zanthoxylum bungeanum*. All the medicines were mixed and put into the traditional Chinese medicine fumigation. In the steaming instrument, add an appropriate amount of water until the instrument generates steam, and instruct the patient to fully expose the painful area and perform fumigation. During this process, keep 50 cm between the patient's skin and the steam outlet to avoid burns, 25 min/time, once/day. (4) Rehabilitation training. The principle of step-by-step will be strictly implemented. During the initial treatment process, the staff can provide basic suggestions, such as left and right rotation of the neck, shoulder circumference exercises, quadriceps isometric contraction training, etc., 15 minutes/time, once/day. As the patient's condition gradually improves, the staff can advise the patient on daily Increase the training time, and then recommend the patient to join back stretching, straight leg raising and slow walking training, 30 minutes each time, 2 times a day if conditions permit; however, the staff needs to remind the patient to strictly control the daily time and intensity based on self-tolerance, and not to rush for quick success to avoid other accidental injuries. Observation time: 14th.

2.3. Evaluation indicators

- (1) Among patients with neck, shoulder, waist and leg pain, compare the differences in VAS scores (visual analog scale for pain) between the two groups before and after the intervention. The total score is 10. The level of the measured data is inversely proportional to the patient's pain level;
- (2) To compare the clinical efficacy, the setting levels and judgment criteria are ^[4]: Significantly effective level: The patient's neck, shoulder, hip, and knee joint functions have returned to normal, and disease symptoms have basically disappeared; Generally effective level: The patient's pain symptoms and other discomfort symptoms have significantly improved, and limb functions have significantly improved; Ineffective level: The patient's indications have not changed in all aspects, and there are signs of aggravation.
- (3) Compare the quality of life scores. The specific dimensions include: social function, psychological function, physical function, and material life; the total score of each item is 100. The measured data are directly proportional to the quality of life of patients with neck, shoulder, waist, and leg pain.

2.4. Statistical analysis

After sorting out the measurement data and counting data obtained in this study, they were analyzed under SPSS 25.0 software. Among them, the VAS score and quality of life score of patients with neck, shoulder, waist and leg pain were tested by the t-test, and the clinical efficacy was tested by the chi-square test. The above information is represented in the form of mean $\pm$ standard deviation (SD), (%), and $P < 0.05$ indicates that the difference is significant.

3. Results

3.1. VAS score

As shown in **Table 1**, there was no difference before treatment, $P > 0.05$; after treatment, the experimental group was at a lower level, $P < 0.05$.

Table 1. Comparison of VAS scores between the control group and the experimental group mean $\pm$ standard deviation (SD)

Group	Before treatment (points)	After treatment (points)
Control group (n = 40 cases)	7.03 $\pm$ 1.24	5.41 $\pm$ 1.06
Experimental group (n = 40 cases)	7.05 $\pm$ 1.19	3.18 $\pm$ 0.47
<i>t</i>	0.074	12.163
<i>P</i>	0.942	0.000

3.2. Clinical efficacy

As shown in **Table 2**, the total effective rate of treatment for patients with neck, shoulder, waist and leg pain was higher in the experimental group, $P < 0.05$.

Table 2. Comparison of clinical efficacy between the control group and the experimental group (%)

Group	Significantly effective	Generally effective	Invalid	Total effectiveness (%)
Control group (n = 40 cases)	18(45.00)	14(35.00)	8(20.00)	32(80.00)
Experimental group (n = 40 cases)	21(52.50)	17(42.50)	2(5.00)	38(95.00)
χ^2	-	-	-	4.114
<i>P</i>	-	-	-	0.043

3.3. Quality of life

As shown in **Table 3**, the scores of the experimental group were at a higher level, $P < 0.05$.

Table 3. Comparison of quality of life scores between the control group and the experimental group (mean $\pm$ SD, points)

Group	Social function	Psychological function	Physical function	Material life
Control group (n = 40 cases)	78.59 $\pm$ 4.56	79.63 $\pm$ 4.12	79.95 $\pm$ 4.33	78.64 $\pm$ 4.05
Experimental group (n = 40 cases)	88.17 $\pm$ 3.94	90.05 $\pm$ 2.13	89.87 $\pm$ 2.44	88.45 $\pm$ 3.12
<i>t</i>	10.054	14.209	12.623	12.136
<i>P</i>	0.000	0.000	0.000	0.000

4. Discussions

After analysis of neck, shoulder, waist and leg pain, the causative factors are relatively complex. The core indicators include: cervical spondylosis, lumbar disc herniation, osteoporosis, rheumatoid arthritis, muscle strain, metabolic diseases, etc. After clinical occurrence, it will cause great trouble to the patient's normal life and have a serious negative impact on the patient's physical and mental health^[5].

In the research results of this article, the observation indicators show:

- (1) Before clinical treatment, the comparison results of VAS scores showed that there was no difference between the two groups, $P > 0.05$; after treatment, the control group was (5.41 $\pm$ 1.06 points) and the experimental group was (3.18 $\pm$ 0.47 points). It can be seen that the latter was lower, $P < 0.05$;
- (2) After statistics of the total effective rate, the data of patients with neck, shoulder, waist and leg pain in the experimental group (95.00%, 38/40) were higher than those in the control group (80.00%, 32/40), $P < 0.05$;
- (3) In terms of quality of life, there was a significant difference in the data of patients with neck, shoulder, waist and leg pain in the two groups, and the experimental group was at a higher level, $P < 0.05$. The specific analysis is as follows:

In the treatment of neck, shoulder, waist and leg pain, conventional Western medicine is ibuprofen sustained-release capsules, which have obvious anti-inflammatory and analgesic effects.

However, the safety factor is low when taken for a long time, and the overall effect is not good. During physical rehabilitation treatment, medium-frequency electrotherapy can be used to intervene with professional medical equipment, which can effectively stimulate the patient's painful parts and regulate the patient's muscle contraction ability, thereby improving muscle spasm and alleviating discomfort^[6]. At the same time, acupuncture intervention in traditional Chinese medicine can better dredge the meridians and achieve the goal of "normalizing without pain"; and during the fumigation process of traditional Chinese medicine, safflower can activate blood and regulate Menstruation, improve microcirculation, *Ligusticum chuanxiong* dispels wind and relieves pain, promotes Qi and activates blood circulation, Fangfeng dispels wind and cold, and Aracenia dispels wind and relieves spasm. In clinical application, it can be supplemented with papaya, Bupleurum and other drugs for intervention, thereby better helping patients reconcile qi and blood and regulate organ function; and during this intervention, the warming effect of steam can further promote the absorption of inflammatory factors in the patient's body as quickly as possible, thereby alleviating the patient's pain symptoms^[7]. In addition, step-by-step rehabilitation training measures can also better improve the patient's body metabolism, better improve the patient's joint functions, increase joint flexibility, enhance muscle strength, and consolidate the treatment effect^[8]; the combination of the above programs has obvious synergy, and can better alleviate discomfort symptoms and shorten the recovery process for patients with neck, shoulder, waist, and leg pain. However, in clinical practice, staff still need to pay attention to patients' psychological needs, patiently comfort and encourage them, briefly introduce disease knowledge and the necessity of rehabilitation treatment, help patients correctly understand relevant information, improve cooperation, and better ensure patient prognosis and efficacy.

5. Conclusion

In summary, in the treatment stage of neck, shoulder, waist and leg pain, it is of great significance to carry out physical rehabilitation programs, which specifically include: medium frequency electrotherapy, acupuncture intervention, traditional Chinese medicine fumigation and rehabilitation training sessions. The combination of the above measures can help reduce patients' pain symptoms and other discomforts, and can improve the overall effectiveness. At the same time, this measure can also ensure the best quality of life for patients, and is worthy of further clinical promotion.

Disclosure statement

The author declares no conflict of interest.

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A Study on the Effect of Nurse-Patient Communication in the Nursing of Elderly Diabetic Patients and Its Impact on Improving Patients' Condition

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Abstract: *Objective:* To analyze the effect of nurse-patient communication in the nursing care of elderly diabetic patients and its impact on improving patients' condition. *Methods:* A total of 72 diabetic patients admitted to our hospital from August 2023 to August 2025 were enrolled and divided into two groups by random sampling. The control group received routine nursing, while the observation group was additionally given nurse-patient communication. The differences in blood glucose control, self-management ability and quality of life between the two groups were compared. *Results:* After nursing, the blood glucose levels (fasting blood glucose, glycosylated hemoglobin and 2-hour postprandial blood glucose) in the observation group were lower than those in the control group ($P < 0.05$). Compared with before nursing, the scores of T2-CSO and GQOLI-74 in both groups were increased after nursing, and the increase in the observation group was more significant ($P < 0.05$). *Conclusion:* Nurse-patient communication can effectively improve the condition of elderly diabetic patients, help strengthen blood glucose control, enhance self-management ability and improve quality of life.

Keywords: Nurse-patient communication; Elderly diabetes; Blood glucose; Nursing effect; Condition improvement

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1. Introduction

Diabetes mellitus is a chronic metabolic disease induced by the combined effects of multiple factors, including genetic susceptibility, environmental factors and obesity. Its core pathogenesis is persistent hyperglycemia resulting from decreased insulin sensitivity and impaired β -cell function^[1]. Long-term metabolic disorders can damage multiple organs; during the disease course, the retina, kidneys, nerves, and cardiovascular and cerebrovascular systems are frequently involved, significantly increasing the risk of cardiovascular events and multiple organ dysfunction. Elderly diabetic patients exhibit great individual differences, often accompanied by multiple chronic diseases and cognitive decline. Blood glucose regulation is more complicated due to physical and metabolic conditions, which further increase the treatment burden and adversely affect quality of life and prognosis^[2]. Statistics show that the prevalence rate is approximately 28.8% among people aged 60–69 years and 31.8% among those aged 70 years and above^[3]. In addition to medication, diabetes

treatment requires long-term patient cooperation in diet, exercise, blood glucose monitoring and psychological adjustment. Effective nurse-patient communication can enhance patients' understanding and compliance, thereby promoting their active participation and self-management and improving nursing outcomes. Relevant studies have shown that positive communication helps alleviate negative emotions such as anxiety and depression, improve psychological status and enhance self-care ability ^[4]. This study investigates the impact of enhanced nurse-patient communication on the basis of routine nursing on blood glucose, self-management ability and quality of life in diabetic patients.

2. Materials and methods

2.1. General data

A total of 72 patients with diabetes mellitus were enrolled as research subjects and divided into two groups by a random sampling method ($n = 36$). There were no statistically significant differences in general data between the two groups ($P > 0.05$), as shown in **Table 1**.

Table 1. Comparison of general data [mean $\pm$ standard deviation (SD), cases (n)]

Group	n	Male/Female	Age (years)	Course of disease (years)	Type 1 / Type 2	Body mass index (kg/m ²)
Observation group	36	20/16	63.98 $\pm$ 7.22	4.43 $\pm$ 0.91	2/34	24.23 $\pm$ 2.41
control group	36	23/13	61.71 $\pm$ 8.44	4.19 $\pm$ 0.73	1/35	23.86 $\pm$ 2.67
t/χ^2		0.520	1.226	1.234	0.293	0.617
P		0.471	0.224	0.221	0.589	0.539

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Met the diagnostic criteria for diabetes mellitus ^[5]; (2) Aged ≥ 60 years old, conscious, and able to cooperate with the investigation and nursing intervention; (3) With complete clinical data; (4) Signed informed consent.

Exclusion criteria: (1) Complicated with severe cardiac, cerebral, hepatic or renal dysfunction, or malignant tumor; (2) Accompanied by severe mental disorders or cognitive impairment, unable to communicate and evaluate normally; (3) Experienced acute complications in the recent period, such as ketoacidosis, hyperosmolar coma, etc.; (4) Complicated with other severe diseases that affect blood glucose management or quality of life; (5) Poor compliance and failed to complete nursing as required.

2.3. Methods

The control group received routine nursing care:

- (1) Medical staff formulated basic diet and medication plans according to patients' conditions, instructed patients to take medications regularly as prescribed, and supervised medication administration to avoid missed doses or unauthorized dose adjustment.
- (2) Patients were guided to conduct scientific diet management. On the basis of retaining daily eating habits, dietary structure was adjusted to control total daily calorie intake, reduce consumption of carbohydrates, fats and high-salt foods, and encourage intake of fresh fruits and vegetables, low-sugar foods and coarse grains. Small and frequent meals as well as a light diet were recommended.
- (3) Appropriate exercise regimens were formulated according to patients' age, physical strength and disease conditions. Patients were guided to adhere to regular exercise to improve insulin sensitivity, and were reminded to pay attention to exercise intensity and duration to prevent hypoglycemia or fatigue discomfort.

- (4) During nursing care, blood glucose, glycosylated hemoglobin and other indicators were monitored regularly, blood glucose control was evaluated on time, and suggestions on diet, activity and medication were adjusted accordingly.
- (5) Diabetes health education was provided for patients, including disease knowledge, diet control, exercise management, blood glucose monitoring and complication prevention, to enhance their self-care awareness and health management ability. The learning effect was strengthened through forms such as publicity, lectures or peer communication.
- (6) Patients were instructed to perform proper foot care and skin protection, observe blood pressure, blood lipid and other related indicators, identify risks early, and prevent the occurrence of diabetic foot, cardiovascular and other complications.

Observation Group: Additional Nurse-Patient Communication:

- (1) Nursing staff received patients with a friendly attitude, offered active greetings, listened patiently, and spoke in a gentle tone to shorten psychological distance. They learned about patients' medical history, personality traits, hobbies, and family conditions, and developed communication strategies tailored to different patients. For patients with obvious mood swings, they guided emotional expression in a gentle manner; for those with good cognitive function, emphasis was placed on condition explanation and shared decision-making. Non-verbal communication, such as smiling, nodding, and appropriate physical contact, was used to enhance trust, enabling patients to gain a sense of security and support during hospitalization.
- (2) Patients' anxiety, depression, and treatment resistance were observed. Listening, empathy, and encouraging language were adopted to relieve psychological pressure or provide psychological counseling, helping patients correctly understand their disease and the importance of long-term management, boosting treatment confidence, and preventing emotional factors from affecting blood glucose control and compliance.
- (3) Through face-to-face explanations, health education leaflets, and small lectures, diabetes-related knowledge was popularized to patients and their families, including pathogenesis, the significance of blood glucose monitoring, complication prevention, medication administration, and key points of self-management. Meanwhile, easy-to-understand language was used, combined with graphic demonstrations of the correct use of blood glucose meters, guiding patients to record blood glucose changes and improving their disease cognition and active management ability.
- (4) Individualized dietary plans were formulated jointly with nutritionists, clarifying food selection, cooking methods, and meal principles, emphasizing low-oil and low-fat diets, restricted intake of sugar and animal offal, and advocating small, frequent meals with fixed timing and quantity. Dietary compliance was evaluated 2–3 times per month with follow-up corrections. For patients with resistance, the necessity of diet control was explained through patient communication to standardize dietary behavior and stabilize blood glucose.
- (5) Appropriate exercise plans were formulated according to patients' age, physical condition, and hobbies, such as walking, Tai Chi, jogging, and swimming, with emphasis on the role of exercise in improving blood glucose, body weight, and cardiovascular function. Nursing staff provided continuous follow-up and encouragement, and accompanied patients during short-term activities in the early stage to enhance persistence and initiative. Meanwhile, precautions before and after exercise and hypoglycemia prevention measures were discussed.
- (6) The mechanism, usage, and possible adverse reactions of different hypoglycemic drugs and insulin were explained in detail to patients, guiding them to take medicine on time and in the correct dosage to avoid missed doses, wrong administration, or unauthorized dose adjustment. Nursing staff regularly checked implementation, communicated and solved problems on time, and offered affirmation and encouragement to improve medication compliance.

Both groups received continuous nursing care for 3 months, followed by 3 months of telephone follow-up after discharge.

2.4. Observation Indicators

- (1) Blood glucose control: Fasting blood glucose (FBG) was measured by collecting 5 mL of venous blood on the next morning after at least 8 hours of fasting. The serum was separated by centrifugation at 3000 r/min for 10 minutes, and detected by the glucose oxidase method using an automatic biochemical analyzer (Mindray BS-800M). For 2-hour postprandial blood glucose (2hPG), after fasting blood sampling, patients orally took 75 g of glucose solution or had

a routine breakfast, and 5 mL of venous blood was drawn again 2 hours later with the same detection method. For glycosylated hemoglobin (HbA1c) determination, 5 mL of venous blood sample was collected and analyzed by high-performance liquid chromatography (HPLC).

- (2) Self-management ability: The Type 2 Diabetes Self-Management Behavior Scale (T2-CSO) was used for evaluation before and after nursing. The scale consists of four dimensions: diet control, exercise implementation, blood glucose monitoring, and medication management. A 5-level scoring method was adopted, with a total score ranging from 26 to 130. A higher score indicates better self-management ability of patients.
- (3) Quality of life: The Generic Quality of Life Inventory-74 (GQOLI-74) was used for assessment before and after nursing, covering four dimensions: physical function, psychological function, social function, and material life. Each dimension was scored on a 100-point scale, and an increase in the total score indicates improved quality of life.

2.5. Statistical Analysis

After data entry, statistical analysis was performed using SPSS 25.0 software. Enumeration data were described as n(%) and compared using the χ^2 test. Measurement data were expressed as mean $\pm$ standard deviation (SD). After tests for normality and homogeneity of variance, the t-test was used to evaluate intergroup differences. The significance level for the two-sided test was set at $P < 0.05$.

3. Results

3.1. Blood glucose control

The blood glucose levels in the observation group after nursing were lower than those in the control group ($P < 0.05$). See Table 2.

Table 2. Comparison of blood glucose control (mean $\pm$ SD)

Group	n	Fasting Blood Glucose (mmol/L)		Glycated Hemoglobin (%)		2-hour Postprandial Blood Glucose (mmol/L)	
		Before Nursing	After Nursing	Before Nursing	After Nursing	Before Nursing	After Nursing
Observation group	36	9.65 $\pm$ 1.42	7.04 $\pm$ 0.93*	9.85 $\pm$ 1.33	7.46 $\pm$ 0.87*	11.23 $\pm$ 1.78	8.15 $\pm$ 1.41*
Control group	36	9.28 $\pm$ 1.26	7.61 $\pm$ 0.85*	9.42 $\pm$ 1.18	8.08 $\pm$ 0.92*	11.04 $\pm$ 1.59	9.28 $\pm$ 1.08*
<i>t</i>		1.169	2.714	1.451	2.938	0.478	3.817
<i>P</i>		0.246	0.008	0.151	0.005	0.634	< 0.001

Note: Compared with before nursing within the same group, * $P < 0.05$

3.2. Self-management Ability

Compared with before nursing, the T2-CSO scores of both groups were increased after nursing, and the increase in the observation group was more significant ($P < 0.05$). See Table 3.

Table 3. Comparison of T2-CSO scores (mean $\pm$ SD, scores)

Group	n	Before Nursing	After Nursing	<i>t</i>	<i>P</i>
Observation group	36	61.07 $\pm$ 6.54	78.51 $\pm$ 7.59	10.444	< 0.001
Control group	36	59.65 $\pm$ 5.23	70.13 $\pm$ 5.71	8.121	< 0.001
<i>t</i>		1.017	5.294		
<i>P</i>		0.313	< 0.001		

3.3. Quality of Life

Compared with the control group, the observation group had a higher GQOLI-74 score after nursing ($P < 0.05$). See **Table 4**.

Table 4. Comparison of GQOLI-74 scores (mean $\pm$ SD, scores)

Group	n	Psychological Function		Physical Function		Social Function		Material Life Status	
		Before Nursing	After Nursing	Before Nursing	After Nursing	Before Nursing	After Nursing	Before Nursing	After Nursing
Observation group	36	47.49 $\pm$ 8.41	70.09 $\pm$ 8.37*	46.16 $\pm$ 10.40	61.09 $\pm$ 6.07*	54.80 $\pm$ 7.89	71.98 $\pm$ 5.32*	50.76 $\pm$ 6.40	76.09 $\pm$ 8.06*
Control group	36	48.54 $\pm$ 7.37	64.88 $\pm$ 5.44*	47.03 $\pm$ 9.78	55.25 $\pm$ 5.24*	53.75 $\pm$ 7.36	63.31 $\pm$ 5.47*	50.03 $\pm$ 7.08	66.25 $\pm$ 5.64*
<i>t</i>		0.563	3.131	0.366	4.370	0.584	6.817	0.459	6.002
<i>P</i>		0.575	0.003	0.716	< 0.001	0.561	< 0.001	0.648	< 0.001

Note: Compared with before nursing in the same group, * $P < 0.05$

4. Discussion

Diabetes mellitus is a chronic metabolic disease characterized by persistent hyperglycemia, which is closely associated with multiple metabolic disorders of glucose, lipids and proteins. It is mainly caused by insulin resistance and impaired β -cell function, among which type 2 diabetes accounts for approximately 95% of all cases [6]. Long-term hyperglycemia can lead to multisystem damage and induce complications such as retinopathy, diabetic nephropathy, neuropathy, and cardiovascular and cerebrovascular diseases. In severe cases, it may even progress to multiple organ dysfunction. Elderly diabetic patients often suffer from cognitive decline, reduced physical fitness, unreasonable dietary structure, and poor compliance, making their conditions more prone to fluctuation. Affected by financial pressure and long-term treatment stress, they generally lack sufficient self-management ability, making it difficult to achieve effective disease control and maintain quality of life. Therefore, clinical nursing should emphasize communication and interaction, understand patients' medical history, psychological status and behavioral habits, to formulate individualized nursing measures and implement comprehensive nursing from physiological, psychological, and social aspects. As a key link in improving nursing quality, nurse-patient communication helps medical staff obtain patients' real needs on time through verbal and non-verbal communication, strengthens patients' understanding of disease management knowledge, relieves negative emotions, and promotes the standardization of diet, exercise and medication behaviors, thereby improving disease conditions [7].

The present study showed that the blood glucose levels in the observation group were lower than those in the control group after nursing, and the scores of T2-CSO and GQOLI-74 were higher than those in the control group ($P < 0.05$), which is consistent with the findings of Shi Jingting [8]. This indicates that nurse-patient communication can strengthen blood glucose management and promote the improvement of quality of life.

Effective communication between nurses and patients helps to establish a good trust relationship, enabling patients to gain a sense of support and security during hospitalization. It can reduce psychological anxiety and stress levels, which is conducive to alleviating the negative impact of excessive sympathetic nerve excitation on blood glucose regulation, while improving treatment compliance. In addition, the in-depth understanding of individual differences during communication makes health education more targeted. Patients can accurately grasp the key points of blood glucose monitoring, diet control and exercise management, thus enhancing their awareness of self-management [9]. In medication management guidance, clear information transmission and compliance supervision were provided to patients, deepening their understanding of the necessity and safety of treatment, reducing irrational medication behaviors, which helps to lower blood glucose levels and improve quality of life [10].

5. Conclusion

In summary, nurse-patient communication in the nursing care of elderly diabetic patients can improve patients' understanding of disease knowledge and management strategies, promote the standardized implementation of diet, exercise and medication behaviors, thereby improving blood glucose control and enhancing self-management ability. Active interaction and emotional support optimize patients' psychological and living status, significantly improving their quality of life, reflecting the positive role of nurse-patient communication in ameliorating disease conditions and nursing outcomes.

Disclosure statement

The author declares no conflict of interest.

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Application of Platelet-Rich Fibrin in Soft Tissue Management of Oral Implantation

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Abstract: Platelet-rich fibrin (PRF) possesses the functions of regulating the local microenvironment, promoting soft tissue repair and maintaining tissue stability by virtue of its three-dimensional fibrin network structure and the sustained release of active ingredients, laying a favorable application foundation in the soft tissue management of oral implantation. This article reviews the structural characteristics and biological properties of PRF, as well as its applications in wound closure of implant sites, soft tissue augmentation and keratinized gingiva reconstruction.

Keywords: Platelet-rich fibrin; Oral implantation; Soft tissue management

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1. Introduction

The long-term success of oral implant rehabilitation relies not only on the osseointegration of implants, but is associated with the peri-implant soft tissue conditions^[1]. Stable and sufficient soft tissue can form an effective biological barrier, reduce the risk of bacterial invasion, and play a vital role in maintaining the gingival margin morphology and prosthetic aesthetics. In clinical practice, however, affected by periodontitis destruction, prolonged edentulous time, absorption of hard and soft tissues after tooth extraction, and individual differences, the implant site is often complicated by insufficient soft tissue volume, inadequate width of keratinized gingiva, and difficulty in wound closure of the surgical area, all of which tend to impair the stability and long-term efficacy of implant rehabilitation. For the management of deficient soft tissue conditions in implant areas, conventional therapeutic methods at present mainly include connective tissue grafting, free gingival grafting and local flap techniques. Nevertheless, such surgical approaches are accompanied by drawbacks such as relatively large surgical trauma, high operational sensitivity and limited patient acceptance. Platelet-rich fibrin (PRF), first proposed by Dohan et al. in 2006, is a platelet concentrate prepared by centrifugation of autologous venous blood without the addition of anticoagulants or exogenous activators^[2]. Based on a three-dimensional fibrin network, it contains platelets, leukocytes and a variety of growth factors. It can form a bio-scaffold with a certain supporting effect locally and release active ingredients sustainably, thereby participating in the process of wound healing and tissue regeneration^[3]. For this reason, PRF has been gradually applied in implant-related soft tissue management and achieved favorable clinical outcomes in wound healing and improvement of local soft tissue conditions. Therefore, based on the

biological mechanism of PRF in implant soft tissue repair, this article reviews its applications in wound management of implant sites, soft tissue augmentation and keratinized gingiva reconstruction.

2. Biological basis of PRF in implant soft tissue regeneration

2.1. Structural characteristics and bioactive components of PRF

PRF is a second-generation platelet concentrate obtained by centrifugation of autologous venous blood, and its formation process simulates the physiological coagulation reaction of the human body. Without the addition of anticoagulants, blood is divided into three layers after centrifugation: the upper layer is platelet-poor plasma, the middle layer is PRF gel, and the lower layer is the red blood cell layer. Among them, PRF is located in the middle area and presents a milky white gel state. This structure derives from the three-dimensional network formed by the gradual polymerization of fibrin, in which platelets and various cellular components are stably embedded, constructing a biological scaffold with certain elasticity and mechanical supporting capacity. The fibrin network can form a relatively stable spatial structure in tissue defects and closely adhere to the surrounding tissues. It provides mechanical support for local tissues in the early healing stage, and meanwhile offers attachment sites for cell adhesion and tissue ingrowth. Zhang Wentao et al. ^[4] observed in the repair of severe alveolar ridge defects in the maxillary anterior region that the application of PRF achieved favorable soft tissue coverage and enhanced wound stability. Its three-dimensional fibrin network supports cell migration and tissue ingrowth, as well as sustains the continuous release of active ingredients. Accordingly, the symmetry of the gingival margin contour and the fullness of the gingival papillae are improved, the risk of “black triangle” formation is relatively reduced, and the local tissue morphology is maintained more stably. In terms of histological configuration, the most prominent feature of PRF is its three-dimensional fibrin network structure. Composed of cross-linked fibrin fibers with uniformly distributed internal pores, this structure can effectively capture and store platelets, leukocytes and a variety of cytokines ^[5]. This structure endows PRF with good plasticity, allowing it to be clinically compressed into membrane materials or directly applied to wound filling in the form of gel, while providing a suitable microenvironment for cell adhesion, migration and proliferation. Compared with traditional platelet concentrates, PRF requires no exogenous coagulation activators, and its fibrous structure is more similar to that of natural blood clots, which is conducive to maintaining the continuity and stability of the tissue repair process.

In terms of composition, PRF is rich in cellular components, such as platelets and leukocytes. The α -granules of platelets store a variety of growth factors, including platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). As essential biological regulatory molecules, these growth factors bind to cell surface receptors and participate in the regulation of cell proliferation, chemotaxis, differentiation, and extracellular matrix synthesis. Released in a relatively coordinated manner at different stages, they exert synergistic effects on the proliferation, adhesion and mineralization of osteoblasts ^[6]. Meanwhile, leukocytes contained in PRF can secrete multiple inflammation-related factors and participate in the regulation of local inflammatory responses and immune processes, thereby maintaining a microenvironment conducive to tissue repair. In addition, PRF exerts regulatory effects on various cell types, including osteoblasts, periodontal ligament cells, gingival fibroblasts, oral epithelial cells and mesenchymal stem cells, which provides the biological basis for bone tissue repair and soft tissue healing ^[7]. Notably, the fibrin network formed by PRF possesses a slow degradation property. The encapsulated growth factors are released sustainably rather than in an abrupt burst within a short period. This maintains stable biological activity signals in the early stage of wound healing and continuously regulates cellular behaviors and tissue reconstruction, which serves as a crucial feature distinguishing PRF from traditional platelet concentrates.

2.2. Mechanism of PRF-mediated soft tissue healing

At the cellular behavioral level, PRF exerts a promotive effect on gingival fibroblasts. A variety of growth factors released by PRF enhance cell proliferative activity and accelerate cell migration, enabling cells at the wound margin to

rapidly accumulate toward the defective area. Meanwhile, the capacity of fibroblasts to secrete collagen is improved with increased deposition of type I collagen, which gradually restores the tension and structural stability of soft tissues and lays the foundation for soft tissue reconstruction. In terms of matrix remodeling, the fibrin scaffold provided by PRF presents a spatial structure similar to that of natural blood clots and serves as a support for cell adhesion and spreading. With the gradual degradation of the scaffold, the local extracellular matrix is continuously replaced by newly formed collagen, transforming the wound from a loose clot structure into dense connective tissue, which manifests as enhanced tissue continuity and improved quality of wound closure. Angiogenesis is also significantly regulated. Vascular-related growth factors sustainably released from PRF accelerate the formation and uniform distribution of new capillaries in the wound area. The establishment of microcirculation shortens the duration of ischemia, facilitates the delivery of oxygen and nutrients, and thereby creates favorable conditions for epithelial coverage and connective tissue maturation. Wu Jing et al.^[8] also pointed out that PRF is rich in growth factors such as PDGF, VEGF and TGF- β , which can promote the proliferation of vascular endothelial cells and the secretion of pro-angiogenic factors, participate in extracellular matrix synthesis, and exert positive effects on tissue repair and regeneration. In the regulation of inflammatory responses, leukocytes enriched in PRF and various cytokines released by them jointly participate in the local immune response, enabling the wound to form a relatively ordered inflammatory state at the early stage. Studies have shown that during PRF-assisted treatment, the levels of inflammatory factors such as IL-1 β , IL-8 and TNF- α are significantly decreased, indicating that PRF can modulate the release of inflammatory mediators in the early stage of injury and reduce the degree of local inflammatory tissue damage^[9]. The release rhythm of inflammatory mediators is precisely regulated, which not only ensures the necessary initiation of inflammation after injury, but also avoids tissue destruction caused by excessive persistent inflammatory response, so as to alleviate local exudation and cellular injury.

3. Application efficacy of PRF in soft tissue management of oral implantation

3.1. Wound closure of implant site and socket preservation after tooth extraction

After the formation of an extraction wound, the wound surface is mostly covered by a blood clot. With a relatively loose structure, the clot is susceptible to displacement or rupture due to the oral environment and mechanical stimuli, resulting in unstable wound margin adaptation and delayed healing. When PRF is placed into the extraction socket or covered over the wound surface, it forms a dense local fibrin network that closely adheres to the wound. It provides early mechanical support to the wound margin, reduces marginal collapse, and enables more continuous epithelial migration toward the wound center. Deng Xuelian et al.^[10] indicated that the molecular components of PRF resemble those of natural blood clots. It acts as a biological scaffold to provide a microenvironment for cell proliferation and differentiation, improves local healing by promoting angiogenesis and tissue repair, and thereby facilitates wound stability and continuous tissue regeneration. As healing progresses, the fibrin matrix formed by PRF is gradually replaced by newly regenerated tissue, allowing a smoother transition from the initial clot state to dense connective tissue. Meanwhile, wound contraction is accelerated, and the incidence of wound dehiscence and bleeding is reduced, maintaining the continuity of local tissues. Clinically, this is manifested as shortened wound healing time and improved healing quality. Wang Fang et al.^[11] confirmed that the application of PRF at extraction sites markedly shortens wound healing time. The growth factors contained in PRF promote the repair of traumatic regions, favor local tissue recovery and structural maintenance, and optimize the overall wound healing process. Previous studies have also found that PRF application alleviates postoperative swelling and pain, which is associated with improved local microcirculation and regulated inflammatory responses. Pu Lili et al.^[12] supported this viewpoint, reporting that the use of PRF after mandibular impacted third molar extraction significantly reduces postoperative pain and swelling, achieves better soft tissue healing, and lowers the incidence of complications compared with conventional treatment.

3.2. Soft tissue augmentation and keratinized gingiva reconstruction

Tooth loss is often accompanied by alveolar ridge resorption, which leads to reduced soft tissue volume and a thinner gingival biotype. This weakens the resistance of peri-implant tissues to mechanical stimulation and dental plaque, further increasing the risk of marginal bone resorption and soft tissue recession. Relevant studies have indicated that insufficient peri-implant soft tissue thickness reduces the tissue buffering capacity against external stimuli, impairs anti-inflammatory and reparative potential, and renders tissues more vulnerable to plaque aggression, thereby raising the likelihood of peri-implant tissue destruction^[13]. Under such compromised soft tissue conditions, the dependence on regenerative materials increases. When PRF is placed around implants or in the submucosal space, it can form stable adhesion with the recipient tissues. Its fibrin network provides early spatial support and is gradually replaced by newly synthesized collagen during healing, resulting in increased local soft tissue thickness. Wang Huichao et al.^[14] further confirmed that PRF helps improve peri-implant soft tissue attachment and local stability. Two months after treatment, partial or complete gingival coverage was achieved at the implant neck, accompanied by increased width of keratinized gingiva. There is a significant reduction in probing depth and sulcus bleeding index compared with baseline. PRF also exerts favorable effects on keratinized gingiva reconstruction. In the second-stage implant surgery or soft tissue contouring procedure, PRF can be used as a covering material or combined with flap elevation to expand the area of keratinized tissue and reduce surgical site contraction and wound margin retraction. Tang Qiong et al.^[15] compared the clinical outcomes of extraction sockets filled with fresh blood clot versus PRF gel. The results showed that the PRF group presented a more prominent increase in keratinized gingiva width, improved gingival soft tissue thickness, and relatively less wound shrinkage during postoperative follow-up, verifying that PRF possesses superior advantages in maintaining soft tissue volume and promoting keratinized gingiva formation.

4. Summary

PRF has demonstrated favorable clinical efficacy in the soft tissue management of oral implantation. Owing to its fibrin network structure and bioactive components, PRF presents considerable application value in wound closure, soft tissue augmentation, and keratinized gingiva reconstruction. Its clinical performance is closely correlated with centrifugation parameters, material form selection and specific application methods. Differences in operational conditions lead to variations in the structural characteristics and the release pattern of bioactive ingredients of PRF. Further standardization of preparation parameters and application protocols is still required to improve the stability of its clinical application.

Disclosure statement

The author declares no conflict of interest.

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Construction and Application of Early Rehabilitation Protocol for Post-stroke Dysphagia Based on the Closed-loop Management of “Assessment-Intervention-Monitoring”

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Abstract: *Objective:* To analyze the efficacy and clinical value of an early rehabilitation protocol based on the closed-loop management mode of “Assessment-Intervention-Monitoring” in patients with post-stroke dysphagia. *Methods:* A total of 78 patients with post-stroke dysphagia admitted to our hospital from October 2023 to October 2024 were enrolled and randomly divided into two groups by the random number table method, with 39 cases in each group. The control group received routine rehabilitation treatment, while the observation group adopted the early rehabilitation protocol based on the closed-loop management of “Assessment-Intervention-Monitoring”. Nutritional indicators and immune function were compared between the two groups. *Results:* After treatment, the nutritional status of both groups was significantly improved compared with baseline ($P < 0.05$). The incidence of complications in the observation group was lower than that in the control group ($P < 0.05$). In terms of immune function indexes and clinical effectiveness rate, the observation group was significantly superior to the control group ($P < 0.05$). *Conclusion:* For patients with post-stroke dysphagia, the early rehabilitation protocol based on “Assessment-Intervention-Monitoring” closed-loop management can effectively improve nutritional status and immune function, reduce complications, and enhance the comprehensive therapeutic effect.

Keywords: Closed-loop management; Early rehabilitation protocol; Stroke; Dysphagia

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1. Introduction

Stroke is a severe neurological disease threatening human health worldwide. It interrupts cerebral blood supply and results in impairments of cognition, language, swallowing and limb motor function. Among these sequelae, dysphagia not only interferes with patients’ normal oral intake, but also causes complications such as dehydration, malnutrition and aspiration pneumonia, which may be lifethreatening in severe cases^[1]. At present, conventional clinical rehabilitation mainly focuses on the recovery of limb movement and vital signs, while the assessment and intervention of swallowing function are often initiated relatively late. Moreover, it lacks individualized and dynamic adjustment mechanisms, leading to unsatisfactory rehabilitation outcomes. In recent years, the concept of early rehabilitation has gained increasing attention; nevertheless,

existing protocols still present problems such as disconnection among the links of **assessment–intervention–monitoring** and insufficient interdisciplinary collaboration. Therefore, based on the theory of closedloop management, this study constructed an integrated early rehabilitation protocol covering assessment, intervention and monitoring. By means of dynamic evaluation, targeted intervention and continuous monitoring, a systematic rehabilitation closed loop was established. With a randomized controlled design enrolling patients with poststroke dysphagia, this study observed the effects of the protocol on nutritional status, immune function, complication incidence and clinical efficacy, so as to provide evidencebased references for optimizing rehabilitation strategies for poststroke dysphagia. The purpose of this paper is to verify the clinical application value of this early rehabilitation protocol based on closedloop management.

2. Materials and methods

2.1. General data

A total of 78 patients with post-stroke dysphagia admitted to Huishan District Rehabilitation Hospital of Wuxi from October 2023 to October 2024 were enrolled as the research subjects. They were divided into the observation and control groups by the random number table method, with 39 cases in each group. There were no statistically significant differences in the general data (gender, age, disease course) between the two groups ($P > 0.05$), indicating baseline comparability, as shown in **Table 1**. This study was approved by the Medical Ethics Committee of the hospital, and informed consent was signed by all patients or their family members. Sample size estimation was based on the preliminary experiment, with an effective rate of 85% in the observation group and 60% in the control group. Setting $\alpha = 0.05$ and $\beta = 0.20$, the calculated minimum sample size was 36 cases per group. Considering a 10% dropout rate, 39 cases were finally included in each group.

Table 1. Baseline general data (mean $\pm$ SD), case (%)

Group	n	Male/Female	Age (years)	Disease course (d)
Observation group	39	22/17	59.26 $\pm$ 2.05	4.01 $\pm$ 0.33
Control group	39	20/19	59.34 $\pm$ 2.43	4.15 $\pm$ 0.27
t/χ^2	—	0.206	0.157	0.915
P	—	0.649	0.875	0.106

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Patients met the diagnostic criteria for stroke specified in the “*Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018*”^[2] and “*Chinese Guidelines for the Diagnosis and Treatment of Cerebral Hemorrhage 2019*,” and the diagnosis was confirmed by cranial CT or MRI; (2) Stable vital signs and clear consciousness; (3) Grade 3 or above according to the Kubota Water Swallowing Test, with definite swallowing dysfunction. Exclusion criteria: Patients complicated with severe pulmonary infection, consciousness disorder, or inability to cooperate with rehabilitation training; those with severe insufficiency of cardiac, hepatic, renal and other vital organs; those complicated with other neurological or psychiatric diseases leading to poor cooperation; and those who refused to sign the informed consent form.

2.3. Methods

The control group received routine rehabilitation treatment, including pharmacological interventions such as circulation improvement and neurotrophic therapy. Patients were given a liquid diet via nasogastric tube. Basic oral massage and passive swallowing stimulation were performed by rehabilitation therapists once a day for 20 minutes each time, with a continuous treatment course of 4 weeks.

The observation group was administered an early rehabilitation protocol based on the closed-loop management model

of **Assessment–Intervention–Monitoring**, with specific measures as follows.

- (1) Prior assessment and protocol formulation: Within 24 hours after admission, the Kubota water swallowing test, videofluoroscopic swallowing study (VFSS), and clinical swallowing evaluation were completed to clarify the type and severity of dysphagia. An individualized rehabilitation plan was jointly formulated by rehabilitation physicians, speech therapists and dietitians.
- (2) Targeted intervention and closed-loop training:
 - (a) Muscle training: Tongue resistance training (press the tongue body down with a tongue depressor, and ask the patient to lift the tongue upward with maximum effort; 10 times per set, 2 sets per day); buccinator muscle training (bulge both cheeks and maintain for 5 seconds, repeated 10 times); laryngeal elevation training (falsetto phonation practice and laryngeal lifting resistance training; 5 times per set, 2 sets per day).
 - (b) Posture adjustment: According to the VFSS results, compensatory swallowing postures such as chin-down swallowing (chin close to the sternum) or head-turning swallowing (turn the head toward the affected side) were adopted, with 5 minutes of training per meal.
 - (c) Swallowing exercises: Alternating training of dry swallowing and saliva swallowing (5 minutes each time, 3 times per day); effortful swallowing (instruct patients to forcibly squeeze the tongue base and posterior pharyngeal wall).
 - (d) Oral and pharyngeal rehabilitation: Ice cotton swabs were used to stimulate the soft palate, tongue base and posterior pharyngeal wall, twice a day for 5 minutes each time; breathing training (abdominal breathing and forced exhalation), twice a day with 10 breaths per session. The total duration of the above training was 30 minutes each session, twice a day, 5 days a week, for a continuous course of 4 weeks.
- (3) Nutritional support and interdisciplinary collaboration: Dietitians formulated individualized dietary regimens (such as paste-like food and soft food) according to patients' nutritional status and dietary preferences, and guided family members in implementation. A multidisciplinary team meeting was held once a week to adjust the rehabilitation protocol.
- (4) Continuous monitoring and dynamic adjustment: Events such as choking during eating and aspiration were recorded daily. The Kubota Water Swallowing Test and nutritional indicators were re-evaluated every week, and VFSS examination was performed every two weeks. Training intensity and postural strategies were timely adjusted based on monitoring outcomes, so as to form a closed-loop management mode of **assessment–intervention–monitoring**.

2.4. Observation indicators

- (1) Nutritional status indicators: Fasting elbow venous blood of 5 mL was collected from all patients in the early morning before treatment and after 4 weeks of treatment. The levels of serum total protein, hemoglobin and albumin were determined by nephelometry.
- (2) Incidence of complications: The cases of aspiration, aspiration pneumonia, abdominal distension and diarrhea in the two groups during treatment were recorded, and the total incidence rate was calculated. Aspiration was defined as choking or dyspnea occurring during eating or training; aspiration pneumonia was confirmed by chest imaging examination.
- (3) Immune function indicators: Enzyme-linked immunosorbent assay (ELISA) was adopted to detect serum IgG and IgM levels before and after treatment. The assay kits were purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd., and all operations were performed strictly in accordance with the manufacturer's instructions.
- (4) Clinical efficacy: The Kubota Water Swallowing Test was used to evaluate swallowing function before and after treatment. Markedly effective: swallowing function improved by grade 2 or above; Effective: swallowing function improved by grade 1; Ineffective: no improvement or deterioration. Total effective rate = (Markedly effective cases + Effective cases) / Total cases × 100%.

2.5. Statistical analysis

SPSS 25.0 software was used for data analysis. Measurement data conforming to the normal distribution were expressed as mean $\pm$ standard deviation (SD), and independent sample *t*-test was adopted for inter-group comparison. Enumeration data were presented as case (%), and the chi-square (χ^2) test was used for comparison between groups. A *P* value less than 0.05 was considered statistically significant.

3. Results

3.1. Nutritional status indicators

Before treatment, there were no statistically significant differences in the levels of serum total protein, hemoglobin and albumin between the two groups ($P > 0.05$). After treatment, the above three indicators in the observation group were significantly higher than those in the control group, with statistical differences ($P < 0.05$). Compared with the baseline in the same group, the nutritional indicators of both groups were significantly improved after treatment ($P < 0.05$). See **Table 2**.

Table 2. Nutritional status indicators (mean $\pm$ SD, g/L)

Group	n	Total serum protein		Hemoglobin		Albumin	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	39	60.15 $\pm$ 4.28	65.64 $\pm$ 7.80	89.12 $\pm$ 2.80	97.61 $\pm$ 5.36	30.21 $\pm$ 3.25	35.14 $\pm$ 4.70
Control group	39	60.11 $\pm$ 4.30	61.39 $\pm$ 7.21	89.15 $\pm$ 2.77	92.13 $\pm$ 3.48	30.18 $\pm$ 3.85	32.11 $\pm$ 4.10
<i>t</i>	—	0.041	2.498	0.047	5.355	0.037	3.033
<i>P</i>	—	0.967	0.014	0.962	0.000	0.970	0.003

Note: Compared with the pre-treatment level in the same group, $P < 0.05$.

3.2. Complications

The total incidence rate of complications in the observation group was 5.13%, which was significantly lower than 23.08% in the control group, and the difference was statistically significant ($\chi^2 = 5.185$, $P = 0.022$). See **Table 3**.

Table 3. Incidence of complications [n(%)]

Group	n	Aspiration	Aspiration Pneumonia	Abdominal Distension and Diarrhea	Total Incidence Rate (%)
Observation group	39	1(2.56)	0(0.00)	1(2.56)	5.13
Control group	39	4(10.26)	2(5.13)	3(7.69)	23.08
χ^2	—	—	—	—	5.185
<i>P</i>	—	—	—	—	0.022

3.3. Immune function indicators

Before treatment, there were no significant differences in the levels of IgG and IgM between the two groups ($P > 0.05$). After treatment, the levels of IgG and IgM in the observation group were significantly lower than those in the control group, with statistically significant differences ($P < 0.05$). Compared with the baseline before treatment in the same group, the levels of IgG and IgM decreased significantly in both groups after treatment ($P < 0.05$). See **Table 4**.

Table 4. Immune function indicators (mean $\pm$ SD, g/L)

Group	Case number	IgG		IgM	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	39	11.23 $\pm$ 0.56	8.70 $\pm$ 0.40	1.77 $\pm$ 0.31	1.40 $\pm$ 0.29
Control group	39	11.28 $\pm$ 0.50	9.34 $\pm$ 0.42	1.78 $\pm$ 0.28	1.55 $\pm$ 0.22
<i>t</i>	—	0.415	6.891	0.149	2.573
<i>P</i>	—	0.678	0.000	0.881	0.012

Note: Compared with baseline before treatment in the same group, $P < 0.05$.

3.4. Clinical efficacy

The total clinical effective rate of the observation group was 92.31%, which was higher than 74.36% of the control group. The difference was statistically significant ($\chi^2 = 4.523$, $P = 0.033$). See **Table 5**.

Table 5. Clinical efficacy [n(%)]

Group	n	Markedly Effective	Effective	Ineffective	Total Effective Rate (%)
Observation group	39	20 (51.28)	16 (41.03)	3 (7.69)	92.31
Control group	39	15 (38.46)	14 (35.90)	10 (25.64)	74.36
χ^2	—	—	—	—	4.523
<i>P</i>	—	—	—	—	0.033

4. Discussion

4.1. Research background and objectives

Dysphagia after stroke can lead to severe complications such as aspiration pneumonia and malnutrition, which adversely affect patients' prognosis and quality of life. The traditional rehabilitation model focuses on the recovery of limb function, with delayed initiation of swallowing intervention and a lack of dynamic adjustment mechanisms. The concept of closed-loop management emphasizes the cyclic optimization of assessment, intervention and monitoring, and has achieved favorable outcomes in the management of chronic diseases. However, its application in the early rehabilitation of post-stroke dysphagia remains insufficient^[3]. This study constructed an early rehabilitation protocol based on the closed-loop management of **assessment–intervention–monitoring**, and adopted a randomized controlled trial to verify its effects on patients' nutritional status, immune function, complications and clinical efficacy.

4.2. Result analysis and literature comparison

This study showed that after treatment, the levels of serum total protein, hemoglobin and albumin in the observation group were higher than those in the control group ($P < 0.05$), suggesting that the early rehabilitation protocol based on closed-loop management can significantly improve the nutritional status of patients. The possible reasons are as follows: this protocol improves the efficiency and safety of actual food intake through targeted swallowing muscle training and postural adjustment. Meanwhile, individualized dietary guidance provided by dietitians ensures adequate intake of energy and protein and avoids gastrointestinal intolerance related to nasogastric feeding. These findings are consistent with those reported by Zhang Qiqi, who found that early comprehensive rehabilitation can ameliorate nutritional indicators in patients^[4].

This study also found that the total incidence of complications (aspiration, aspiration pneumonia, abdominal distension and diarrhea) in the observation group was significantly lower than that in the control group (5.13% vs. 23.08%, $P = 0.022$). The underlying reasons were analyzed as follows: the continuous monitoring mechanism in closed-loop management can promptly identify the risk of aspiration and implement interventions by adjusting feeding posture

or suspending oral intake. Meanwhile, systematic oropharyngeal rehabilitation training enhances the laryngeal protective reflex and reduces the probability of aspiration.

Shang Na et al. also confirmed that swallowing training combined with rehabilitation exercises can lower the incidence of aspiration pneumonia, which is consistent with the results of the present study ^[5].

In terms of immune function, the levels of IgG and IgM in the observation group were lower than those in the control group after treatment ($P < 0.05$). Immunological disturbance commonly occurs in post-stroke patients due to stress and malnutrition, and elevated IgG and IgM may reflect a state of chronic inflammation. The lower immunoglobulin levels in the observation group indicated alleviated inflammatory response and gradual normalization of immune function. Dai Yanyan et al. ^[6] demonstrated that comprehensive rehabilitation could improve immune indicators. The more marked decline of IgG and IgM in the observation group of this study may be attributed to the fact that closed-loop management reduced infectious complications, thereby decreasing persistent activation of the immune system. In terms of clinical efficacy, the total effective rate of the observation group (92.31%) was significantly higher than that of the control group (74.36%, $P = 0.033$), indicating that the closed-loop management protocol could restore swallowing function more effectively. Compared with the effective rate of approximately 85% reported by Liu Ran et al. ^[7] for comprehensive rehabilitation training, the efficacy in this study was further improved. This may be because the present protocol emphasizes dynamic assessment and timely adjustment, avoiding the plateau stage that may occur with fixed training regimens.

4.3. Conclusions and future research directions

In conclusion, the early rehabilitation protocol based on the **assessment–intervention–monitoring** closed-loop management can significantly improve nutritional status and immune function, reduce the incidence of complications, and enhance clinical efficacy in patients with post-stroke dysphagia. Further multicenter, large-sample studies should be conducted in the future with prolonged follow-up duration to explore the effects of this protocol on patients' long-term quality of life, social rehabilitation rate, and health economic indicators.

4.4. Research value and limitations

This study innovatively integrated the concept of closed-loop management into the early rehabilitation of patients with post-stroke dysphagia and constructed an operable and replicable protocol, which provides evidence-based references for clinical practice. Meanwhile, several limitations of the present study should be acknowledged: it was designed as a single-center trial with a relatively small sample size; the follow-up period was only 4 weeks, and the long-term efficacy remains unclear; moreover, the blinding method was not adopted in outcome evaluation, which may lead to performance bias. Further well-designed studies are required to verify the robustness of the research conclusions.

Disclosure statement

The author declares no conflict of interest.

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Research Progress of Transcutaneous Auricular Vagus Nerve Stimulation in the Treatment of Depression

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Abstract: Depression is one of the most prevalent and severe mental disorders worldwide, with its epidemiological burden increasing significantly. Existing treatment modalities are associated with issues such as prolonged treatment duration, drug tolerance, and poor adherence. Transcutaneous auricular vagus nerve stimulation (taVNS) is a safe, low-cost, and non-invasive physical therapy developed from vagus nerve stimulation techniques. This review primarily elucidates the regulatory effects of transcutaneous auricular vagus nerve stimulation on depression and its applications in the treatment of depression.

Keywords: taVNS; Depression; Research progress

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1. Introduction

The epidemiological status and social burden of depression

Depression is a common chronic mental disorder characterized by persistent low mood, loss of interest, and cognitive impairment ^[1]. According to the World Health Organization (WHO) report, over 300 million patients worldwide have been affected, with a lifetime prevalence rate of 6.8% in China. It is projected that by 2030, it will become the second-largest disease burden after cardiovascular diseases ^[2]. According to the Global Burden of Disease (GBD) study data, in China, the number of depression cases increased from 34.4 million to 53.1 million between 1990 and 2021, a rise of 54%; the overall prevalence was approximately 2.9%, with women (3.5%) higher than men (2.2%), and the prevalence was even higher among the elderly aged 55 and above (6.5%). The detection rate of anxiety with depressive symptoms in adolescents also showed an upward trend, which was further exacerbated during the pandemic ^[3,4]. This disease not only leads to a decline in patients' quality of life but also imposes a significant socioeconomic burden, including healthcare expenditures, productivity losses, and increased suicide risk, making it a major global public health challenge.

1.1. Existing treatment modalities (pharmacological, psychological, and physical therapy) and their limitations

The first-line treatment of depression includes pharmacotherapy, psychotherapy, physical therapy, etc.

Pharmacotherapy is the most commonly used intervention for depression, with frequently employed medications including selective serotonin reuptake inhibitors (SSRIs, such as fluoxetine and sertraline), serotonin-norepinephrine reuptake inhibitors (SNRIs, such as venlafaxine), tricyclic antidepressants (TCAs), and newer agents like bupropion. These drugs exert their effects by modulating monoamine neurotransmitters. The STAR*D study (Sequenced Treatment Alternatives to Relieve Depression) demonstrated that only approximately 30% of patients achieve remission after the first phase of antidepressant treatment, with the remission rate further declining to around 25% in the second phase. After four cumulative phases, the total remission rate remains at approximately 67%, with the probability of remission progressively decreasing after each dose change or dose escalation. Multiple meta-analyses have further confirmed that about 30% of major depressive disorder (MDD) patients fail to achieve clinical remission after receiving adequate doses and durations (at least 8 weeks) of two or more antidepressant medications^[5,6]. Additionally, pharmacotherapy is associated with significant adverse effects and adherence issues. Long-term use may also lead to drug resistance, cognitive impairment, and increased risk of metabolic syndrome.

Psychotherapy is one of the core non-pharmacological interventions recommended in the depression guidelines, primarily including Cognitive Behavioral Therapy (CBT), Interpersonal Therapy (IPT), and Mindfulness-Based Cognitive Therapy (MBCT). Cognitive Behavioral Therapy (CBT), through techniques such as identifying and correcting negative cognitive biases and behavioral activation, has been demonstrated by numerous randomized controlled trials (RCTs) to significantly improve depressive symptoms^[7-9]. A systematic review^[10] has shown that CBT can improve depressive symptoms by more than 50%, especially in patients with mild-to-moderate MDD or drug intolerance. Its short-term efficacy is comparable to that of pharmacotherapy, while its long-term advantage in preventing relapse is particularly evident. However, psychotherapy faces multiple barriers in its practical promotion. First is the severe shortage of professionals: the number of psychological counselors/therapists worldwide and in China is far from meeting the demand^[11], resulting in waiting times of several months or even longer. The second issue is patient compliance^[12,13]: While CBT emphasizes homework (e.g., cognitive records, behavioral experiments), multiple studies indicate a completion rate of only 40%–60%. Key barriers include time conflicts, lack of motivation, difficulty in task execution during severe symptoms, and misconceptions about the treatment process.

Physical therapy has developed rapidly in recent years, mainly including repetitive transcranial magnetic stimulation (rTMS). rTMS, which stimulates the left dorsolateral prefrontal cortex (DLPFC) through non-invasive magnetic fields, has been approved by the FDA and China's NMPA for the treatment of TRD and MDD. Relevant studies have shown^[14,15] that standard high-frequency rTMS (10Hz) or intermittent theta burst stimulation (iTBS) can elicit responses in approximately 50% of patients and achieve remission in 30%, particularly effective for drug-resistant cases with mild side effects (primarily headache and scalp discomfort).

1.2. Origin and development of Vagus Nerve Stimulation (VNS)

Vagus nerve stimulation (VNS) was first used for epilepsy treatment in the 1880s. In 1997, the U.S. FDA approved implantable VNS (iVNS) for refractory epilepsy, and in 2005, its application was expanded to adjunctive therapy for chronic or recurrent depression. iVNS involves surgical implantation of electrodes to stimulate the main trunk of the cervical vagus nerve, which can improve activity in brain regions related to mood regulation. However, issues such as surgical trauma, infection risks, and high costs have limited its widespread adoption.

1.3. Advantages and research significance of transcutaneous Vagus Nerve Stimulation (taVNS)

taVNS (transcutaneous electrical vagus nerve stimulation) delivers electrical stimulation to the auricular branch of the vagus nerve (ABVN) via the skin of the ear, offering non-invasive, portable, low-cost, and minimal side-effect advantages,

enabling home-based self-management. Compared to iVNS (intracranial vagus nerve stimulation), taVNS demonstrates similar efficacy with enhanced safety and has been studied in various conditions, including epilepsy, depression, and migraine^[16].

2. Theoretical basis of transcutaneous Vagus Nerve Stimulation

2.1. Theoretical basis of Traditional Chinese Medicine

2.1.1. The connection between auricular points and visceral meridians

The “Yin-Yang Eleven Meridian Moxibustion Classic” unearthed from the Western Han Dynasty tomb at Mawangdui in Changsha first documented the “ear meridian,” which is associated with the upper limbs, eyes, cheeks, and throat. This represents the earliest discussion on the relationship between the ear and meridians. The “Yellow Emperor’s Inner Canon” further systematically elaborated on the connection between the ear and the body’s internal organs and meridians. The “Ling Shu: Oral Questions” explicitly states: “The ear is the convergence point of the Zong meridians,” indicating that all twelve meridians directly or indirectly pass through the ear, making it the convergence point of the body’s meridians. The “Ling Shu: Pathogenic Factors, Visceral Diseases, and Manifestations” also mentions: “The twelve meridians and 365 collaterals, whose blood and Qi all ascend to the face and traverse the orifices... their collateral Qi travels to the ear to enable hearing.” This demonstrates the close connection between the ear and all meridians.

In the theory of ear-organ correspondence, the “Suwen·Jingui Zhenyan Lun” states: “The southern red color connects to the heart, which opens to the ear.” Although the heart normally opens to the tongue, the tongue is not a natural orifice, so the “orifice is associated with the ear.” This theory established the foundation for the connection between the ear and heart in the treatment of emotional disorders. Meanwhile, the theory that the kidneys open to the ear has been emphasized by medical practitioners throughout history. The “Comprehensive Medical Treatise of Ancient and Modern Times” quotes Chao Yuanfang: “The kidney is the meridian of the foot-Shaoyin, and its essence and Qi connect to the ear.” The Qing Dynasty’s “Essential Techniques of Correct Massage” further proposed that the back of the ear corresponds to the five zang organs, linking the anatomical position of the auricle to the functions of the five zang organs, thereby forming a systematic theory of ear acupoints and zang-fu relationships.

2.1.2. Syndrome of heat

Depression falls under the category of “Yuzheng” (Stagnation Syndrome) in Traditional Chinese Medicine (TCM). Its pathogenesis primarily involves emotional distress and Qi stagnation, with affected organs including the heart, liver, and spleen. The “Compendium of Acupuncture and Moxibustion” records: “When the mind is preoccupied, the spirit has a destination, and the righteous Qi stagnates, leading to Qi accumulation,” elucidating the pathogenic characteristics of Qi stagnation caused by emotional internal injury.

Acupoints closely associated with emotional disorders in auricular therapy include Shenmen (MA-TF1), Xin (CV1), and Jiaoyang (LI1), whose functional localization largely overlaps with the distribution of the vagus nerve in the auricular region. Historically, Auricular Shenmen (MA-TF1) has been recognized as a pivotal point for calming the mind and regulating emotions, commonly employed in clinical practice to stabilize mood and alleviate stress. Modern research confirms that stimulating Auricular Shenmen can modulate autonomic nervous system function, thereby improving emotional disturbances. The Xin point (CV1) is grounded in the theoretical concepts of “the heart storing spirit” and “the heart governing clarity,” which helps alleviate depressive states by regulating mental focus.

2.1.3. The relationship between auricular acupoints Shenmen, Xin, Jiaoyang and other points and emotional disorders

Based on the Traditional Chinese Medicine (TCM) theories of “the ear as the convergence of ancestral meridians” and “treating ear disorders with brain-based therapies,” modern researchers have combined traditional auricular stimulation

techniques with vagus nerve stimulation technology to develop transcutaneous auricular vagus nerve stimulation (taVNS) therapy. Professor Rong Peijing's team ^[17] systematically elucidated the theoretical connotation of 'brain-ear therapy', 'pointing out that auricular acupoints, as regions on the body surface where the vagus nerve is distributed, can activate the 'ear-vagus nerve-islet nucleus-brain network' pathway through electrical stimulation, thereby regulating neurological disorders such as depression. Acupuncture at the auricular points can achieve therapeutic effects such as nourishing the heart and calming the mind, as well as promoting Qi circulation and relieving stagnation by unblocking meridians and harmonizing the yin-yang balance of the viscera.

2.2. Fundamentals of modern medicine

2.1. Anatomical distribution and function of the vagus nerve

The vagus nerve (the Xth cranial nerve) is the longest cranial nerve in the body, containing approximately 80% of the afferent fibers. It originates from the dorsal nucleus and ambiguous nucleus of the medulla oblongata and is widely distributed to thoracic and abdominal organs. Its primary functions include regulating heart rate, gastrointestinal motility, immune and inflammatory responses, and emotional homeostasis. The afferent fibers mainly project to the nucleus tractus solitarius (NTS), which then forms extensive connections with brainstem nuclei such as the locus coeruleus (LC) and dorsal raphe nucleus (DRN), as well as the limbic system (amygdala, hippocampus, prefrontal cortex), thereby achieving integrated regulation of autonomic function, inflammation, and emotion ^[16].

2.2. Distribution characteristics of the auricular branch of the vagus nerve in the auricular region

Anatomical studies demonstrate that the auricular branch of the vagus nerve (ABVN) is primarily distributed in the cymba conchae (100% exclusively innervated by ABVN), the cavity conchae (approximately 45%), the tragus (approximately 45%), and the anterior wall of the external auditory canal. Regions such as the auricle are mainly innervated by the great auricular nerve or the lesser occipital nerve, with no distribution of ABVN. This distribution pattern provides precise superficial stimulation targets for taVNS ^[18].

2.3. Regulatory pathways of taVNS on the central nervous system

Studies have shown that taVNS stimulation of the anterior ventral nucleus (ABVN) relays signals through the nucleus tractus solitarius (NTS) to the locus coeruleus (LC) (which releases norepinephrine) and dorsal raphe nucleus (DRN) (which releases serotonin), thereby modulating depression-related brain regions such as the prefrontal cortex, cingulate cortex, and hippocampus ^[19-23]. Simultaneously activates the cholinergic anti-inflammatory pathway ($\alpha 7$ nicotinic acetylcholine receptor) and inhibits peripheral and central inflammatory factors (e.g., TNF- α , IL-6). fMRI studies have confirmed that taVNS enhances internal connectivity within the DMN, reduces abnormal connections between the DMN and the insula, and upregulates BDNF expression, thereby promoting neural plasticity.

3. Advances in mechanism research

In recent years, mechanistic studies have been conducted from multiple dimensions, including neuroimaging, molecular biology, and animal models. In terms of neuroimaging ^[19,24-28], resting-state fMRI demonstrated that taVNS could reduce functional connectivity (FC) between the posterior cingulate cortex and the middle frontal gyrus, which was significantly associated with improved HAMD scores. Another study confirmed that taVNS modulates the topological structure of visual networks, reducing feature path lengths and enhancing degree centrality. Studies on the gut microbiota-brain-gut axis demonstrate that transcranial vagus nerve stimulation (taVNS) can improve gut microbiota diversity in depression model mice, reduce lipopolysaccharide (LPS) translocation, and regulate short-chain fatty acid levels. Electrophysiological studies further confirm that taVNS enhances γ -aminobutyric acid (GABA)ergic inhibition, thereby balancing excitatory-inhibitory dysregulation. These findings indicate that taVNS exerts antidepressant effects through multi-target and multi-

pathway synergistic mechanisms. However, further exploration is required regarding parameter optimization (frequency 20–30 Hz, pulse width 200–500 μ s, current 0.5–2 mA) and individual variability.

4. Clinical application and efficacy studies

Multiple randomized controlled trials (RCTs) and meta-analyses have confirmed the clinical efficacy of transcutaneous electrical nerve stimulation (taVNS). In 2013, Hein et al.^[29] first demonstrated in a randomized controlled trial (RCT) that 2-week transcranial electrical stimulation (taVNS) significantly reduced the Beck Depression Inventory (BDI) scores. Rong et al.^[30] carried out a large-scale study in China in 2016 (91 cases in the real stimulation group), and HAMD-24 scores decreased significantly after 12 weeks of treatment compared with the sham stimulation group, and the improvement continued to the follow-up period. The 2023 meta-analysis by Tan et al.^[31] included 12 randomized controlled trials (RCTs) ($n = 838$) and demonstrated that transcranial vagus nerve stimulation (taVNS) significantly increased the response rate compared to sham stimulation ($RR = 12.30$) and showed a large effect size in HAMD score reduction (Hedges' $g = -1.47$). Compared with antidepressant medications (ATDs), taVNS exhibited equivalent or higher response rates ($RR = 1.22$) with small to moderate HAMD score reduction effects. When combined with ATDs, taVNS demonstrated superior HAMD improvement ($g = -0.95$). Subgroup analysis revealed significant benefits in patients with mild to moderate depression and post-stroke depression. Other studies^[32–34], such as open-label trials for treatment-resistant depression, demonstrated that approximately 40%–60% of patients achieved response criteria after 8 weeks of transcranial electrical nerve stimulation (taVNS), with some patients maintaining efficacy for 3–6 months. In general, taVNS is indicated for patients with drug intolerance or treatment-resistant depression (TRD), with a treatment duration of 4 to 12 weeks and a daily session of 20 to 30 minutes.

5. Safety and adverse effects

The 2022 systematic review by Kim et al.^[35] included 177 studies (6,322 cases), reporting an extremely low overall incidence of adverse events (AEs) with transcutaneous vagus nerve stimulation (taVNS) (12.84 per 100,000 stimulation person-minutes-day). The most common AEs were earache, headache, tingling, and skin erythema, all of which were mild, transient, and self-limiting. There was no significant difference in the risk of adverse events (AE) between the true stimulation group and the sham stimulation group or control group (risk difference $RD = 0.013$). No severe AEs (such as cardiac events or epileptic seizures) were directly associated with taVNS, with only 2 potentially relevant events failing to meet the causal determination criteria. Occasional dizziness and nausea were occasionally observed during clinical trials and resolved after discontinuation. Compared to iVNS or ECT, taVNS demonstrated significantly higher safety, making it suitable for long-term use.

6. Conclusion

Transcutaneous auricular vagus nerve stimulation (taVNS), as an emerging technology in the field of neuromodulation, integrates traditional Chinese medicine (TCM) auricular acupoint theory with modern vagus nerve stimulation techniques, offering significant advantages of being non-invasive, safe, convenient, and cost-effective. Current evidence indicates that taVNS can effectively ameliorate mood symptoms in patients with depression, demonstrating efficacy comparable to antidepressant medications while maintaining good safety profiles, particularly suitable for patients with drug intolerance or treatment-resistant depression. Its mechanisms of action involve multiple pathways, including monoamine neurotransmitter regulation, HPA axis modulation, promotion of neural plasticity, suppression of neuroinflammation, and brain network remodeling. Although current research faces limitations such as insufficient parameter standardization and a lack of long-term evidence, with the advancement of large-scale clinical studies and deeper mechanistic investigations, taVNS is poised to become a crucial component in the comprehensive prevention and treatment system for depression, providing novel strategies to alleviate the global burden of depression.

Disclosure statement

The author declares no conflict of interest.

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Nursing Care of a Patient with Severe Acute Pancreatitis after EVAR for Thoracoabdominal Aortic Penetrating Ulcer

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Abstract: To summarize the nursing care of a patient with severe acute pancreatitis after endovascular aortic repair (EVAR) for a thoracoabdominal aortic penetrating ulcer. Nursing points: Adopt a dual strategy of restrictive fluid resuscitation combined with goal-directed fluid management to effectively maintain hemodynamic stability; implement effective airway management and early use of high-flow oxygen therapy to maintain adequate oxygenation; implement a stepped pain management strategy, combined with the Meridian Flow Theory of Traditional Chinese Medicine to optimize the analgesic program and reduce symptoms of abdominal pain and bloating; according to the enteral nutrition tolerance classification and management requirements, develop a personalized diet plan to ensure energy supply. After multidisciplinary treatment and meticulous care, the patient recovered well and was successfully discharged from the hospital on the 21st day after surgery. During the follow-up visit 1 month later, the patient recovered well and had no recurrence of symptoms, such as abdominal pain and bloating.

Keywords: Penetrating aortic ulcer; Acute pancreatitis; Goal-directed fluid management; Enteral nutrition; Critical care

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1. Introduction

Aortic penetrating ulcer refers to a pathological condition in which the intima of the aorta ruptures, resulting in ulcer-like protrusions on the aortic wall. It is caused by the erosion of aortic atherosclerotic plaques and inflammation of the aortic wall. As the disease progresses, it can eventually lead to aortic rupture. In order to prevent adverse events such as aortic rupture and the need for surgical treatment, endovascular aortic repair (EVAR) has been widely used in the treatment of aortic penetrating ulcers^[1]. Acute pancreatitis is a common digestive system disease worldwide. Severe acute pancreatitis accounts for about 5%-10% of acute pancreatitis cases. It has a rapid onset and rapid disease progression. Systemic inflammatory response syndrome and multiple organ dysfunction syndrome appear in the early stage of the disease, and the mortality rate is as high as 20–30%^[2]. Our hospital admitted a patient with a thoracoabdominal aortic penetrating ulcer who was complicated by severe acute pancreatitis after surgery on April 16, 2025. The nursing experience is now reported as follows.

2. Clinical data

2.1. General information

The patient, a 75-year-old female, was admitted to the hospital on April 16, 2025, due to “chest pain and discomfort for more than 10 days.” The admission diagnosis was “thoracic and abdominal aortic ulcer, type 2 diabetes, coronary atherosclerosis, and hypertension 2-level (very high risk).” On April 18, thoracoabdominal EVAR was performed at the vascular surgery department, and two stents were inserted into the thoracic aorta during the operation. On the first day after surgery, the patient complained of upper abdominal pain, nausea and vomiting. The abdominal pain was not relieved after vomiting. An emergency blood amylase test showed 1372.7 μL . Abdominal CT showed peripancreatic exudation and a small amount of pleural effusion on both sides. Acute pancreatitis was diagnosed. Symptomatic treatments such as fluid replenishment, fasting, gastrointestinal decompression, inhibition of pancreatic enzyme secretion, and anti-infection were given according to the doctor’s instructions. The patient’s abdominal pain worsened on the second postoperative day, and he was transferred to our department for treatment. At the time of admission, the patient was conscious, with an acutely painful face, shortness of breath, positive tenderness under the xiphoid process that radiated to the left shoulder, and a small amount of crackles could be heard at the base of both lungs. The body temperature was 36.4°C, the heart rate was 113 beats/min, the blood pressure was 165/92 mmHg (1 mmHg = 0.133 kPa), the mask oxygen inhalation was 8L/min, and the blood oxygen saturation was 89%. Laboratory test results showed: hemoglobin 86 g/L, white blood cells $21.64 \times 10^9/\text{L}$, blood urea nitrogen 14.91 mmol/L, blood creatinine 241 $\mu\text{mol/L}$; blood gas analysis showed: pH value 7.30, arterial oxygen partial pressure 63mmHg, alkali remaining -4.6 mmol/L.

2.2. Treatment and outcome

After admission, the patient’s blood pressure fluctuated between 160–175/90–105 mmHg. He complained of abdominal pain and distension, and his BISAP score (Bedside Index of Severity of Acute Pancreatitis) was 3. The doctor advised that the patient was critically ill and immediately administered high-flow humidified oxygen therapy, adjusting the oxygen concentration to 40%, establishing a 3-way intravenous channel, and actively replenishing fluids to maintain the function of important organs. Continuous micro-pump infusion of nitroglycerin was used to control blood pressure at the target level, antibiotics were upgraded to imipenem to fight infection, traditional Chinese medicine acupoint application was used to promote intestinal peristalsis, and raw rhubarb retention enema was used to promote excretion. On April 21st and 22nd, the patient’s abdominal pain was still unrelieved, with a pain score of 5. The reexamination of blood creatinine was 183.7 $\mu\text{mol/L}$, indicating that the renal function was still damaged, the blood pressure fluctuated between 140-160/90-100mmHg, and the oxygenation index fluctuated between 190–220 mmHg. A reexamination of the abdominal CT showed that peripancreatic leakage increased and there was still effusion in the thoracic cavity on both sides, and the diagnosis was severe acute pancreatitis. Multidisciplinary consultations are organized according to the patient’s condition, and dual strategies of restrictive fluid resuscitation and goal-oriented fluid management are adopted to optimize the infusion plan to dynamically regulate blood volume and prevent related complications. Pay close attention to airway management, and take effective measures based on the patient’s oxygenation index value to guard against the occurrence of acute respiratory distress syndrome. According to the “three-step analgesic method”, follow the doctor’s advice to upgrade the analgesics from non-steroidal drugs to central analgesics to improve the analgesic effect and reduce the impact on blood pressure. The albumin was rechecked on April 25 and dropped from 30.4 g/L at admission to 25.8 g/L. Enteral nutrition was started immediately and changes in abdominal circumference and intra-abdominal pressure were closely monitored. On May 2, the patient’s abdominal pain and distension were significantly relieved, and he began to take imported food. On May 7, the white blood cell count was $7.33 \times 10^9/\text{L}$. The antibiotic was downgraded to cefotaxime and the patient was encouraged to exercise moderately at the bedside. After active symptomatic treatment and care, the patient’s condition improved and he was discharged from the hospital on the 21st day after surgery, and he recovered well after 1 month of follow-up.

3. Nursing

3.1. Adopt the dual strategy of restrictive fluid resuscitation combined with goal-directed fluid management to effectively maintain hemodynamic stability

Early fluid therapy in acute pancreatitis is particularly critical, as it can effectively improve tissue perfusion and prevent pancreatic necrosis and multi-organ failure. This patient is elderly and has a history of coronary heart disease. He is currently undergoing EVAR surgery for a penetrating aortic ulcer, and his postoperative blood pressure is always at a high level. To a certain extent, he needs to avoid excessive fluid resuscitation, control blood volume, and reduce vascular tension. The nursing team quickly sorted out the condition and promoted multidisciplinary consultation. Specialist nurses from the Department of Gastroenterology, Vascular Surgery, Cardiovascular Medicine, and Endocrinology checked the patient at the bedside and decided to initiate a restrictive fluid resuscitation plan^[3]. The infusion volume was precisely controlled at an infusion rate of no more than 5 mL/kg/h. At the same time, based on the goal-oriented strategy for fluid infusion proposed in the guideline^[4], the doctors and nurses jointly set a target heart rate of < 100 beats/min and a systolic blood pressure of < 150 mmHg. The nursing team established 3 intravenous channels, 1 channel of octreotide was pumped in a small amount at 250 µg/h, 1 channel was pumped in a small amount of nitroglycerin at a starting dose of 500 µg/h, and the 3rd channel was arranged for the intravenous infusion of crystal gel liquid according to the patient's condition. During the early resuscitation process, the resuscitation effect is evaluated every half hour, a bedside infusion response monitoring sheet is established, and heart rate, blood pressure, pulse oxygen, urine output, laboratory test-related indicators, etc., are monitored^[5]. By flexibly adjusting the infusion speed and dynamically adjusting the hourly dose of nitroglycerin pumped, precise control of blood volume management is achieved.

3.2. Implement effective airway management and use high-flow oxygen therapy early to maintain adequate oxygenation

When the patient entered the hospital, she complained of chest pain and tightness, heart rate 113 beats/min, respiration 23 beats/min, blood oxygen saturation 89%, a small amount of crackles auscultated at the base of both lungs, chest CT showed a small amount of pleural effusion, and blood gas analysis showed: PaO₂: 63 mmHg, PaCO₂: 45 mmHg, and oxygenation index was 153 mmHg. Based on the patient's past medical history and physical signs, to rule out acute coronary syndrome and pulmonary artery thrombosis, bedside electrocardiography and emergency pulmonary artery CTA examination were performed promptly, and no abnormalities were found. Acute respiratory distress syndrome is prone to occur in the early stages of acute pancreatitis. To be alert to the occurrence of this complication, the nursing team quickly evaluated the patient's lungs using the modified Marshall scoring system. The score was 3 points, indicating severe impairment of lung function. At this time, the patient's airway management has become the focus of clinical nursing. The nursing measures are as follows:

- (1) Raise the head of the bed 45° to move the diaphragm downward, reduce the pressure on the chest cavity, and improve the patient's pulmonary ventilation function.
- (2) Carry out high-flow humidified oxygen therapy, set the initial oxygen concentration to 40%, and closely monitor the oxygenation situation.
- (3) Follow the doctor's advice and give atomized treatment with acetylcysteine and budesonide to eliminate phlegm and relieve asthma, and assist the patient with effective cough training every day.
- (4) Assist the patient to turn over and pat his back to promote the effective discharge of lung secretions, clear the airway on time, and ensure effective ventilation. After the above measures, the patient's arterial blood oxygen partial pressure increased from 63 mmHg on April 2 to 128 mmHg on May 2, and the oxygenation function was corrected in time.

3.3. Implement a stepped pain management strategy and optimize the analgesic plan combined with the Meridian Flow Theory of Traditional Chinese Medicine

Pain is the main symptom of acute pancreatitis, and pain relief is a clinically important treatment goal. The patient's physical examination was positive for tenderness under the xiphoid process when he was admitted to the hospital, radiating

to the lower back, and the pain score was 6 points. The abdominal CT reexamination on the second day after admission showed that the peripancreatic exudate continued to increase, which aggravated the stimulation of the pancreatic capsule and peritoneal nerve endings. The continuous pain stimulated the patient's blood pressure to increase, aggravating the risk of intraluminal aortic stent leakage and displacement. Based on the patient's clinical manifestations, the nursing team followed the doctor's advice and upgraded the antibiotic imipenem to control the infection and reduce the inflammatory reaction caused by pancreatitis. According to the "three-step analgesic method", the analgesics were upgraded from non-steroidal anti-inflammatory analgesics to the central analgesic drug nisonodorolac tromethamine according to the doctor's instructions to improve the analgesic effect. In order to relieve the patient's symptoms of abdominal distension and pain, the nursing team combined traditional Chinese medicine to promote the recovery of gastrointestinal function ^[6]. The nursing measures are as follows:

- (1) Apply Glauber's salt externally to the abdomen every day to improve pancreatic blood circulation, promote intestinal peristalsis, and reduce symptoms of abdominal distension.
- (2) Based on the patient's usual morning defecation habits, the nursing team selected acupoints on time based on the theory of Meridian flow. The acupoints were Zusanli, Pishu, Weishu, and Zhongwan. Because Qi and blood flow into the large intestine meridian at Mao hour (5–7 a.m.), the night shift nurse is scheduled to use Chinese medicine containing rhubarb, hemp seed, citrus aurantium, and borneol for acupoint application on the patient between 6–7 o'clock every day to promote intestinal peristalsis. The application time is 2–4 hours each time.
- (3) Raw rhubarb retention enema has the effect of purging fire and detoxifying, clearing away dampness and heat, purging the bowels and relieving pain to a certain extent in patients with acute pancreatitis. In order to further extend the retention time of raw rhubarb for enema, the nursing team improved the conventional enema method: 50g of raw rhubarb was boiled in 200ml of boiling water for 10 minutes to remove the residue, and the liquid was cooled to about 40°C for later use ^[6].

The enema tool was changed to a 50 mL syringe + sputum suction tube, the intubation depth is 30–40 cm, and the patient is instructed to adopt a rotational position, that is, raise the buttocks 10 cm during enema, take the left lateral decubitus position (slowly inject 2/3 of the liquid) → supine position → right lateral decubitus position (slowly inject the remaining 1/3 of the liquid), and then lie on the right side for 20 minutes. In the end, the patient's pain was effectively controlled, and the pain score dropped from 6 points to 2 points after 1 week of the above intervention. The patient's treatment compliance and subjective comfort were improved.

3.4. Develop a personalized diet plan based on enteral nutrition tolerance classification and management requirements

Acute pancreatitis is highly catabolic, and early initiation of enteral nutrition can reduce the incidence of infectious complications, multiple organ dysfunction syndrome, and death ^[7]. This patient had early abdominal pain, obvious distension, and weak intestinal function. Parenteral nutrition was used first, and intravenous nutrition preparations such as albumin and Lejia were supplemented as needed. On the 6th day after admission, the patient's abdominal pain and distension were relieved, bowel sounds were 2–3 times/min, and the albumin was reduced to 25.8 g/L in the re-examination. A nutritional risk screening was performed and the NRS-2002 score was 4. The patient was immediately consulted by the nutrition department and a nasojejunal tube was inserted for trial enteral nutrition. The patient in this case is 157 cm tall. According to the energy calculation formula ^[8], the daily energy requirement is 1300–1560 kcal. Based on the grading and management plan of enteral nutrition tolerance, the nursing team dynamically assessed every 6 hours during enteral nutrition. On the first day of enteral nutrition, a small amount of normal saline was introduced on a trial basis. The patient had no intolerance. According to the doctor's instructions, 500 mL of BIPLA was administered through a nasogastric pump at 30 mL/h. On the second day of enteral nutrition, the patient developed abdominal distension, vomited gastric contents once, a volume of about 200 mL, and auscultated bowel sounds 1–2 times/min, and enteral nutrition was suspended. On the 3rd day, bowel sounds were auscultated 3 times/min. The patient had no complaints of abdominal pain

and distension. He continued to receive 30 mL/h nasogastric feeding of Beprex as directed by the doctor. On the 4th day, the patient was adjusted to 50 mL/h nasogastric pumping of Beprex. The patient had no intolerance, and then gradually increased to the target amount. On the 8th day, the patient began to take oral food, and the nursing team formulated a personalized recipe for him, as follows: Breakfast was 20 g of whey protein powder + 200 g of vegetarian noodles, and 25 g of sugar-free lotus root starch was added as a snack at 9:00 in the morning. Lunch is 120 g of millet cake + 200 mL of boiled vegetable soup, and an additional meal of 200ml of mixed vegetable juice at 15:00. Dinner is 150 g of vegetarian wontons + 200 mL of thick millet soup, and 20 g of whey protein powder is added at 20:00. After the above nursing measures, the patient's energy needs basically met the standard during hospitalization, and his blood sugar, albumin, and weight all reached the expected levels.

4. Conclusion

This case is a patient with severe acute pancreatitis combined with hypertension, coronary heart disease, and aortic ulcer after EVAR surgery, which is rare in clinical practice. In the early stage, the patient's symptoms were severe and his lung and kidney functions were damaged. The nursing team evaluated and concluded that there was a conflict between the requirements for adequate fluid resuscitation for pancreatitis and volume management after EVAR. They then adopted predictive care through critical thinking, formulated personalized nursing measures to dynamically regulate blood volume, and actively and effectively intervened in hypoxemia, so that the patient's symptoms could be managed under control. In terms of pain management, the nursing team collaborated with traditional Chinese medicine to innovate and change the traditional rhubarb retention enema method. Based on the Meridian flow theory and the patient's defecation habits, the patient's abdominal pain and distension were effectively relieved by selecting acupuncture points and applying Chinese medicine on time. During the enteral nutrition period, stepwise nutrition management was implemented early, and the patient's nutritional status was improved after intervention with a personalized diet plan in the later period. In the future, further evidence can be accumulated to improve the nursing standards for such rare cases.

Disclosure statement

The authors declare no conflict of interest.

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Current Status of Research Progress on Idiopathic Pulmonary Fibrosis

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Abstract: Idiopathic pulmonary fibrosis (IPF) is a chronic, irreversible interstitial lung disease characterized by diffuse pulmonary interstitial fibrosis and progressive decline in pulmonary function, with its etiology not yet fully elucidated. The pathological process primarily manifests as recurrent injury and abnormal repair of alveolar epithelial cells, sustained activation of fibroblasts, leading to excessive extracellular matrix deposition and structural remodeling of lung tissue in patients. This review focuses on the pathological features, pathogenesis, and key signaling pathways of IPF, systematically summarizing current major clinical treatment strategies to provide theoretical references for further elucidation of IPF pathogenesis and exploration of more effective prevention and therapeutic approaches.

Keywords: Idiopathic pulmonary fibrosis; Pulmonary fibroblasts; Pathogenesis; Signaling pathways; Anti-fibrotic therapy

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1. Introduction

IPF is the most common and worst-prognosed subtype of idiopathic interstitial pneumonia, characterized by complex pathogenesis involving multiple cellular and molecular processes. The median survival after diagnosis is 3–5 years, with a rising global mortality rate ^[1]. The core pathological feature of IPF involves repair dysregulation following persistent alveolar epithelial cell injury, leading to abnormal proliferation of pulmonary fibroblasts and extensive differentiation into pulmonary myofibroblasts. This results in extracellular matrix (ECM) deposition in the pulmonary interstitium, ultimately forming a “honeycomb lung” structure and impairing gas exchange function ^[2].

Due to the insidious early symptoms of IPF, clinical diagnosis is often confused with chronic obstructive pulmonary disease (COPD) and heart failure, with approximately 60% of patients diagnosed at intermediate or advanced stages ^[3]. Currently, there is no curative treatment for IPF. Pirfenidone and nintedanib, as commonly used anti-fibrotic agents, can slow pulmonary function decline but are associated with significant tolerance issues ^[4]. Existing therapies can only delay disease progression, underscoring the clinical importance of investigating IPF’s pathological mechanisms and therapeutic targets. This article summarizes the pathological characteristics, pathogenesis, key signaling pathways, and current treatment options for IPF to provide theoretical foundations for exploring effective therapeutic strategies.

2. Pathological Characteristics of IPF

2.1. Pulmonary interstitial fibrosis

Pulmonary interstitial fibrosis is the most typical pathological feature of IPF, and its progression can be divided into three stages: “damage-inflammation-repair imbalance.” After alveolar epithelial cells are injured by external stimuli, their barrier function is compromised, leading to the release of pro-inflammatory factors and pro-fibrotic factors. Inflammatory cells are recruited to the injury site, exacerbating local inflammatory responses. Pulmonary fibroblasts are activated and differentiate into myofibroblasts, which synthesize large amounts of collagen, fibronectin, and other extracellular matrix (ECM) components. Additionally, the activity of ECM degradation enzymes is inhibited, resulting in excessive ECM deposition in the pulmonary interstitium^[5-7].

2.2. Inflammatory cell infiltration

The immune-inflammatory response serves as a critical defense mechanism of the body and an essential phase in injury repair, maintaining normal physiological functions of tissues and organs by resisting various injuries and infections. Abnormal injury repair is a primary pathological feature of idiopathic pulmonary fibrosis (IPF). The immune-inflammatory response plays a pivotal driving role in the early stages of IPF pathogenesis, where activated inflammatory cells secrete various inflammatory mediators to trigger inflammatory responses, thereby inducing dysregulation of injury healing during IPF progression^[8]. Studies have revealed a significant increase in macrophage count in alveolar lavage fluid from IPF patients^[9]. Macrophages participate in inflammatory regulation, pulmonary tissue injury, and repair through two core pathways, classical polarization and alternative activation—thereby influencing the onset and progression of IPF^[10,11].

3. Pathogenesis of IPF

3.1. Alveolar epithelial cell injury and epithelial-mesenchymal transition

Alveolar epithelial cell injury represents the initial pathological step in the pathogenesis of idiopathic pulmonary fibrosis (IPF), with dysfunction of type II alveolar epithelial cells (AEC II) serving as the core etiological factor. In IPF, oxidative stress, telomere shortening, and genetic mutations may induce “senescence phenotypes” in AEC II, characterized by reduced proliferative capacity, secretory dysfunction, and increased apoptosis^[12,13]. Damaged AEC II can undergo “epithelial-mesenchymal transition” to transform into myofibroblasts. Under the influence of factors such as TGF- β 1 and IL-1 β , AEC II lose epithelial markers and acquire migratory capabilities, subsequently secreting extracellular matrix (ECM) upon entering the pulmonary interstitium, thereby promoting the progression of IPF^[14,15].

3.2. Activation and proliferation of lung fibroblasts

The activation of pulmonary fibroblasts is a pivotal step in the fibrotic process of IPF, and its activation is regulated by multiple factors. Resting pulmonary fibroblasts exhibit weak ECM synthesis capacity; upon stimulation by pro-fibrotic factors such as TGF- β 1 and PDGF, they can activate intracellular signaling pathways, differentiate into myofibroblasts, and secrete large amounts of ECM, thereby exacerbating pulmonary fibrosis accumulation^[16]. TGF- β 1, as a key cytokine responsible for fibrosis^[17], binds to TGF- β receptors on the membrane of pulmonary fibroblasts, activating both Smad-dependent and non-Smad pathways, which promote the expression of downstream fibrotic target genes and drive the progression of pulmonary fibrosis^[18,19].

2.3. ECM remodeling imbalance

Abnormally activated fibroblasts extensively synthesize extracellular matrix components such as collagen and fibronectin, leading to ECM structural remodeling. In IPF patients, the dynamic balance between matrix metalloproteinases and tissue inhibitor of metalloproteinases is disrupted, thereby impairing the normal degradation capacity of ECM and promoting its

persistent abnormal deposition in lung tissue, ultimately accelerating the onset and progression of pulmonary fibrosis^[20].

2.4. Oxidative stress and cellular damage

Oxidative stress is a significant predisposing factor for the pathogenesis of IPF, with its core mechanism involving an imbalance between reactive oxygen species (ROS) generation and clearance in lung tissue. Excessive ROS directly induces oxidative damage to DNA, proteins, and lipids, ultimately leading to cellular injury. In IPF patients, oxidative stress responses in lung tissues are markedly enhanced, characterized by excessive accumulation of superoxide anions and hydrogen peroxide, coupled with dysregulation of the body's antioxidant defense systems, which accelerates pulmonary fibrosis progression^[21]. Additionally, multiple oxidative stress-related signaling pathways exhibit aberrant regulation in IPF. Activation of the NF- κ B pathway promotes the release of various pro-inflammatory factors, while Nrf2 activity is significantly reduced in IPF patients, resulting in impaired clearance of excess ROS. This creates a vicious cycle of oxidative damage and repair dysregulation, driving sustained progression of pulmonary fibrosis^[22].

2.5. Immune inflammatory response

In patients with idiopathic pulmonary fibrosis (IPF), the number of various inflammatory cells, such as macrophages, T lymphocytes, and neutrophils in lung tissue is significantly increased^[23], releasing large amounts of TNF- α and IL-6 to trigger inflammatory responses^[24], exacerbating pulmonary tissue damage. B lymphocytes and T lymphocytes in the lung tissue of IPF patients exhibit extensive abnormal activation, leading to the production of autoantibodies and immune complex formation, which further aggravate inflammatory reactions and pulmonary tissue injury^[25,26]. During the early stage of alveolar epithelial cell (AEC) injury, neutrophils are extensively recruited to the injury site, where they release pro-inflammatory mediators and neutrophil elastase (NE) to stimulate downstream immune responses, thereby inducing abnormal repair of damaged tissues during IPF progression. Additionally, NE accelerates the formation of pulmonary scar tissue and the progression of pulmonary fibrosis by promoting fibroblast proliferation and differentiation, inducing myofibroblast activation, and upregulating α -SMA expression^[27,28].

3. IPF-related signaling pathways

3.1. TGF- β /Smad signaling pathway

The TGF- β /Smad signaling pathway is a critical pathway in the pathogenesis of fibrosis. TGF- β 1, as a key stimulatory factor^[29], plays a significant role in pulmonary fibrosis. By activating the Smad signaling pathway, TGF- β 1 promotes the proliferation, activation, and migration of pulmonary fibroblasts, as well as upregulates collagen synthesis and secretion, thereby advancing the progression of idiopathic pulmonary fibrosis (IPF)^[30]. The Smad-dependent signaling pathway is a classical mechanism underlying the development of IPF. In IPF patients, the TGF- β /Smad signaling pathway is abnormally activated in lung tissues, with significantly elevated levels of TGF- β 1. TGF- β 1 binds to TGF- β RII, inducing its phosphorylation and recruiting TGF- β RI, which subsequently activates downstream Smad2/3 proteins. These proteins then form complexes with Smad4, translocating from the cytoplasm to the nucleus, where they bind to promoter regions of target genes such as COL1A1, α -SMA, and Snail, regulating gene expression and promoting extracellular matrix (ECM) synthesis and epithelial-mesenchymal transition (EMT) processes^[31,32].

3.2. Wnt/ β -catenin signaling pathway

The Wnt/ β -catenin signaling pathway plays a critical role in embryonic development and tissue repair, with its abnormal activation being closely associated with the fibrotic process in idiopathic pulmonary fibrosis (IPF). Under normal conditions, cytoplasmic β -catenin is phosphorylated and degraded by a complex composed of glycogen synthase kinase-3 β (GSK-3 β) and AXIN, keeping the pathway in an inhibited state. During IPF development, this pathway becomes activated. In IPF patients, expression levels of Wnt3a, β -catenin, and their target genes are significantly elevated in lung tissues. Wnt

ligands such as Wnt3a and Wnt5a bind to cell membrane receptors Frizzled/LRP5/6, inhibiting GSK-3 β protein activity. Consequently, β -catenin fails to be effectively degraded, leading to persistent accumulation in the cytoplasm. Upon entering the nucleus in large quantities, it binds to downstream transcription factors, thereby regulating the proliferation and differentiation of pulmonary myofibroblasts and influencing the fibrotic process^[33].

3.3. Hippo/YAP/TAZ signaling pathway

The Hippo/YAP/TAZ signaling pathway is a critical pathway regulating cell proliferation, apoptosis, and organ size. Recent studies have revealed its significant role in idiopathic pulmonary fibrosis (IPF). In IPF, excessive deposition of pulmonary interstitial extracellular matrix (ECM) inhibits Hippo pathway activity, leading to sustained activation of YAP/TAZ. Activated YAP/TAZ promotes pulmonary fibroblast proliferation and ECM synthesis, induces alveolar epithelial cell senescence, and suppresses reparative functions. Research has demonstrated that YAP gene knockout significantly alleviates pulmonary fibrosis in mice, suggesting that YAP/TAZ may represent a potential therapeutic target for IPF^[34].

3.4. JAK/STAT signaling pathway

In IPF, the JAK/STAT signaling pathway is abnormally activated, regulating the upregulation of downstream pulmonary fibrosis-related genes, leading to increased synthesis of collagen and fibronectin, and reducing ECM degradation by inhibiting MMP expression or promoting TIMP expression. This results in excessive ECM deposition in IPF, exacerbating disease progression^[35]. The JAK/STAT signaling pathway synergistically promotes fibroblast proliferation and activation while inhibiting the AECs' repair, thereby advancing pulmonary fibrosis^[36]. Studies have demonstrated that IL-6 and IL-10 activate JAK2 and STAT3, promoting fibroblast proliferation and differentiation into myofibroblasts, increased ECM synthesis, and subsequent excessive deposition, thereby aggravating the pathological course of IPF^[37]. Furthermore, research confirms that IL-27 significantly downregulates JAK/STAT signaling pathway activation by inhibiting STAT1 and STAT5 phosphorylation, thereby delaying IPF progression^[38]. These findings indicate that JAK/STAT signaling pathway-targeted therapeutic strategies hold significant clinical potential in the treatment of pulmonary fibrosis.

3.5. PI3K/AKT signaling pathway

In patients with idiopathic pulmonary fibrosis (IPF), the expression of PI3K and AKT in lung tissue is significantly elevated. The key pathogenic factor TGF- β in IPF activates the PI3K/AKT signaling pathway, inhibiting apoptosis of alveolar epithelial cells (AECs) and enhancing their migratory capacity. Excessive migration and survival lead to abnormal phenotypic transformation of AECs, thereby promoting the occurrence and progression of epithelial-mesenchymal transition (EMT) and exacerbating IPF development. Tetrahydroindene (TET), as an intervention agent for the PI3K/AKT signaling pathway, can significantly ameliorate silica-induced pulmonary fibrosis models. Studies have demonstrated that TET can target and regulate the PI3K/AKT signaling pathway, downregulating the expression levels of fibrosis-related biomarkers, providing novel therapeutic targets and strategic directions for pulmonary fibrosis treatment^[39].

3.6. MAPK signaling pathway

Extracellular signal-regulated kinase ERK, p38 mitogen-activated protein kinase, and c-Jun N-terminal kinase are components of the MAPK pathway. The ERK signaling pathway promotes fibroblast proliferation and activation, increases extracellular matrix (ECM) synthesis, and drives the progression of idiopathic pulmonary fibrosis (IPF). In bleomycin-induced IPF rat models^[40], the expression levels of ERK1 and ERK2, key members of the ERK signaling pathway, were significantly upregulated, confirming their critical regulatory roles in the pathological process of pulmonary fibrosis. In bleomycin-induced IPF models^[41], JNK expression levels were markedly elevated. The JNK signaling pathway contributes to IPF development by promoting abnormal fibroblast activation, facilitating myofibroblast differentiation, increasing ECM synthesis and secretion, and regulating the release of pro-inflammatory cytokines such as TNF- α and IL-6.

4. Current treatment options for IPF

4.1. Anti-fibrotic drug therapy

Currently, there are no effective drugs available for the treatment of IPF. Pirfenidone and nintedanib are the primary medications capable of alleviating IPF symptoms^[42]. These agents exert their therapeutic effects by inhibiting pulmonary fibroblast activation and ECM synthesis, thereby delaying IPF progression, reducing the risk of acute exacerbations, and lowering mortality rates^[43].

Pirfenidone inhibits the TGF- β /Smad signaling pathway, reduces the secretion of fibrogenic factors and pro-inflammatory factors, thereby suppressing abnormal proliferation and activation of pulmonary fibroblasts, decreasing fibroblast differentiation into myofibroblasts, reducing collagen synthesis, and prolonging patient survival^[44]. Nintedanib blocks downstream signal transduction processes by targeting PDGF receptors, FGFR receptors, and VEGF receptors. Nintedanib inhibits PDGF-mediated fibroblast proliferation and migration, suppresses FGFR-mediated ECM synthesis, inhibits VEGF-mediated angiogenesis, and alleviates pulmonary interstitial inflammation^[45].

4.2. Pulmonary rehabilitation and supportive therapy

Pulmonary rehabilitation therapy is currently an effective method for alleviating IPF, capable of improving patients' dyspnea symptoms, enhancing exercise tolerance, and improving quality of life. IPF patients can improve their quality of life through respiratory training, exercise training, psychological intervention, and oxygen therapy. Supportive treatments also include preventing pulmonary infections, such as influenza vaccination and pneumococcal vaccination, managing comorbidities like gastroesophageal reflux disease, and utilizing proton pump inhibitors for treatment. These measures can reduce the risk of acute exacerbations in IPF and improve patient prognosis^[46].

5. Conclusion

IPF is a disease characterized by complex pathogenesis, poor prognosis, and relatively limited treatment options. Therefore, an in-depth understanding of its pathogenesis and pathological features holds significant theoretical importance for the development of novel therapeutic agents. This article focuses on multiple signaling pathways closely associated with IPF, including TGF- β /Smad and Wnt/ β -catenin pathways. These pathways collectively influence key pathological processes, such as fibroblast activation, extracellular matrix metabolism imbalance, and inflammatory responses, thereby promoting the onset and progression of pulmonary fibrosis. However, the pathogenesis of IPF remains complex. Future research requires systematic exploration of the regulatory mechanisms of these signaling pathways to provide critical theoretical foundations for screening novel biomarkers for early disease diagnosis and identifying clinically valuable therapeutic targets. This will further advance the development of precision diagnosis and treatment systems for IPF and improve the quality of life for the patients.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Comparative Study of Modified Laparoscopic Cervical Cerclage and Transvaginal Cervical Cerclage in the Treatment of Cervical Insufficiency

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Abstract: *Objective:* To observe the clinical effects of modified laparoscopic cervical cerclage and transvaginal cervical cerclage in the treatment of cervical insufficiency. *Methods:* 74 patients with cervical insufficiency in our hospital (from June 2024 to September 2025) were selected and randomly divided into a control group (37 cases) undergoing transvaginal cervical cerclage and an observation group (37 cases) undergoing modified laparoscopic cervical cerclage. The patients' surgical conditions, hospitalization time, pregnancy outcomes, complication rates, neonatal outcomes and quality of life were observed. *Results:* The operation time, intraoperative blood loss, and hospitalization time of the observation group were shorter than those of the control group ($P < 0.05$); the pregnancy outcome of the observation group was better than that of the control group ($P < 0.05$); the incidence of complications in the observation group was lower than that of the control group ($P < 0.05$); the neonatal outcome of the observation group was better than that of the control group ($P < 0.05$); and the quality of life score of the observation group was higher than that of the control group ($P < 0.05$). *Conclusion:* The modified laparoscopic cervical cerclage surgery for patients with cervical insufficiency has good results. It can promote postoperative recovery, improve pregnancy outcomes and neonatal outcomes, reduce the incidence of complications, and improve the quality of life. It is better than transvaginal cervical cerclage treatment and is worth learning from.

Keywords: Modified laparoscopic cervical cerclage; Transvaginal cervical cerclage; Cervical insufficiency

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1. Introduction

Cervical insufficiency is mainly the gradual dilation of the cervix without uterine contractions or pain, which in turn causes the fetal membranes and placenta to protrude into the vagina, easily causing the delivery of immature fetuses and premature rupture of membranes. This disease is an important cause of miscarriage or premature birth in preterm pregnancies^[1]. At this stage, the main treatment for this disease is cervical cerclage. Mechanical reinforcement of the internal cervical is beneficial for prolonging gestational age and improving pregnancy outcomes. Transvaginal cervical cerclage has been the clinical treatment of choice for a long time and has many features, such as ease of operation. However, for some patients with abnormal anatomy or failed transvaginal surgery, open abdominal surgery is often performed. This surgical method has a greater adverse impact on patients, such as obvious trauma and slow recovery. With the continuous development of minimally invasive technology, improved laparoscopic cervical cerclage has attracted

widespread attention. It can avoid vaginal operations and further irritate the cervix, and can seal the cervical canal more firmly. It is an effective treatment measure, and its clinical application effect needs to be studied in depth ^[2].

2. Materials and methods

2.1. General information

A total of 74 patients with cervical insufficiency in our hospital from June 2024 to September 2025 were selected and randomly divided into 2 groups. There were 37 patients in the control group, aged 21 to 36 (28.37 ± 2.81) years old, cervical length 21 to 27 (24.38 ± 2.81) cm, and cervical internal os width 3 to 8 (5.47 ± 1.19) mm. There were 37 patients in the observation group, aged 22 to 37 (28.54 ± 2.67) years old, cervical length 22 to 28 (24.54 ± 2.67) cm, and cervical internal os width 3 to 7 (5.54 ± 1.23) mm. Comparison of general data, $P > 0.05$.

Inclusion criteria: (1) Singleton pregnancy or non-pregnant state; (2) Cervical conditions suitable for cerclage; (3) No history of pelvic surgery; (4) No reproductive tract infection.

Exclusion criteria: (1) severe fetal malformations or genetic diseases; (2) complications during pregnancy; (3) mental illness.

2.2. Method

Control group: The patients were given general spinal anesthesia, kept in the lithotomy position, and their buttocks were appropriately elevated. Do a good job of disinfecting the vulva and vagina, empty the bladder, completely expose the cervix and fornix, and carry out secondary disinfection. The anterior lip of the cervix is gently lifted using oval forceps, and 0.9% saline is injected into the reflexed part of the bladder and cervix to form a water cushion. The vaginal mucosa is transversely incised 0.5 cm below the reflected peritoneum, and the bladder is pushed upward to ensure full exposure of the cervix. Purse-bag suture is used. The needle is inserted at the 1 o'clock position to penetrate the mucosa and reach two-thirds of the cervical myometrium. The needle is inserted at the 5 o'clock position, the needle is inserted at the 11 o'clock position, and the needle is withdrawn at the 7 o'clock position. Finally, a knot is tied at the posterior fornix. During the operation, in order to reduce the postoperative foreign body irritation of the patient, continuous absorbable sutures are usually used when suturing the fornix mucosa, and cerclage wires are embedded in the submucosa.

Observation group: Patients were placed in a supine position with tracheal intubation and intravenous inhalation combined anesthesia, with their legs separated and a urinary catheter indwelling. Make an incision on the upper edge of the umbilicus with a length of 1 cm. At the same time, the Trocar and laparoscope are inserted to establish pneumoperitoneum and ensure that the pressure is maintained at 10 to 13 mmHg. For non-pregnant patients, during the surgical treatment, the uterus is pushed up with a uterine lift to fully expose the field of view, and 5 mm puncture holes are established at the McBurney's point in the right lower abdomen, the corresponding part on the contralateral side, and the lateral side of the left umbilical ligament. The bladder is folded and the peritoneum is opened, and the bladder is pushed down at the same time to fully separate the tissues around the uterine isthmus and clearly display the parametrial blood vessels. Then use the Mersilene band to puncture the inner side of the paracervical blood vessels and the superficial myometrium of the cervical isthmus. Pay attention to going from front to back and bypass the back of the uterine isthmus. Then, puncture the needle inside the contralateral uterine blood vessels from back to front. The final knotting position is in front of the uterine isthmus. The cervical tightness is tested, and the standard is that the No. 6 dilation rod passes without resistance, and the cerclage is repeated according to this standard. The wound was sutured laparoscopically, and a cerclage band was embedded at the same time. For patients with early pregnancy, it is necessary to use a lifting cup to hold the cervix during the uterine lifting process, and the integrity of the round ligament of the uterus is preserved during the operation. In order to create a good operating space, the tip of the forceps needs to be used to push up the rear of the broad ligament. The operator makes a hole at the lifting site, and at the same time penetrates the peritoneum of the front and rear leaves of the broad ligament. The needle insertion and needle removal operations are performed in the hole, and the rest of the steps are the same.

2.3. Observation indicators

(1) Statistics of operation time, intraoperative blood loss, and hospitalization time; (2) Pregnancy outcomes: miscarriage, premature birth, term delivery; (3) Complication rate: vascular injury, cerclage detachment, cervical tear, postoperative infection; (4) Neonatal outcomes: macrosomia, neonatal morbidity; (5) Quality of life: Brief Health Scale (SF-36), the higher the score, the better.

2.4. Statistical methods

SPSS 26.0 software processes data. Measurement data is expressed as mean $\pm$ standard deviation (SD), t test is used. Count data is expressed as: n, %. χ^2 test is used. $P < 0.05$ means the difference is statistically significant.

3. Results

3.1. Comparison of patients' surgical conditions and hospitalization time

The observation group was less than the control group, $P < 0.05$, Table 1.

Table 1. Comparison of patients' surgical conditions and hospital stay

Group	Operation time (min)	Intraoperative blood loss (mL)	length of stay (d)
Control group (n = 37)	68.37 $\pm$ 2.84	36.95 $\pm$ 2.83	7.18 $\pm$ 1.38
Observation group (n = 37)	61.28 $\pm$ 2.86	20.19 $\pm$ 3.28	5.96 $\pm$ 1.23
<i>t</i>	10.700	23.533	4.014
<i>P</i>	0.000	0.000	0.000

3.2. Comparison of pregnancy outcomes

The observation group was better than the control group, $P < 0.05$, Table 2.

Table 2. Comparison of pregnancy outcomes (n%)

Group	Miscarriage	Premature Birth	Term birth
Control group (n = 37)	2 (5.41)	10 (27.03)	25 (67.57)
Observation group (n = 37)	1 (2.70)	2 (5.41)	34 (91.89)
χ^2		7.040	
<i>P</i>		0.030	

3.3. Comparison of complication rates

The observation group was lower than the control group, $P < 0.05$, Table 3.

Table 3. Comparison of complication rates (n%)

Group	Blood vessel damage	The cerclage band fell off	Cervical tear	Postoperative infection	Always happens
Control group (n = 37)	2 (5.41)	3 (8.11)	1 (2.70)	1 (2.70)	7 (18.92)
Observation group (n = 37)	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.70)	1 (2.70)
χ^2	-	-	-	-	5.046
<i>P</i>	-	-	-	-	0.025

3.4. Comparison of neonatal outcomes

The observation group was lower than the control group, $P < 0.05$, **Table 4**.

Table 4. Comparison of neonatal outcomes (n%)

Group	Macrosomia	Neonatal morbidity
Control group (n = 37)	4 (10.81)	6 (16.22)
Observation group (n = 37)	0 (0.00)	1 (2.70)
χ^2	4.229	3.945
P	0.040	0.047

3.5. Quality of life comparison

The observation group was higher than the control group, $P < 0.05$, **Table 5**.

Table 5. Comparison of quality of life (points)

Group	Energy	Emotional function	Somatic pain	Social function	General health	Physiological functions	Mental health	Physiological function
Control group	71.57 ± 2.69	73.74 ± 2.95	73.72 ± 3.94	71.34 ± 2.38	73.84 ± 2.23	71.72 ± 2.94	72.72 ± 2.94	72.34 ± 2.71
Observation group	76.74 ± 3.55	77.94 ± 2.64	75.57 ± 3.83	75.49 ± 2.62	77.40 ± 2.62	76.73 ± 2.93	78.55 ± 2.34	77.82 ± 2.39
t	7.061	6.453	2.053	7.132	6.294	7.342	9.438	9.225
P	0.000	0.000	0.044	0.000	0.000	0.000	0.000	0.000

4. Discussions

Cervical insufficiency is relatively common clinically. The most obvious manifestation after the disease occurs is the painless shortening and opening of the cervix after the second trimester of pregnancy, preventing the pregnancy from being maintained to term. Through analysis of the cause of the disease, it is believed that it is related to many factors, such as congenital cervical dysplasia, hormone level imbalance, etc. Acquired injury is also a very important factor, such as surgery, infection, childbirth, etc. ^[3] In the treatment of diseases, surgery is a common treatment method. However, in clinical practice, it is found that there are many surgical methods that can be used, but there are certain differences in the final effects of different surgical methods. At the same time, due to the continuous development of medical technology, various high-quality surgical treatment methods are constantly emerging ^[4]. Therefore, further research is needed to select more effective and safe surgical methods for patients with cervical insufficiency.

In the results of this study, the operation time, intraoperative blood loss, and hospitalization time of the observation group were shorter than those of the control group ($P < 0.05$). Improved laparoscopic cervical cerclage can perform more precise operations under laparoscopy, further enlarging the pelvic structure, locating the internal cervical os and parametrial blood vessels in a short time, further reducing the time for repeated exploration, and thus shortening the operation time. During transvaginal surgical treatment, the bladder and cervix are separated manually, and the operating space is limited, which easily increases the risk of tissue damage and leads to an increase in intraoperative bleeding ^[5]. Laparoscopy can further refine blood vessels, thereby reducing intraoperative blood loss. The field of view of transvaginal surgery is limited, which can easily cause accidental injury to blood vessels, increase bleeding, and prolong the operation time. Laparoscopic surgery further reduces trauma to patients and reduces postoperative pain, which is beneficial to speeding up postoperative physical recovery and shortening hospitalization time ^[6]. The pregnancy outcome of the observation group was better than that of the control group ($P < 0.05$). The sutures are fixed to the cervical isthmus during modified laparoscopic cervical

cerclage treatment, which in this case can provide stronger mechanical support and better resist the uterine cavity pressure during pregnancy. The transvaginal cerclage thread is mainly located in the cervix and vagina. Its position is low, and it is easy for the cerclage thread to fall off due to cervical shortening or uterine contractions. Moreover, laparoscopic surgery can avoid stimulation of the cervix caused by vaginal surgery, reduce the risk of premature rupture of membranes, increase the full-term birth rate, and reduce the miscarriage and premature birth rates ^[7]. The incidence of complications in the observation group was lower than that in the control group ($P < 0.05$). During transvaginal surgery, it is easy to damage the blood vessels of the bladder or cervix, increasing the risk of postoperative infection or cervical tear. Laparoscopic treatment is performed through the extraperitoneal route without entering the vagina, reducing the risk of complications. Laparoscopic suturing is stronger and the sutures are buried under the peritoneum, thereby reducing the risk of cerclage detachment. The neonatal outcomes of the observation group were better than those of the control group ($P < 0.05$). Modified laparoscopic cervical cerclage treatment is beneficial for increasing the full-term birth rate. In this case, it can improve neonatal lung maturity and reduce the incidence of neonatal diseases. However, transvaginal cervical cerclage has a higher rate of premature birth, which requires more intervention for newborns and increases their prevalence ^[8]. The quality of life score of the observation group was higher than that of the control group ($P < 0.05$). Laparoscopic cervical cerclage has less trauma and less pain, which helps patients to move around as soon as possible after surgery, achieve better postoperative recovery, avoid adverse effects on their daily activities and emotional state, and thus improve their quality of life ^[9].

Therefore, after treatment of patients with cervical insufficiency, compared with transvaginal cervical cerclage treatment, modified laparoscopic cervical cerclage has better surgical effects, promotes postoperative recovery, improves pregnancy outcomes and neonatal outcomes, reduces the incidence of complications, and improves quality of life, which has promotional value.

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Disclosure statement

The author declares no conflict of interest.

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Traditional Chinese Medicine Dietary Therapy for Painful Diabetic Peripheral Neuropathy: Compatibility Principles and Mechanistic Rationale—A Narrative Review

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Abstract: Painful diabetic peripheral neuropathy (PDPN) is one of the most prevalent and refractory chronic complications of diabetes mellitus. Clinically, it is characterized by distal numbness, burning pain, stabbing pain, cold pain, and sensory disturbances, all of which substantially impair quality of life. Although there is no exact disease entity corresponding to PDPN in traditional Chinese medicine (TCM), the condition is generally interpreted within the categories of Xiaoke Bi syndrome, blood Bi, Bi syndrome, numbness, and pain syndrome, based on its diabetic background and manifestations of pain, numbness, and channel obstruction. According to TCM theory, the core pathogenesis of PDPN is defined by a deficiency in origin and excess in superficiality. Long-standing Xiaoke gradually consumes both Qi and Yin, leading to spleen-kidney deficiency, insufficiency of liver blood, and malnourishment of the extremities; meanwhile, phlegm turbidity, blood stasis, cold coagulation, and damp-heat obstruct the channels and collaterals, resulting in pain due to collateral blockage. TCM dietary therapy is grounded in the principle of medicine-food homology and emphasizes syndrome differentiation, mild nourishment, and long-term regulation. Its major therapeutic strategies include replenishing Qi and nourishing Yin, strengthening the spleen and tonifying the kidney, activating blood and unblocking the collaterals, and harmonizing the nutritive and defensive Qi. Recent studies on prescription patterns in diabetic peripheral neuropathy found that *Astragali radix*, *Angelicae sinensis radix*, *Spatholobi caulis*, *Paeoniae radix alba*, *Chuanxiong rhizoma*, and *Achyranthis bidentatae radix* are the main herbs. This shows the treatment idea of supplementing Qi, activating blood, and nourishing the collaterals. At the same time, network pharmacology studies suggest that these compatibility patterns may produce therapeutic effects through interactions among multiple components, targets, and pathways. This review summarizes the TCM pathogenesis of PDPN, the theoretical basis of TCM dietary therapy, representative dietary compatibility patterns, and the supportive evidence from network pharmacology, to provide a theoretical basis for the dietary management of PDPN within the TCM framework.

Keywords: Painful diabetic peripheral neuropathy; Traditional Chinese medicine dietary therapy; Medicine-food homology; Compatibility principles; TCM pathogenesis; Network pharmacology

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1. Introduction

Diabetic neuropathy is a common chronic complication of diabetes mellitus, and distal symmetric polyneuropathy is its most prevalent form. PDPN is characterized by pain-dominant distal sensory symptoms, including burning, stabbing, and cold pain, allodynia, numbness, and sensory abnormalities^[1]. Although current guidelines emphasize glycemic control, risk factor management, and symptomatic analgesia, disease-modifying options for established neural injury and chronic neuropathic pain remain limited, supporting the need for long-term, integrative, and sustainable strategies^[2].

In the TCM framework, PDPN is not an independent local pain disease. It is a chronic disease process with “Xiaoke” as the root, “pain” as the manifestation, and collateral disease running through the whole course. So, treatment should not only focus on pain relief, but also on the regulation of Qi, blood, Yin, Yang, zang-fu function, and the free flow of the channels and collaterals. Dietary therapy is an important part of TCM preventive treatment and rehabilitation. It has a mild effect, is easy for patients to accept, and is suitable for long-term use. So, it is especially suitable for chronic and recurrent diseases such as PDPN. In recent years, studies on medication patterns in diabetic peripheral neuropathy have found that *Astragali radix*, *Angelicae sinensis radix*, *Salviae miltiorrhizae radix et Rhizoma*, *Spatholobi caulis*, *Paeoniae radix alba*, *Chuanxiong rhizoma*, *Cinnamomi ramulus*, and *Achyranthis bidentatae radix* are frequently used herbs. Their treatment ideas mainly focus on supplementing Qi, activating blood, nourishing blood, and dredging the collaterals^[3].

2. TCM pathogenesis of painful diabetic peripheral neuropathy

2.1. Xiaoke with depletion of both Qi and Yin as the fundamental root

In TCM theory, the first cause of Xiaoke is Yin deficiency, with dryness of the internal organs and heat inside the body. As the disease goes on, the loss of Yin affects the movement of Qi and leads to a deficiency of both Qi and Yin. This lack of Qi and Yin causes symptoms of poor nourishment due to Qi deficiency and poor moistening due to Yin deficiency. The distal limbs need Qi, blood, and body fluids to keep normal sensation and movement. So long-term loss of Qi and Yin may show as numbness in the distal limbs, dull pain, reduced sensation, fatigue, and tiredness. Because of this, deficiency of Qi and Yin is one of the basic causes of PDPN.

2.2. Spleen-kidney deficiency and insufficiency of essence and blood as the basis of chronicity

As Xiaoke continues, it uses up Qi and Yin and also harms the spleen and kidney. In TCM, the spleen is the source of Qi and blood and the foundation after birth, while the kidney is the foundation before birth and stores essence. When the spleen and kidney are weak, the body makes less Qi and blood, and the tendons, vessels, and collaterals receive less nourishment. PDPN appears in the distal limbs, but its root lies in zang-fu deficiency. In clinical practice, patients with a long disease course often have weakness of the lower limbs, soreness of the waist and knees, fatigue, and frequent urination at night, which often points to spleen-kidney deficiency or liver-kidney deficiency^[4].

2.3. Blood stasis and phlegm turbidity obstructing the collaterals as the key pathogenic basis of pain

The TCM theory that “chronic disease enters the collaterals” provides a key framework for understanding PDPN-related pain. Although PDPN is rooted in deficiency, its pain is closely linked to excess factors, particularly blood stasis, phlegm turbidity, cold coagulation, and damp obstruction. Consistent prescription pattern analyses have identified *Astragali Radix*-based herb pairs and combinations as representative strategies for supplementing Qi, nourishing blood, activating blood, and unblocking the collaterals^[5].

2.4. Disharmony of the nutritive and defensive Qi, with intertwined cold and heat, as the basis for heterogeneous pain phenotypes

PDPN is characterized by heterogeneous symptoms, including burning pain, cold pain, nocturnal aggravation, tactile

hypersensitivity, numbness, and dysesthesia. In TCM, these features are understood as resulting from Ying-wei disharmony and the intermingling of cold and heat. Root deficiency, including Qi-Yin deficiency, spleen-kidney deficiency, and insufficiency of liver blood, underlies the disorder, whereas phlegm, blood stasis, cold coagulation, and damp-heat obstructing the collaterals constitute the branch, with collateral obstruction and insufficient channel nourishment as the core pathological basis.

3. Theoretical basis and therapeutic logic of TCM dietary therapy for PDPN

The theoretical basis of TCM dietary therapy is grounded in the concept of medicine-food homology. Recent expansions of the official list of dual-use substances in China, including the addition of *Astragali radix* in 2023 and *Rehmanniae radix*, *Ophiopogon radix*, *Asparagi radix*, and *Citri grandis exocarpium* in 2024, have provided practical policy support for dietary interventions based on medicinal-food homologous materials^[6].

From the TCM perspective, dietary therapy for PDPN emphasizes mild nourishment, gradual regulation, and concurrent treatment of root deficiency and branch excess. Its major functions include supplementing Qi and nourishing Yin, strengthening the spleen and harmonizing the middle burner, activating blood and unblocking the collaterals, tonifying the kidney and replenishing essence, and harmonizing nutritive and defensive Qi, thereby contributing to the alleviation of pain and improvement of collateral nourishment. Warming dietary strategies may be particularly suitable for patients with cold-aggravated symptoms or deficiency-cold patterns^[7].

Therefore, TCM dietary therapy for PDPN is better understood as a syndrome-based intervention that supports upright Qi, regulates zang-fu function, nourishes the channels and collaterals, and improves the underlying pathological state of chronic neuropathic pain^[8,9].

4. Representative dietary compatibility patterns

TCM dietary therapy for PDPN should follow syndrome differentiation, mild nourishment, and long-term regulation. Based on the diabetic diet, suitable ingredients can be made into porridge, soup, paste, or drinks.

4.1. Astragalus–Yam–Ophiopogon porridge

Astragali radix is sweet and slightly warm. It is often used to tonify Qi, raise clear Yang, and help Qi move blood. *Dioscoreae rhizoma* is sweet and neutral. It is used to strengthen the spleen and nourish the stomach, lungs, and kidneys. *Ophiopogon radix* is sweet, slightly bitter, and slightly cold. It is used to nourish Yin, produce fluids, moisten dryness, and relieve vexation. As porridge, this combination is suitable for patients with long-term Xiaoke with Qi-Yin deficiency and spleen weakness. Common signs include distal numbness, dull pain, fatigue, and dry mouth. In this diet, *Astragali radix* supports Qi, *Dioscoreae rhizoma* strengthens the spleen and kidney, and *Ophiopogon radix* nourishes Yin and fluids. This may help improve circulation and moisten the collaterals.

4.2. Angelicae–Angelica–Spatholobi therapeutic beverage

Astragali radix helps Qi and helps blood form and move. *Angelicae sinensis radix* nourishes blood, activates blood, and relieves pain. *Spatholobi caulis* nourishes blood, activates blood, and relaxes the channels. Used as a therapeutic drink like a decoction, this combination is suitable for patients with Qi-blood deficiency and collateral blockage. Common signs include stabbing pain, numbness, worse pain at night, and discomfort after activity. This combination has a stronger medicinal nature than the one before, but it still follows the idea of TCM dietary therapy. Food can use the effect of medicine, and medicine can be used in nourishing dietary forms. Its main idea is that enough Qi helps blood move, smooth blood flow opens the collaterals, and open collaterals help reduce pain.

4.3. Cinnamon Twig–White Peony–Fresh Ginger–Jujube dietary decoction

Cinnamomi ramulus is acrid, sweet, and warm, and is used to warm the channels and harmonize the nutritive and defensive Qi. *Paeoniae radix alba* is sour, bitter, and slightly cold, and nourishes blood, preserves Yin, and relieves spasm. Fresh ginger warms the middle and dispels cold, whereas jujube tonifies the middle Qi and nourishes the spleen. Together, these ingredients harmonize Ying and Wei, warm the channels, unblock the collaterals, and alleviate pain. This pattern is particularly suitable for PDPN patients with Yang deficiency, cold coagulation, or disharmony of nutritive and defensive Qi, especially those with cold limbs, cold pain, numbness, worsening after exposure to cold, and greater pain at night.

4.4. Yam–Goji–Polygonatum paste

Dioscoreae rhizoma strengthens the spleen and kidney. *Lycii fructus* nourishes the liver and kidney and also benefits essence and blood. *Polygonati rhizoma* replenishes Qi, nourishes Yin, and tonifies kidney essence. Made as a thick paste or nourishing soup, this combination is suitable for patients with a long disease course, liver-kidney deficiency, weakness of the lower limbs, persistent numbness, and soreness of the waist and knees. In this diet, the main idea is slow and steady supplementation in chronic disease. It aims to replenish liver-kidney essence, nourish the tendons and collaterals, and help relieve the repeated and lasting symptoms of PDPN.

4.5. Yam–Poria–Coix Seed–White Hyacinth Bean porridge

Dioscoreae rhizoma supplements spleen Qi; Poria strengthens the spleen and drains dampness; *Coicis semen* strengthens the spleen and removes dampness; and *Dolichoris album semen* strengthens the spleen, harmonizes the middle, and transforms dampness. This combination is suitable for patients with spleen deficiency and damp retention. Common signs include heaviness of the limbs, dull numbness, poor appetite, and fatigue. In diabetes, a long disease course often weakens the spleen. When damp turbidity builds up inside the body, the channels become more blocked, and the distal limbs receive less nourishment. This pattern mainly treats the root by strengthening the spleen, removing dampness, and helping the body produce Qi and blood.

4.6. Black Bean–Goji–Mulberry drink

Black soybean is sweet and neutral. It is used to benefit the kidneys and the essence. *Lycii fructus* nourishes the liver and kidneys. *Mori fructus* nourishes Yin and blood, produces fluids, and moistens dryness. Together, these ingredients are suitable for patients with Yin-blood deficiency and liver-kidney weakness. They are especially suitable for those with distal numbness, dizziness, tinnitus, insomnia, and irritability. This dietary combination is gentle and moistening. It fits the TCM idea that chronic disease should be regulated slowly, not treated in a strong way.

4.7. Summary of dietary compatibility patterns

From the view of TCM dietary therapy, representative compatibility patterns for PDPN should show two main features. First, the selected ingredients should be medicinal-food homologous substances or mild therapeutic foods that are suitable for long-term use. Second, the compatibility should follow syndrome differentiation and basic treatment ideas, such as supplementing Qi and nourishing Yin, strengthening the spleen and harmonizing the middle, activating blood and unblocking the collaterals, tonifying the kidney and replenishing essence, and harmonizing nutritive Qi and defensive Qi. Different dietary patterns match different syndromes. This shows the TCM way of syndrome-based diet therapy, the combined use of food and medicine, and long-term gradual regulation.

5. Network pharmacological support for the above dietary compatibility patterns

It should be clear that network pharmacology is a modern research tool. It helps show the multi-component, multi-target, and multi-pathway features of TCM compatibility, but it does not replace syndrome differentiation. Here, its value is to

give modern support for representative dietary compatibility patterns, not to redefine the TCM basis of dietary therapy.

Current studies on medication patterns in diabetic peripheral neuropathy show that frequently used herbs include *Astragali radix*, *Angelicae sinensis radix*, *Salviae miltiorrhizae radix et rhizoma*, *Cinnamomi ramulus*, *Chuanxiong rhizoma*, *Spatholobi caulis*, *Paeoniae radix alba*, *Rehmanniae radix*, and *Carthami flos*, with therapeutic strategies centered largely on supplementing Qi, activating blood, and relieving collateral obstruction.

Among these ingredients, *Astragali radix* has received the most network pharmacology attention. It is a representative Qi-tonifying herb and a recognized medicinal-food homologous material^[10–12]. It also has an important place in TCM theory and modern mechanistic research. Network pharmacology studies of Huangqi Chifeng Decoction for diabetic peripheral neuropathy found key targets such as TNF, VEGFA, IL6, AKT1, CASP3, and PPARG. Main pathways included AGE-RAGE, PI3K-Akt, IL-17, TNF, MAPK, and HIF-1 signaling^[13,14]. Studies on the Huangqi-Chuanxiong herb pair also found active compounds such as quercetin, kaempferol, luteolin, and beta-sitosterol. These studies also suggested the involvement of AGE-RAGE and IL-17 signaling pathways^[15]. For dietary patterns such as Astragalus–Yam–Ophiopogon Porridge and Astragalus–Angelica–Spatholobus Beverage, the TCM idea focuses on supplementing Qi, nourishing Yin, or activating blood. Studies on Astragalus also suggest that it may have multi-target regulatory effects.

Modern support for liver-kidney tonifying dietary patterns remains indirect and is mainly derived from studies on *Lycii fructus*. Available network pharmacology and molecular docking evidence suggests a potential regulatory role in type 2 diabetes through multi-component and multi-target mechanisms^[16], but not direct effects on PDPN. Accordingly, these findings should be interpreted as indirect support for improving chronic deficiency-related internal imbalance rather than as evidence of proven efficacy against neuropathic pain^[17].

In contrast, direct network pharmacology evidence is still limited for the Cinnamon Twig–White Peony–Fresh Ginger–Jujube pattern and the Yam–Poria–Coix Seed–White Hyacinth Bean pattern. These dietary combinations are better explained mainly by classical TCM theory and syndrome matching. The first pattern focuses on harmonizing Ying and Wei, warming the channels, and relieving pain caused by cold blockage. The second pattern focuses on strengthening the spleen, removing dampness, and helping the body produce Qi and blood after birth^[18–20].

Overall, current evidence indicates that Astragali Radix-centered dietary patterns, especially in combination with blood-activating herbs, have the strongest support from network pharmacology, whereas patterns based on *Lycii fructus* and other liver-kidney tonics are supported only indirectly. In contrast, patterns for harmonizing nutritive and defensive Qi or strengthening the spleen and resolving dampness remain grounded mainly in TCM theory and prescription patterns. Therefore, TCM theory should remain the primary framework, with network pharmacology serving as supportive evidence rather than a one-to-one explanatory model^[21].

6. Conclusion

In TCM, PDPN is understood as a chronic Xiaoke-related disorder with collateral obstruction, characterized by root deficiency and branch excess. While Qi-Yin deficiency, spleen-kidney deficiency, and insufficiency of liver blood constitute the root, phlegm, blood stasis, cold, and damp-heat obstructing the collaterals represent the branch. Accordingly, TCM dietary therapy emphasizes mild nourishment, gradual regulation, and simultaneous treatment of both root and branch. Its main methods include supplementing Qi and nourishing Yin, strengthening the spleen and harmonizing the middle, activating blood and unblocking the collaterals, tonifying the kidney and replenishing essence, and harmonizing nutritive Qi and defensive Qi. In practice, diet therapy can use medicinal-food materials such as *Astragali radix*, *Dioscoreae rhizoma*, *Ophiopogonis radix*, *Lycii fructus*, *Angelicae sinensis radix*, *Spatholobi caulis*, *Cinnamomi ramulus*, and *Paeoniae radix alba*, and they can be prepared as porridge, soup, paste, or therapeutic drinks based on syndrome differentiation^[22]. At present, research on TCM dietary therapy for PDPN still depends mainly on theory, prescription pattern studies, and network pharmacology studies of related herbs or formulas. Direct high-quality studies on specific dietary patterns, clear TCM syndromes, and pain outcomes are still lacking. Future research should focus on standardized

syndrome stratification, more rigorous dietary protocol design, more objective clinical endpoints, and multi-level mechanistic validation ^[23], to promote TCM dietary therapy for PDPN from experience-based application toward a more evidence-informed framework ^[24].

Disclosure statement

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Molecular Subtyping of Hepatocellular Carcinoma and Precision Systematic Treatment Strategies

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Abstract: Hepatocellular carcinoma (HCC) is a highly heterogeneous malignant tumor determined by multiple molecular driver events and tumor microenvironment remodeling. Multidisciplinary integrated studies have systematically revealed that HCC can be classified into several functional subtypes with internal consistency in multi-level molecular characteristics but significant differences among subtypes, including Wnt/ β -catenin activated type, proliferative/chromosomal instability type, metabolic/hepatocyte-like type, and immune microenvironment-dominant type. These subtypes exhibit fundamental differences in signaling pathway dependence, immune ecological architecture, and therapeutic sensitivity, directly determining the efficacy of targeted therapy and immunotherapy. Current systemic therapies still face significant challenges in patient selection and resistance control, highlighting the necessity of precision treatment based on molecular subtyping. This review summarizes the biological basis of major molecular subtypes of HCC, focuses on subtype-guided strategies for immunotherapy combination, targeted therapy combination, and metabolic intervention, and emphasizes the potential value of dynamic subtyping and resistance monitoring in precision systemic therapy.

Keywords: Hepatocellular carcinoma, Molecular subtyping, Tumor microenvironment, Precision system therapy

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1. Etiological evolution and biological heterogeneity basis of hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer globally, with its occurrence closely associated with a background of chronic liver disease, including viral hepatitis, cirrhosis, and the increasingly prominent metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH). With improved prevention and control of viral hepatitis and the increasing burden of metabolism-related liver diseases, the etiological composition and disease spectrum of HCC exhibit continuous evolution and significant heterogeneity ^[1].

In clinical practice, the majority of hepatocellular carcinoma (HCC) patients are diagnosed at intermediate or advanced stages and often present with varying degrees of hepatic dysfunction. This condition partially limits the efficacy of radical local therapies and imposes higher requirements on the safety and tolerability of systemic treatments ^[2].

At the biological level, high-throughput sequencing and multi-omics integration studies have demonstrated that hepatocellular carcinoma (HCC) is not a single disease entity but rather consists of multiple tumor subpopulations with systematic differences in driver gene events, differentiation status, metabolic characteristics, and tumor microenvironment (TME) [3-5]. This multidimensional heterogeneity not only determines tumor invasion behavior and patient survival outcomes but also profoundly influences the efficacy of targeted therapy, immunotherapy, and metabolic interventions. Therefore, systematic molecular and biological typing of HCC is a critical prerequisite for understanding its heterogeneity and advancing precision systemic treatment strategies [6,7].

2. Functional molecular subtypes and biological characteristics of hepatocellular carcinoma

The molecular subtyping of early hepatocellular carcinoma is primarily established based on transcriptomic studies, such as Boyault's G1-G6 subtyping, Hoshida's S1-S3 subtyping, and Chiang's five-category classification system. Subsequently, multi-omics integrated studies have further systematically refined and functionally annotated these subtypes [8]. Different subtypes exhibit highly consistent and reproducible systematic differences in driver gene profiles, activation status of key signaling pathways, genomic stability, epigenetic regulatory background, tumor microenvironment composition, and metabolic phenotypes, which are closely associated with histological differentiation degree, clinical aggressiveness, and treatment sensitivity [9]. The following section focuses on hepatocellular carcinoma subtypes that have been repeatedly validated across multiple independent studies, demonstrating clear biological significance and potential clinical translational value.

2.1. Wnt/ β -catenin activation type: Carcinogenic signal-driven and immune rejection phenotype

This subtype has been repeatedly identified across multiple typing systems (e.g., Boyault's G5/G6, Chiang's CTNNB1-related class, and Hoshida's S3). The classic molecular feature involves mutations in the hot region of CTNNB1 (encoding β -catenin), such as in exon 3, which lead to β -catenin stabilization and nuclear translocation, subsequently activating the expression of downstream Wnt/ β -catenin signaling genes (e.g., GLUL, LGR5, AXIN2) [10].

At the histological level, this subtype predominantly manifests as moderately to highly differentiated tumors, with some retaining hepatocyte-specific metabolic functions, relatively low cellular proliferative activity, and overall high genomic stability [11]. Although its growth rate may be relatively slow, it exhibits a highly characteristic immune rejection state from an immunological perspective.

Extensive studies have demonstrated that Wnt/ β -catenin-activated hepatocellular carcinoma (HCC) is typically associated with significantly reduced immune cell infiltration, exhibiting an immune-excluded or immune-desert phenotype. Mechanistic research suggests that Wnt signaling may limit effector T cell infiltration into the tumor core by suppressing chemokine expression and impairing dendritic cell (DC) recruitment and antigen presentation function, thereby leading to primary resistance to PD-1/PD-L1 immune checkpoint inhibitors (ICI). However, single-cell transcriptomics and spatial transcriptomics studies further reveal significant spatial structural and cellular state heterogeneity within this subtype [12]. Consequently, this subtype is widely regarded as a critical research model for exploring Wnt pathway regulation, tumor microenvironment (TME) remodeling, and immunotherapy combination strategies.

2.2. Proliferative/chromosomal instability type: Genomic aberration-driven highly aggressive phenotype

This subtype roughly corresponds to Boyault's G1~G3, Chiang's proliferation type, and Hoshida's S1/S2 subtypes. Its core molecular characteristics include significant upregulation of genes related to cell cycle regulation and DNA damage repair, TP53 mutations, and widespread chromosomal copy number variations [13,14].

Furthermore, this subtype is often associated with amplification or aberrant activation of proto-oncogenes such as

MYC, CCND1, and FGF19/FGFR4, which further drive rapid tumor cell proliferation, invasive growth, and treatment resistance [13–15]. Multiple large-scale multi-omics studies, including TCGA, have consistently demonstrated the high concordance of this subtype across genomic, transcriptomic, and clinical outcomes. Its hallmark features include poor prognosis, significantly elevated risk of early recurrence, and pronounced heterogeneity in response to systemic therapy [13].

In terms of histological and clinical characteristics, this subtype predominantly exhibits poorly differentiated status, with a higher incidence of vascular invasion and satellite nodules, often accompanied by elevated serum alpha-fetoprotein (AFP) levels [16,17]. From a treatment dependency perspective, these tumors are highly dependent on proliferative, vascular, and growth signaling pathways, making multi-target tyrosine kinase inhibitors (TKIs) and anti-angiogenic therapies (e.g., VEGF/VEGFR inhibitors) potentially beneficial for patients. However, due to widespread signal pathway redundancy and compensatory activation, single-targeted agents often fail to maintain long-term efficacy, necessitating exploration of combination or sequential cross-pathway inhibition strategies based on subtype matching [15,18]. Notably, the FGF19-FGFR4 pathway demonstrates clear targeting potential in patients with specific molecular backgrounds, representing one of the key directions in current translational research and clinical trials [19].

2.3. Metabolic/Hepatocyte-like phenotype: Differentiation lineage and metabolic program characteristics

Metabolic status serves as a critical dimension for understanding the biological heterogeneity and therapeutic response of hepatocellular carcinoma (HCC). Metabolic/hepatocyte-like subtypes typically retain or partially retain hepatocyte-specific metabolic functions, including cytochrome P450 (CYP) enzyme system activity, bile acid metabolism, and fatty acid oxidation capacity. These tumors exhibit higher histological differentiation, relative genomic stability, and generally favorable prognosis [20]. In contrast, certain HCC cases demonstrate significant metabolic reprogramming features, such as enhanced glycolytic pathways or abnormal activation of specific lipid metabolism routes. Such tumors are often associated with activation of pro-proliferative and dedifferentiation signaling pathways, including PI3K/AKT/mTOR, NOTCH, and TGF- β , and are closely linked to aggressive phenotypes and poor prognosis.

The integration of single-cell sequencing with multi-omics studies enables the identification of subtypes with strong metabolic-immune coupling, such as glycan-HCC, characterized by glycosylation-related pathways or lipid-HCC, dominated by abnormal lipid metabolism. These findings suggest that tumor metabolic states can shape the immune microenvironment through multiple mechanisms and influence treatment sensitivity [20–23]. Consequently, metabolic targeted therapies and metabolic-immune combination interventions are increasingly becoming key research directions for this type of hepatocellular carcinoma.

2.4. Immune and microenvironment-dominant type: Structural features of tumor microenvironment and immune ecology characteristics

The tumor microenvironment is one of the key factors driving the heterogeneity of hepatocellular carcinoma (HCC) and exerts a decisive influence on its immunological phenotype. From an immunological ecology perspective, HCC exhibits a continuum ranging from immune-hot (characterized by abundant activated CD8⁺ T cells, activated dendritic cells (DCs), and NK cells accompanied by IFN- γ signaling) to immune-excluded or immune-desert states (where immune cells are obstructed by dense stroma or abnormal vascular architecture) [24].

Patients with immune-hot tumors are generally more likely to benefit from immune checkpoint inhibitors (ICIs) monotherapy or ICI combination therapy with anti-angiogenic agents. In contrast, immune-cold or immune-excluded tumors exhibit limited efficacy of single ICI therapies due to tumor-associated fibroblasts (CAF)-mediated stromal barriers, enrichment of immunosuppressive myeloid cells, and abnormal vascular architecture, which hinder effective infiltration of effector immune cells into the tumor core [25]. Studies have demonstrated that the immune-vascular combination strategy (atezolizumab + bevacizumab) significantly improves overall survival and progression-free survival in patients with unresectable hepatocellular carcinoma, establishing a robust clinical foundation for tumor microenvironment (TME)-

guided therapy^[26].

There is a clear coupling relationship between molecule-driven events and TME status. For instance, CTNNB1 activation is typically associated with immune rejection phenotypes, while proliferative/chromosomal instability tumors are more likely to exhibit enhanced VEGF-A/VEGFR signaling and an immunosuppressive microenvironment^[27]. Therefore, systematically incorporating TME features into the classification framework can facilitate more accurate prediction of ICI and targeted therapy efficacy, while providing critical biological insights for elucidating drug resistance mechanisms^[28].

3. Limitations of current systemic therapies against molecular heterogeneity

3.1. Impact of molecular and immune heterogeneity on systemic therapeutic efficacy

The multidimensional heterogeneity of hepatocellular carcinoma directly leads to significant differences in systemic treatment responses among various subtypes. The Wnt/ β -catenin activated type, immune-hot/immune-cold type, metabolic reprogramming type, and proliferative/chromosomal instability type exhibit fundamental distinctions in tumor microenvironment (TME) characteristics and pathway dependence, profoundly influencing the therapeutic efficacy of immune checkpoint inhibitors (ICI) and targeted therapies^[25]. Taking the Wnt/ β -catenin activated subtype as an example, its inadequate intratumoral T-cell infiltration and impaired dendritic cell (DC) recruitment partially explain its inherent resistance to PD-1/PD-L1 therapy^[29,30]. Therefore, reliance solely on traditional clinical or pathological indicators fails to adequately account for heterogeneous responses to systemic treatments across patients, highlighting the necessity of incorporating molecular and immunological subtypes into clinical classification systems.

3.2. Mechanisms of targeted therapy resistance and the necessity of combination therapy

Multitarget TKIs (such as sorafenib and lenvatinib) have partially improved survival outcomes in patients with advanced hepatocellular carcinoma (HCC), but their efficacy is often limited by tumor clone evolution, compensatory activation of signaling pathways, and drug resistance mediated by factors such as the tumor microenvironment (TME). Proliferative/chromosomal instability tumors typically exhibit multiple driver pathways (including VEGF, FGF19/FGFR4, PI3K/AKT/mTOR, and RAS/MAPK), with compensatory activation among pathways and tumor stem cell characteristics collectively contributing to rapid failure of single TKI therapy^[31]. Additionally, redistribution of immunosuppressive cells within the TME, cytokine imbalance, and enhanced stromal barriers promote TKI and immune checkpoint inhibitor (ICI) resistance to varying degrees, particularly in immunosuppressive or immune-rejection HCC^[24].

The REFLECT study (lenvatinib versus sorafenib) demonstrated that, despite comparable overall efficacy, significant variations in benefit levels were observed among different patients, further highlighting the necessity of stratification strategies to identify more suitable treatment populations^[32]. Therefore, stratification-based combination therapies with cross-pathway inhibitors or sequential treatment strategies, as well as combination therapies targeting both tumor cells and the microenvironment, represent key approaches to overcoming hepatocellular carcinoma resistance.

3.3. Bottlenecks in the translation of molecular subtyping into clinical decision-making

Although classification systems such as those developed by Boyault, Hoshida, and Chiang have been repeatedly validated in both biological and predictive aspects, they have not yet been widely incorporated into routine clinical guidelines or transformed into standardized clinical decision-making tools^[31]. Key limitations include heterogeneity across different study cohorts, lack of unified and operational biomarker detection standards, and insufficient prospective validation data. To achieve a precision treatment pathway encompassing “classification-treatment matching-dynamic monitoring-real-time adjustment,” it is imperative to establish classification methods implementable on clinical testing platforms and conduct systematic prospective validation in multicenter cohorts^[28].

4. Precision systematic treatment strategy for hepatocellular carcinoma based on molecular subtyping

4.1. Individualized immunotherapy strategies based on immunotypic analysis

Precision immunotherapy should be based on accurate identification of immune subtypes in hepatocellular carcinoma. By integrating immune activity scores, ICI-related gene signatures, and molecular subtyping information, it is possible to more accurately predict ICI benefit populations and guide personalized immunotherapy regimens. For immune-hot tumors, ICI monotherapy or ICI combined with anti-angiogenic therapy is typically the first-line approach. In contrast, for non-inflammatory (non-inflamed) tumors, particularly immune-rejection subtypes with high Wnt signaling, monotherapy with ICI alone is often insufficient to restore effector T cell function. Combined strategies, such as ICI combined with anti-VEGF, anti-TGF- β agents, or therapies promoting dendritic cell (DC) recruitment and activation, are preferred to enhance T-cell infiltration and improve immune responses^[25,33]. Emphasizing standardized detection of candidate biomarkers (e.g., CTNNB1 status, immune cell infiltration characteristics, and IFN- γ -related signatures) will facilitate the practical application of immune subtyping in clinical decision-making^[12].

4.2. Targeted combination therapy strategy guided by molecular driving pathways

Targeted combination therapy with subtype-specific matching for specific driver pathways is one of the core strategies for achieving precision systemic treatment. For proliferative/chromosomal instability tumors, given the significant activation of VEGF-A/VEGFR and FGF19/FGFR4 pathways, the combination of VEGF inhibitors with ICI or the introduction of FGFR4 inhibitors in FGF19-positive patients may provide additional benefits by improving the tumor microenvironment (TME) and enhancing immune responses^[34]. In the Wnt-high subtype, although direct inhibition of the Wnt pathway remains technically challenging, immune rejection can be indirectly overcome through downstream effect modulation, RNA interference strategies, or combined TME remodeling approaches^[35]. Overall, a rational combination of molecular targeting and immunomodulation must be based on robust biological evidence and validated for safety and efficacy through prospective clinical trials.

5. Conclusion

In summary, hepatocellular carcinoma is not a single disease entity, but rather a highly heterogeneous collection of molecular subtypes formed through the combined effects of multiple molecular driver events and dynamic remodeling of the tumor microenvironment. The molecular classification system established through multi-omics integration systematically delineates the biological characteristics and therapeutic response differences among various subtypes from dimensions such as signaling pathway dependence, immune ecology, and metabolic programs, thereby providing a mechanistic foundation for precision systemic therapy.

Current evidence-based medical studies indicate that traditional treatment models relying on clinical staging and pathological characteristics struggle to explain significant interpatient variability in therapeutic outcomes. Although molecular subtype-guided stratification strategies demonstrate value in optimizing patient selection and improving efficacy prediction, single treatment approaches often fail to sustain long-term efficacy due to factors such as tumor clonal evolution, compensatory activation of signaling pathways, and adaptive remodeling of the microenvironment. Treatment resistance remains a critical factor limiting long-term prognosis.

Therefore, the key to precision therapy lies in establishing an integrated framework of “classification-intervention-monitoring”: developing a standardized and clinically accessible molecular classification system to achieve treatment matching; designing cross-pathway combination intervention strategies based on subtype-driven mechanisms to overcome drug resistance; and leveraging liquid biopsy, single-cell, and spatial multi-omics technologies to enable dynamic monitoring of molecular classification and temporal optimization of treatment strategies.

Overall, the integrated application of molecular typing, tumor microenvironment analysis, and dynamic monitoring constitutes a critical foundation for advancing hepatocellular carcinoma treatment from empirical approaches to mechanism-driven precision medicine, while providing a methodological framework for continuous optimization of therapeutic strategies in intermediate-and advanced-stage patients.

Disclosure statement

The authors declare no conflict of interest.

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Observation on the Efficacy of Budesonide Formoterol Powder Inhalation as an Adjuvant Treatment for COPD Associated with Pulmonary Heart Disease

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Abstract: *Objective:* In this study, we deeply explore the value of budesonide and formoterol powder inhalation as adjuvant therapy for patients with COPD and cor pulmonale. *Methods:* The time node was selected from 2021.5 to 2023.2, and a total of 50 patients were included, all with COPD and pulmonary heart disease. Two groups were divided into two groups by random grouping, taking budesonide formoterol powder inhalation and conventional treatment, respectively, and then the efficacy was compared. *Results:* The treatment effect of the observation group was higher than that of the control group, and the result comparison was $P < 0.05$. The pulmonary function indicators were all higher than those of the control group, $P < 0.05$; the PaCO₂ index of the observation group decreased and was lower than that of the control group; the PaO₂ index increased, and was higher than that of the control group, $P < 0.05$; the incidence of adverse reactions in the observation group was lower than that of the control group, $P < 0.05$. *Conclusion:* When treating COPD patients with cor pulmonale, taking budesonide formoterol powder inhalation can improve the therapeutic effect, improve lung function indicators and PaCO₂ and PaO₂ indices, reduce adverse reactions, and ensure the safety of patients during treatment.

Keywords: Budesonide formoterol powder inhalation; COPD with pulmonary heart disease; Efficacy

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease in the respiratory system. The disease has a high incidence rate and a certain degree of infectivity. The disease has the characteristics of recurrence and is not easy to cure. After the patient develops the disease, he will show symptoms such as cough, sputum, shortness of breath, etc., resulting in damage to his heart and lung function. Therefore, COPD patients with pulmonary heart disease are very common, which harms the patient's normal life and reduces their quality of life. The pathogenesis of COPD with cor pulmonale is very complex. At this stage, clinical treatment is mainly based on drug treatment. The main ingredients are β_2 receptor agonists and glucocorticoids^[1]. Usually, once the drugs contain these two substances, the condition of COPD patients with cor pulmonale will be improved. In recent years, inhalant drugs have become very popular. They can affect the patient's body only through the airway and effectively reduce the patient's gastrointestinal reaction. Therefore, this type of drug is

frequently used by doctors. Budesonide and formoterol powder inhalation is one of these drugs. After the drug enters the patient's body, it fully exerts its corresponding effect, which can not only ensure the safety of the patient's use of the drug, but also ensure the therapeutic effect^[2]. Based on this, this article focused on a group study of 50 COPD patients with cor pulmonale. The two groups of patients received different treatment methods, focusing on exploring the therapeutic effect of budesonide and formoterol powder inhalation. The report is as follows.

2. Materials and methods

2.1. General information

The time node was selected from 2021.5 to 2023.2, and a total of 50 patients were included, and they were divided into two groups by random grouping. In the control group, there were 13/12 male and female cases; the age range was 49 to 77 years old, with an average age of (59.57 ± 9.65) years; in the observation group, there were 14/11 male and female cases; the age range was 50 to 79 years old, with an average age of (59.67 ± 14.31) years. Comparison of baseline data between the 2 groups: $P > 0.05$.

Inclusion criteria: (1) All patients meet the diagnostic criteria for COPD with cor pulmonale; (2) Have not taken glucocorticoids, β_2 receptor agonists and other drugs in the recent past; (3) Patients are informed of this study and sign an informed consent form.

Exclusion criteria: (1) Patients with severe respiratory infections; (2) Patients who have taken glucocorticoids, β_2 receptor agonists and other drugs without authorization in the recent past; (3) Patients have severe cardiovascular disease or severe liver and kidney dysfunction; (4) Patients are allergic to the drugs in this study.

2.2. Treatment methods

The control group received conventional symptomatic treatment, including anti-infection, acid-base, and electrolyte supplementation^[3]. At the same time, measures such as antiasthmatic, oxygen inhalation, and expectoration are implemented according to the patient's specific symptoms.

On the basis of the control group, patients in the observation group were additionally treated with budesonide and formoterol powder inhalation. Among them, the budesonide formoterol powder inhalation is produced by AstraZeneca AB^[4], with the national drug approval number HJ20140458. Specifications: Each inhalation contains 320 μg of budesonide and 9.0 μg of formoterol fumarate. It is treated by inhalation, twice a day, and rinsing the mouth with water after completion.

A course of treatment lasts for 7 days, and patients in both groups continued to receive treatment for 3 courses.

2.3. Observation indicators

- (1) Treatment effect: Markedly effective: The patient's symptoms are eliminated and all lung function test indicators are normal; Effective: The symptoms are significantly relieved, but there are still slight abnormalities in lung function indicators, and continuous medication is required; Ineffective: There is no significant change in symptoms and lung function indicators before and after treatment.
- (2) Lung function indicators: including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and rate in one second ($\text{FEV1}/\text{FVC}$)^[5].
- (3) Blood gas indicators: including arterial blood carbon dioxide partial pressure (PaCO_2), arterial blood oxygen partial pressure (PaO_2)
- (4) Adverse reactions: Statistics include nausea, headache, dizziness, infection, etc.

2.4. Statistical methods

The SPSS 26.0 software was used to process the data involved in the study. Measurement data were expressed as "mean $\pm$

standard deviation (SD)” and tested by “*t*”; count data were expressed as “[n/(%)]” and tested by “ χ^2 ”. $P < 0.05$ indicated that the difference was significant.

3. Results

3.1. Treatment effects of two groups of patients

The total probability of treatment effect for patients in the observation group is 96.00%, which is obviously 76.00% higher than that of the control group. The difference is $P < 0.05$. See **Table 1** for details.

Table 1. Treatment effects of two groups of patients

Group	n	Effective	Valid	Invalid	Total probability
Observation group	25	22 (88.00%)	2 (8.00%)	1 (4.00%)	24 (96.00%)
Control group	25	8 (32.00%)	11 (44.00%)	6 (24.00%)	19 (76.00%)
χ^2					4.1528
<i>p</i>					0.0420

3.2. Improvement of lung function in two groups of patients

The FEV1, FVC and FEV1/FVC of the observation group were significantly higher than those of the control group, with a difference of $P < 0.05$. See **Table 2** for details.

Table 2. Pulmonary function index of two groups of patients

Group	FEV1(L)		FVC(L)		FEV1/FVC(%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n = 25)	0.85 ± 0.15	1.86 ± 0.24	1.54 ± 0.53	2.34 ± 0.45	46.54 ± 4.45	66.75 ± 5.46
Control group (n = 25)	0.86 ± 0.21	1.49 ± 0.27	1.52 ± 0.56	1.96 ± 0.42	46.52 ± 4.73	61.43 ± 5.85
<i>t</i>	0.1937	5.1211	0.1296	3.0866	0.0153	3.3241
<i>p</i>	0.8472	0.0000	0.8973	0.0034	0.9878	0.0017

3.3. Blood gas indicators of two groups of patients

The PaCO₂ index of the patients in the observation group decreased and was lower than that of the control group; the PaO₂ index increased and was higher than that of the control group, with a difference of $P < 0.05$. See **Table 3** for details.

Table 3. Blood gas indicators of the two groups of patients

Group	n	PaCO ₂		PaO ₂	
		Before intervention	After intervention	Before intervention	After intervention
Observation group	25	7.56 ± 1.35	5.45 ± 0.68	6.79 ± 1.36	9.86 ± 0.68
Control group	25	7.78 ± 1.36	6.64 ± 0.74	6.84 ± 1.47	8.79 ± 0.75
<i>t</i>		0.5740	5.9204	0.1248	5.2846
<i>p</i>		0.5686	0.0000	0.9012	0.0000

3.4. Adverse reactions of patients in the two groups

The total probability of adverse reactions in the observation group was 4.00%, which was significantly lower than the

28.00% in the control group. The difference was $P < 0.05$. See **Table 4** for details.

Table 4. Adverse reactions of patients in the two groups

Group	n	Disgusting	Dizziness	Headache	Infection	Total probability
Observation group	25	1 (4.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Control group	25	2 (8.00%)	1 (4.00%)	3 (12.00%)	1 (4.00%)	7 (28.00%)
χ^2						5.3571
p						0.0210

4. Conclusion

COPD with cor pulmonale is a chronic inflammatory disease involving multiple systems, with complex pathological mechanisms and diverse clinical manifestations. The core feature of this disease is extensive inflammatory infiltration in pulmonary blood vessels, alveoli, and airways. These inflammatory reactions will continuously release pro-inflammatory factors such as leukotrienes and IL-8, leading to airway remodeling, increased pulmonary vascular resistance, and progressive decline in lung function. Patients often present with persistent cough, sputum production, dyspnea and other symptoms. In severe cases, they can develop into respiratory failure and right ventricular dysfunction, which greatly affects the patient's quality of life [6]. From the perspective of pathogenesis, COPD with cor pulmonale is the result of multiple factors such as genetic susceptibility, environmental exposure, and immune regulation imbalance. This complex etiological background makes the development of treatment options face many challenges. Although there are currently a variety of clinical treatments such as bronchodilators, glucocorticoids, and oxygen therapy, the treatment effects are often difficult to achieve expectations due to individual differences, drug tolerance, adverse reactions, and other issues. In addition, long-term use of certain drugs may lead to the development of drug resistance and even potential damage to liver and kidney function, further limiting treatment options [7]. With the development of precision medicine and molecular biology technology, treatment strategies for COPD with cor pulmonale are gradually moving towards individualization and targeting. Cutting-edge technologies such as biomarker-based drug screening, the development of new anti-inflammatory drugs, and gene therapy provide new possibilities for improving patient prognosis. In the future, how to minimize drug side effects while ensuring efficacy will become the core goal of clinical research. Through multidisciplinary collaboration and in-depth exploration of evidence-based medicine, it is expected to provide patients with safer and more durable treatment options, thereby significantly improving their quality of life and prolonging their survival.

The treatment of COPD with pulmonary heart disease mainly focuses on controlling the symptoms of the disease, reducing the probability of potential dangers as much as possible, and comprehensively improving the patient's physical fitness and exercise endurance. In the treatment of COPD with cor pulmonale, oral medication is a very effective treatment method, and the inhaled method can allow the drug to have corresponding effects on the patient's airway. Budesonide and formoterol powder inhalation is an innovative compound drug for respiratory diseases such as chronic obstructive pulmonary disease (COPD) and pulmonary heart disease. Its unique design combines the dual action mechanisms of budesonide and formoterol, which significantly improve the therapeutic effect through synergistic effects, optimize the drug's onset speed and duration of action, and provide patients with a more efficient treatment plan [8]. Budesonide, a potent glucocorticoid, plays a key role in the management of lung inflammation. It can directly act on inflammatory cells and inhibit the release of inflammatory factors, thereby reducing lung tissue damage. In addition, budesonide's stabilizing effect on mast cells further inhibits the production of inflammatory mediators and significantly improves airway patency. This mechanism is particularly important in COPD patients because it can effectively reduce airway hyperresponsiveness and reduce the risk of acute exacerbation, thereby improving the patient's quality of life. Formoterol is a long-acting β_2 receptor agonist that rapidly expands the bronchi and improves the patient's respiratory function

by enhancing the transcriptional expression function of β_2 receptors. Its unique hydrophilic and lipophilic properties enable it to rapidly penetrate into target tissues and maintain stable drug concentrations over a longer period of time. This property not only improves the bioavailability of the drug but also reduces the patient's medication frequency and improves treatment compliance. The mechanism of action of formoterol is not limited to bronchodilation. It can also activate adenylyl cyclase to convert adenosine triphosphate (ATP) into cyclic adenosine monophosphate (cAMP), thereby relaxing vascular smooth muscle and improving pulmonary hemodynamics. This process helps relieve patients' dyspnea symptoms, effectively reduces pulmonary hypertension, and reduces the pathological burden of pulmonary heart disease. Budesonide formoterol powder inhalation delivers the drug directly to the lungs via inhalation, maximizing its local effects while minimizing systemic side effects. This method of administration not only improves the targeting of the drug, but also reduces the distribution of the drug throughout the body, thereby reducing potential adverse reactions^[9]. The drug's dual-effect mechanism not only significantly improves the patient's lung function, but also provides patients with a more comprehensive therapeutic effect by reducing inflammatory reactions and relieving airway obstruction symptoms. Moreover, both drugs have the effect of dilating the trachea and anti-inflammatory. When used together, the drug effects can overlap and have a better effect of relieving cough and resolving phlegm. Patients will also have fewer side effects after inhalation. Through group comparison in this study, it was found that the efficacy of conventional treatment is still mainly limited to improvement of typical symptoms such as dyspnea and edema, and it is also helpful to improve the survival rate in the acute phase. However, the medication in the observation group was extremely helpful in suppressing airway inflammation and reducing mucosal edema, delaying the progression of COPD from the source, thereby indirectly reducing the possibility of progression of arterial hypertension. This differentiation obviously provides a reliable basis for this adjuvant treatment^[10]. Therefore, from a review of the overall clinical treatment status in the past, conventional treatment emphasizes life-saving as the basis, while focusing on controlling heart failure and preventing acute attacks. It is also the current irreplaceable basic treatment measure for COPD with pulmonary heart disease.

In summary, the most important value of adjuvant budesonide and formoterol lies in the long-term control and management of the disease. For example, after conventional treatment, anti-inflammatory airway expansion can delay the progression of the disease. Therefore, the optimal strategy is not to choose one of the two, but to add it to the conventional treatment. The effect of the auxiliary application is obviously better.

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Advances in Polymerase Engineering and Their Biotechnological Applications

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Abstract: DNA and RNA polymerases are essential enzymes responsible for nucleic acid replication, transcription, and amplification, and they play indispensable roles in molecular biology, biotechnology, and synthetic biology. However, the natural properties of polymerases are often limited by their evolutionary origins, resulting in constraints in catalytic efficiency, substrate compatibility, thermostability, and replication fidelity. In recent years, advances in protein engineering and structural biology have enabled the development of diverse strategies to enhance polymerase performance. This review summarizes recent progress in polymerase engineering aimed at structural optimization and functional enhancement. Major engineering strategies, including directed evolution, rational and semi-rational design, computational protein engineering, and domain fusion approaches, are discussed in terms of their principles and applications. In addition, the rapidly expanding applications of engineered polymerases are highlighted, particularly in molecular diagnostics, enzymatic DNA synthesis, artificial genetic systems, and medical and industrial biotechnology. Overall, the continuous integration of high-throughput screening technologies, structural analysis, and artificial intelligence-assisted design is expected to accelerate the development of next-generation polymerases with improved performance and expanded catalytic capabilities. These advances will further promote innovations in synthetic biology, nucleic acid diagnostics, genome engineering, and the development of novel biotechnological tools.

Keywords: Polymerase engineering; Directed evolution; Rational design; Synthetic biology; Molecular diagnostics

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1. Introduction

Polymerases are a class of essential enzymes involved in nucleic acid metabolism, playing critical roles in DNA replication, RNA transcription, and in vitro nucleic acid amplification. Owing to their catalytic capability in synthesizing nucleic acids with high specificity and efficiency, polymerases have been widely applied in basic molecular biology research, clinical diagnostics, genome sequencing, and synthetic biology^[1–3]. For example, Taq DNA polymerase, which exhibits excellent thermostability, plays an indispensable role in PCR amplification^[4]. Phi29 DNA polymerase, characterized by its strong strand-displacement activity and proofreading capability, has been extensively used in single-cell whole-genome amplification^[5]. In addition, T7 RNA polymerase occupies an irreplaceable position in in vitro transcription systems due to its high transcription efficiency and promoter specificity^[6].

However, the functionality of natural polymerases is often constrained by their evolutionary origins and physiological

environments. As a result, many polymerases exhibit limitations in substrate recognition range, thermal stability, catalytic rate, extension capability, and replication fidelity ^[7]. For instance, some polymerases are prone to thermal inactivation at elevated temperatures, restricting their applications in complex biochemical environments. Conversely, certain high-fidelity polymerases maintain replication accuracy at the expense of reduced catalytic speed. These trade-offs between structural stability and catalytic efficiency limit the broader application of polymerases in emerging biotechnological fields. Consequently, engineering polymerases to improve their catalytic properties has become an important research direction in protein engineering and synthetic biology. With the rapid development of structural biology, computational modeling, and high-throughput screening technologies, a variety of polymerase engineering strategies have been developed. Directed evolution enables high-throughput screening of polymerase variants by establishing a physical linkage between genotype and phenotype ^[8]. Rational and semi-rational design, guided by three-dimensional structural information, conserved sequence analysis, and energy calculations, allows precise prediction of beneficial mutation sites to improve catalytic efficiency or structural stability. In addition, domain engineering and terminal truncation strategies can modulate spatial conformation and interdomain interactions, thereby improving polymerase processivity and template-binding efficiency ^[9].

In this review, we summarize recent advances in the structural engineering and functional enhancement of polymerases. First, major strategies for polymerase engineering are discussed, including directed evolution, rational and semi-rational design, and structure-guided computational approaches. These strategies provide powerful tools for improving catalytic activity, stability, fidelity, and substrate adaptability. Subsequently, we highlight the emerging applications of engineered polymerases in molecular diagnostics, enzymatic DNA and XNA synthesis, and medical and industrial biotechnology. Understanding these advances not only provides insights into the structure–function relationships of polymerases but also offers guidance for the future design of high-performance enzymes for diverse biotechnological applications.

2. Major strategies for polymerase engineering

With the rapid development of protein engineering and bioinformatics, researchers have increasingly explored strategies to improve polymerase performance and expand their functional capabilities through structural optimization. Various approaches have been developed to engineer polymerases, among which directed evolution and rational or semi-rational design represent the two most widely used strategies ^[10]. Each method has its own advantages and limitations. In practical research, these strategies are often applied in combination to achieve more efficient and targeted polymerase engineering.

2.1. Directed evolution

Directed evolution is one of the most classical and widely used strategies for enzyme engineering. This approach introduces mutations into proteins lacking detailed structural information through methods such as random mutagenesis, DNA recombination, and saturation mutagenesis, thereby generating large mutant libraries from which improved variants can be selected through high-throughput screening ^[11,12]. Common mutagenesis techniques used in directed evolution include error-prone PCR, chemical mutagenesis, DNA shuffling, and saturation mutagenesis. One major advantage of directed evolution is its minimal dependence on structural knowledge. It enables the discovery of beneficial mutations that are often difficult to predict through rational design approaches, particularly for improving catalytic activity. However, directed evolution also has several limitations. The experimental workload can be substantial, screening efficiency may be relatively low, and beneficial mutations obtained through random mutagenesis are sometimes difficult to interpret mechanistically. Therefore, this strategy is often most suitable for random optimization of enzyme performance within established screening systems and experimental conditions.

In recent years, several innovative directed evolution methods have been developed, greatly accelerating polymerase engineering. Techniques such as compartmentalized self-replication (CSR) and orthogonal replication systems have significantly expanded the capabilities of polymerase evolution. Compartmentalized self-replication (CSR) is an efficient

in vitro directed evolution method that encapsulates individual genes and their expression products within water-in-oil emulsion droplets, forming microreactors. In this system, each gene encoding a polymerase variant is transcribed and translated within a separate droplet, and the resulting polymerase catalyzes the replication of its own encoding gene. Only polymerase variants with sufficiently high catalytic activity can produce enough copies of their genes to survive subsequent rounds of selection and amplification. Using isothermal CSR, Povilaitis et al.^[13] successfully evolved phi29 DNA polymerase variants with improved catalytic activity and stability. Abil et al.^[14] developed the compartmentalized partnered replication (CPR) strategy for directed evolution of genetic elements and circuits, providing a framework for evolving complex biological systems. CSR-based approaches have been widely applied to polymerase engineering, including improving the performance of *Thermus thermophilus* DNA polymerase I^[15] and investigating the salt tolerance of phi29 DNA polymerase using microfluidic platforms^[16]. In addition, in vitro CSR-based directed evolution of *Thermus aquaticus* DNA polymerase produced mutants capable of translesion synthesis, enabling DNA replication across damaged templates^[17]. Subsequent studies by Naccache^[18,19] and Dramé-Maigné^[20,21] further demonstrated the enormous potential of CSR for ultra-high-throughput screening and evolution of strand-displacing polymerases and other enzymes.

To achieve continuous and autonomous evolution in complex cellular environments, researchers have also developed orthogonal replication systems. These systems operate within host cells but remain independent of the host genome, thereby providing a dedicated evolutionary platform for target genes. Diercks et al.^[22] constructed an orthogonal T7 replication system that enables continuous hypermutation and rapid evolution in *Escherichia coli*, representing a new strategy for in vivo directed evolution. Similarly, Ma and Lin^[23] achieved orthogonal RNA replication in mammalian cells, representing a major breakthrough that enables directed evolution within more complex eukaryotic cellular environments.

Directed evolution is increasingly being integrated with emerging genome-editing technologies such as CRISPR, enabling more precise and efficient mutagenesis and screening. For example, Chen et al.^[24] developed a CRISPR–DNA polymerase-assisted targeted mutagenesis system that allows controllable laboratory evolution by introducing genetic diversity at specific genomic loci. In addition, Pu et al.^[25] engineered split RNA polymerases through directed evolution to construct multifunctional biosensor platforms, demonstrating the potential of polymerase engineering in biosensing applications.

Directed evolution has led to remarkable advances in polymerase functional expansion and performance optimization, significantly influencing the development of synthetic biology and chemical biology^[26]. For example, Maola et al.^[27] successfully obtained an efficient threose nucleic acid (TNA) polymerase through homologous recombination and directed evolution, thereby expanding the chemical boundaries of genetic materials. Directed evolution has also been used to alter the promoter recognition specificity of bacteriophage RNA polymerases^[28], improve the salt tolerance of phi29 DNA polymerase^[16], and systematically expand the functionality of T7 RNA polymerase to meet diverse demands for in vitro nucleic acid synthesis^[29].

In the future, as research into fundamental questions related to the origin of life—such as RNA replication and RNA polymerase ribozymes^[30] continues to deepen, and as universal intracellular evolution platforms become more sophisticated, engineered polymerases are expected to play increasingly important roles in synthetic biology, disease diagnostics, drug development, and the exploration of fundamental biological principles.

2.2. Rational and semi-rational design

In contrast to directed evolution, rational and semi-rational design strategies rely on structural insights and computational analyses to guide targeted mutations. By integrating information from protein three-dimensional structures, bioinformatics analysis, and molecular dynamics simulations, researchers can predict mutation sites that are likely to improve enzyme performance. Through detailed analysis of polymerase structure and catalytic mechanisms, both residues near the active site and distal residues involved in structural stability can be rationally optimized. Common rational and semi-rational strategies used in polymerase engineering include structure- and energy-based computational design, domain fusion and terminal truncation engineering, and hotspot prediction based on sequence conservation analysis. These approaches

provide a systematic framework for improving polymerase activity, stability, fidelity, and substrate recognition.

2.2.1. Structure- and energy-based computational design

Computational approaches based on structural and energetic analyses not only provide powerful tools for mechanistic investigation but also actively guide polymerase engineering. By integrating three-dimensional protein structures with energy evaluation models, these strategies enable the prediction of how specific mutations influence conformational stability and catalytic performance. At the atomic level, such computational methods facilitate detailed analysis of the structure–function relationships of polymerases, their conformational dynamics, and their interactions with substrates or inhibitors. These insights provide a theoretical framework for the precise and efficient optimization of enzyme stability, catalytic activity, fidelity, and specificity.

Significant progress has been achieved using computational design for improving enzyme stability and activity. For example, by combining iterative mutagenesis with computational design, researchers successfully optimized both the expression level and thermal stability of terminal deoxynucleotidyl transferase (TdT). In another study, computational protein design was used to generate a TdT variant exhibiting both high thermostability and high catalytic activity, enabling the synthesis of long de novo DNA molecules. These studies complement previous computational investigations aimed at improving the stability and practical applications of thermophilic DNA polymerases. In addition, structure-guided engineering has been used to enhance the performance of polymerases in specific biotechnological applications. Based on detailed structural insights, researchers successfully engineered a novel DNA polymerase from *Clostridium thermocellum*, significantly improving its performance in loop-mediated isothermal amplification (LAMP) assays. Together with semi-rational evolution strategies and programmable site-directed mutagenesis techniques with single-amino-acid precision^[9], these computational approaches constitute a powerful toolbox for the targeted engineering of polymerases.

2.2.2. Domain fusion and terminal truncation strategies

Domain fusion is a commonly used strategy in polymerase engineering, in which exogenous protein domains are introduced into the original polymerase structure to improve enzyme solubility, expression level, stability, and catalytic performance. One frequently used fusion partner is Sso7d, a small DNA-binding protein derived from Hyperthermophilic archaea. Fusion of Sso7d with high-fidelity Pfu DNA polymerase or the widely used Taq DNA polymerase has been shown to significantly enhance amplification efficiency and increase the length of amplified DNA products. Špibida et al. fused the DNA-binding domain of *Pyrococcus furiosus* DNA ligase to Taq Stoffel polymerase, generating an engineered enzyme capable of efficiently amplifying complex DNA templates^[31]. Similarly, Maksum et al. reported that fusion of an N-terminal maltose-binding protein (MBP) tag enabled soluble overexpression of *Thermus thermophilus* (Tth) DNA polymerase in *Escherichia coli*^[32]. In addition, fusion with proteins possessing specific functional properties can generate multifunctional chimeric enzymes or significantly enhance polymerase performance. For example, Fei et al. demonstrated that fusion of Taq DNA polymerase with the CL7 protein from *E. coli* markedly improved DNA amplification efficiency^[33].

Terminal truncation is another commonly used strategy for polymerase engineering. By removing regions at the N-terminus or C-terminus, truncation can improve protein expression levels, eliminate non-essential structural regions, enhance protein solubility, and, in some cases, increase polymerase fidelity. Villbrandt et al. generated two N-terminal truncation variants of Taq DNA polymerase: $\Delta 288$, lacking the first 288 amino acids, and $\Delta 413$, lacking the first 413 amino acids^[34]. Both truncated enzymes retained polymerase activity; however, the $\Delta 413$ variant showed significantly reduced specific activity and thermostability. Sethy et al. engineered several terminal deoxynucleotidyl transferase (TdT) variants by deleting approximately 140 amino acids from the N-terminus^[35]. This truncation significantly improved expression levels, increasing protein yield by 9.5-fold and 23-fold compared with the wild-type enzyme while maintaining similar catalytic efficiency. In another study, Barnes removed 235 amino acids from the N-terminal exonuclease domain of Taq polymerase, which resulted in a twofold increase in replication fidelity.

2.2.3. Hotspot prediction and conservation analysis

semi-rational polymerase engineering. This approach identifies residues that are either critical for enzyme function or tolerant to mutation by comparing evolutionary conservation patterns and structural energy features across homologous sequences. Through multiple sequence alignment, researchers can locate regions that play essential catalytic roles as well as regions that may accommodate mutations, thereby guiding targeted polymerase engineering and performance optimization.

Sequence analyses of multisubunit RNA polymerases have revealed that residues located in the catalytic center are highly conserved, whereas surrounding regulatory regions exhibit greater variability. Consequently, engineering efforts typically focus on low-conservation regions while avoiding highly conserved catalytic residues, thereby minimizing the risk of disrupting the enzyme's active center. Using customized multiple sequence alignment strategies, researchers have successfully improved the performance of Taq DNA polymerase. Conservation-based analysis has also been applied to study viral polymerases. Oany et al. identified highly conserved regions within the RNA polymerase of the Ebola virus through sequence alignment and conservation scoring. Molecular docking analyses further revealed that these conserved residues play key roles in substrate recognition and catalytic activity^[36].

Similarly, comparative sequence analysis combined with molecular dynamics simulations has been used to investigate the structure–function relationships of DNA polymerases in pathogenic fungi. Satpati et al. demonstrated that conserved residues tend to form stable interaction networks at structural interfaces, whereas non-conserved regions are often involved in subunit regulation and conformational flexibility^[37]. These variable regions can therefore serve as promising targets for protein engineering. In practice, conservation-based strategies have been successfully applied in polymerase engineering. For example, conservation-guided design has been used to engineer psychrophilic polymerases optimized for nanopore long-read sequencing, as well as thermophilic polymerases used in synthetic biology applications. These examples highlight the importance of understanding evolutionary conservation patterns when designing polymerase variants with improved performance and novel functionalities.

3. Applications of polymerase functional improvement

3.1. Molecular diagnostics and PCR technologies

With advances in polymerase engineering and structural optimization, the application of polymerases in molecular diagnostics has expanded from conventional PCR to a variety of highly sensitive nucleic acid detection platforms. The fidelity, thermostability, and processivity of polymerases directly affect the sensitivity and specificity of amplification systems. Therefore, recent studies have focused on developing engineered polymerases to support rapid detection, high accuracy, and simplified one-pot diagnostic reactions.

Polymerase stability and amplification efficiency are particularly important for miniaturized diagnostic platforms. Immobilization of polymerases on nanomaterials or mesoporous carriers can improve enzyme thermostability and reaction uniformity, thereby enhancing the robustness of PCR systems. Meanwhile, ultrafast PCR technologies based on plasma heating or microfluidic devices significantly shorten amplification time, enabling rapid nucleic acid detection suitable for point-of-care testing (POCT). In addition, nanoparticle–polymerase interactions can enhance signal amplification and improve detection sensitivity. For instance, polymerase-mediated end-labeling strategies have enabled single-molecule detection of DNA strand breaks, providing new approaches for studying DNA damage and developing ultrasensitive diagnostic methods.

Isothermal amplification technologies have also become important alternatives to conventional PCR because they eliminate the need for complex thermal cycling equipment. Loop-mediated isothermal amplification (LAMP) enables rapid and sensitive detection of bacterial, plant, and animal pathogens due to the strong strand-displacement activity of polymerases. To further improve specificity, probe-based detection strategies and high-resolution melting analysis have been introduced to distinguish single-nucleotide variations. Other isothermal methods, such as helicase-dependent

amplification (HDA) and recombinase polymerase amplification (RPA), further expand polymerase-based diagnostic systems and support rapid field detection.

In recent years, the integration of polymerase-based amplification with CRISPR detection systems has enabled highly sensitive nucleic acid detection without complex instrumentation. These platforms have been applied to the detection of viruses, parasites, and foodborne pathogens, demonstrating strong potential for public health surveillance and emergency diagnostics. In addition, polymerase-driven biosensors and one-pot RT-qPCR systems simplify workflows and enable low-copy nucleic acid detection. With the development of AI-assisted diagnostic platforms and automated detection technologies, polymerase-based molecular diagnostics is expected to become faster, more portable, and increasingly intelligent.

3.2. Enzymatic synthesis of DNA and RNA

With the rapid development of synthetic biology and artificial genetic systems, the functions of polymerases have expanded from conventional DNA replication to the synthesis of artificial DNA and xenonucleic acids (XNAs). Engineered polymerases obtained through rational design or directed evolution often exhibit broader substrate compatibility, improved catalytic efficiency, and enhanced template adaptability, providing important tools for de novo DNA synthesis and the construction of artificial genetic systems.

In enzymatic DNA synthesis, terminal deoxynucleotidyl transferase (TdT) has attracted considerable attention because of its template-independent catalytic activity. Structural analysis and mutagenesis studies have significantly improved the processivity and substrate selectivity of TdT, enabling efficient extension on complex 3'-end substrates. Protein engineering has further enabled TdT to incorporate non-natural nucleotides, expanding its applications in artificial gene synthesis and molecular encoding technologies. For example, directed evolution has produced high-activity TdT variants suitable for commercial enzymatic DNA synthesis, offering a more environmentally friendly alternative to conventional chemical synthesis methods.

Template-dependent polymerase systems have also been developed for controlled DNA synthesis. Polymerase-based strategies combined with modified nucleotides have enabled stepwise DNA synthesis with improved accuracy and efficiency. These approaches have also been applied in emerging areas such as DNA data storage, where high-fidelity polymerases ensure reliable information writing and reading processes. More recently, automated and high-throughput enzymatic DNA synthesis platforms have been developed, significantly improving DNA assembly efficiency and scalability for synthetic biology applications.

Polymerase reactions can also be coupled with cell-free transcription–translation systems to construct artificial replication cycles. Such systems enable repeated information replication and expression *in vitro*, providing experimental models for artificial cells and synthetic life systems. In addition, engineered thermophilic polymerases capable of incorporating modified nucleotides have enabled the synthesis of labeled DNA, artificial RNA molecules, and chemical biology probes.

Beyond natural DNA synthesis, engineered polymerases also play important roles in XNA synthesis. Enzymes such as engineered Phi29 polymerase and XNA polymerases can catalyze the synthesis of various artificial nucleic acids, demonstrating remarkable structural plasticity and substrate adaptability. These systems enable the creation of novel nucleic acid polymers with improved stability and functional diversity. Furthermore, polymerases capable of incorporating chemically modified nucleotides have significantly expanded the chemical diversity of nucleic acid synthesis reactions.

3.3. Applications in medical and industrial fields

Engineered DNA polymerases have shown broad potential in medical diagnostics and industrial detection. In clinical diagnostics, novel viral polymerases identified through metagenomic mining exhibit improved thermostability and broader substrate recognition, enabling the development of highly sensitive RT-PCR detection systems. Several diagnostic platforms have also been developed to simplify nucleic acid testing. For example, portable polymerase-based detection

systems have enabled rapid blood-based detection of the Ebola virus, while simplified RNA extraction and RT-qPCR workflows have significantly reduced the technical barriers for SARS-CoV-2 testing. In addition, single-enzyme RTX-PCR systems that integrate reverse transcription and amplification into one reaction have further improved detection efficiency and accuracy. Advances in detection devices have also enhanced polymerase-based diagnostic platforms. Photothermal temperature-control systems and microfluidic integrated detection platforms allow polymerase amplification reactions to operate under low-power conditions, making them suitable for point-of-care testing (POCT). Furthermore, digital bioluminescent POCT devices based on pyrophosphate signals released during polymerase reactions demonstrate the growing trend toward intelligent and integrated diagnostic technologies.

Protein engineering has further expanded polymerase applications in epigenetic analysis and complex environmental detection. For instance, engineered DNA polymerases capable of recognizing m⁶A modifications provide new approaches for epigenetic sequencing. Charge-engineered polymerases with improved stability under high-salt conditions have also been developed for industrial detection environments. In addition, polymerase-based systems combined with magnetic nanoparticles enable automated signal amplification and detection, while polymerase inhibition effects have been used to develop probe-free methods for quantitative drug analysis, such as heparin detection. Polymerase-driven nanobiotechnology systems also show promise in biomedical research. DNA nanostructures generated through polymerase reactions have been used for long non-coding RNA imaging and cancer therapy, highlighting the potential of nucleic acid nanomaterials in medicine.

Beyond medical diagnostics, polymerase-based nucleic acid detection technologies play important roles in agriculture and environmental monitoring. Portable isothermal amplification systems have been widely applied for rapid detection of plant and animal pathogens in field conditions. Commercial diagnostic platforms and continued advances in polymerase engineering further support the large-scale commercialization of nucleic acid diagnostics. In addition, CRISPR-guided polymerase systems capable of generating targeted mutagenesis *in vivo* provide new opportunities for industrial biotechnology and genome engineering.

4. Conclusion

Polymerase engineering has become a central area of research in protein engineering and synthetic biology. Advances in structural biology, computational modeling, and high-throughput screening technologies have greatly improved our ability to modify polymerases with enhanced catalytic efficiency, stability, fidelity, and substrate compatibility. Strategies such as directed evolution, rational design, domain engineering, and conservation-based mutation analysis have provided powerful approaches for optimizing polymerase performance and expanding their functional diversity. These engineered polymerases have significantly broadened the application scope of nucleic acid technologies. In molecular diagnostics, improved polymerases have enabled highly sensitive PCR, isothermal amplification, and CRISPR-based detection systems. In synthetic biology, engineered polymerases facilitate enzymatic DNA synthesis, artificial genetic systems, and XNA replication. Furthermore, polymerase-based technologies are increasingly applied in medical diagnostics, industrial biotechnology, agriculture, and environmental monitoring. Despite these advances, challenges remain in achieving precise control over enzyme activity, substrate selectivity, and structural stability under complex reaction conditions. Future research combining artificial intelligence-assisted protein design, high-throughput evolution platforms, and structural mechanistic studies will further accelerate the development of next-generation polymerases. Such advances will continue to expand the boundaries of nucleic acid biotechnology and enable innovative applications across diverse scientific and industrial fields.

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Research on the Application of PTFE Material in Medical Devices

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Abstract: This paper systematically studies the application value of tetrafluoroethylene (PTFE) in medical devices based on its special chemical structure and physical properties, with a focus on its advantages such as good biocompatibility, low friction, and stable chemical inertness. In the context of clinical scenarios, the article elaborates on the practical application of PTFE coating technology and porous structure design in the production of medical devices. The study structure shows that proper modification and processing of PTFE can significantly reduce friction between medical devices and human tissues, while enhancing the bonding effect of implants to bones. This paper also analyzes the application techniques of PTFE in medical sealing and reconstructive surgery, providing a corresponding technical basis for understanding the important role of this material in high-end medical equipment.

Keywords: Polytetrafluoroethylene; Expanded polytetrafluoroethylene; Medical devices; Biocompatibility; Surface modification; Interventional devices

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1. Introduction

PTFE (Polytetrafluoroethylene), with excellent comprehensive performance, has become indispensable in modern medical equipment manufacturing macromolecule material. As a perfluorinated polymer, it has a very low coefficient of friction and good biological inertness, and can remain stable for a long time in the complex physiological environment of the human body. The following is a systematic introduction to the material properties of PTFE, as well as its specific application forms and technical points in multiple medical specialties.

2. Introduction to PTFE materials

PTFE is a high-molecular-weight compound formed by the polymerization of tetrafluoroethylene monomers. In its molecular structure, fluorine atoms tightly wrap around carbon chains to form a stable spatial barrier, giving the material excellent chemical stability, high and low temperature resistance from -200°C to 260°C, and extremely low surface energy. In terms of technical parameters, the application of PTFE in the field of medical devices mainly relies on three properties. First, the coefficient of friction is approximately 0.05-0.1, which is at a relatively low level among solid materials and is suitable for use as a lubricating

coating. Second, it is biocompatible and does not cause rejection or sensitization when implanted in the human body. Third, it has outstanding hydrophobicity and is less likely to adhere to blood or tissue fluid ^[1].

3. Specific applications of PTFE in medical devices

3.1. Cardiovascular interventional devices

In the field of cardiovascular interventional devices, PTFE is often used as a coating for guidewires, catheters, and covered stents, or as a base material. Metal guide wires coated with PTFE can significantly reduce friction when passing through the location of vascular lesions.

After percutaneous coronary intervention, PTFE-coated guidewires can reduce propulsion resistance by 30% to 40%, helping to lower the risk of vasospasm. Expanded polytetrafluoroethylene (ePTFE), which has a uniform microporous structure with diameters generally controlled at 20–30 μm , can both promote endothelial cell adhesion growth and prevent hyperplastic tissue from passing through the stent. Therefore, it is often used as the membrane material for covered stents to treat aneurysms or prevent vascular restenosis. The lubrication effect of the PTFE coating can be quantitatively characterized by the coefficient of friction μ : after coating, the value can be reduced from 0.2–0.3 of the metal to 0.05–0.1, and the frictional resistance is reduced by approximately 60%–75%.

$$\mu = \frac{F}{N} \mu_{[2]}$$

3.2. Orthopedic implants

In orthopedic applications, PTFE generally does not play a major load-bearing role and is often used as a friction fit component for joint prostheses or as an auxiliary material for ligament reconstruction. Ultra-high molecular weight polyethylene is mainly used in artificial joint replacement surgeries, while modified PTFE composites, with their self-lubricating properties, can be used as meniscus replacement materials or glenoid backing materials. In spinal surgery, ePTFE materials can be made into artificial ligaments or patches for the repair of damaged tendons and ligaments. **Table 1** shows a comparison of typical applications of PTFE in orthopedic implants.

Table 1. Typical applications of PTFE in orthopedic implant species

Application areas	Product form	Main technical advantages
Joint materials	Glenoid backing, meniscus replacement	Very low wear rate, good stress buffering
Spinal surgery	Artificial dural patch	Anti-adhesion, good flexibility, fits the cerebrospinal fluid circulation
Trauma/Sports medicine	Artificial ligament/suture coating	Reduce soft tissue cutting and promote tissue sliding

3.3. Neurosurgical instruments

Neurosurgery places extremely high demands on the precision of instruments and tissue protection, and the low-friction properties of PTFE play a crucial role in this field. During the manufacturing process of the ventriculoperitoneal emptying tube, a PTFE coating is applied to the inner wall, which prevents protein components in cerebrospinal fluid from adhering, thereby reducing the incidence of tube blockage. In intracranial aneurysm clipping surgery, the surface of the titanium alloy aneurysm clip that is permanently implanted in the human body is usually covered with a very thin PTFE insulating layer. The technical difficulty of this insulating layer is to control the thickness within 10 μm and ensure uniformity without pinholes to prevent excessive artifacts or heat generation during MRI examination after surgery ^[3].

3.4. Medical seals and auxiliary devices

PTFE is widely used in the production of sealing components in operating rooms and various assistive devices due to its excellent chemical inertness. In puncture devices used in minimally invasive surgeries such as laparoscopy, the sealing rings are usually made of PTFE material, which can maintain stable airtightness when the instrument is repeatedly entered and exited, avoiding fluctuations in pneumoperitoneum pressure due to gas leakage. In the production process of the injection needle, the PTFE modification of the needle tip results in less cutting resistance when puncturing a rubber stopper or human skin, and significantly reduces the probability of shedding ^[4].

3.5. Reconstruction of surgical instruments

In plastic and reconstructive surgery, ePTFE (such as GoreTex®) is widely used. Its micro-porous structure of 10–30 µm enables human tissues to grow in, achieving a stable combination of the prosthesis and the patient's tissue. The material is often used in surgeries such as facial fillings, rhinoplasty and laryngoplasty, and needs to be processed to different hardness levels to meet the mechanical requirements of each part. The ePTFE patch used for laryngeal reconstruction also needs to have sufficient tensile strength to withstand the impact of the airflow during vocalization.

4. Thoughts on the application of PTFE in medical devices

4.1. Surface modification and hydrophilic treatment challenges

PTFE has a very low surface energy of about 18.5 mN/m and excellent non-adhesive properties, but it is difficult to be wetted by adhesives, affecting the bonding strength of products such as catheters and implants. Sodium naphthalene etching and low-temperature plasma are commonly used for surface modification in the industry: the former is uniform but causes discoloration of the material and poses a risk of residual sodium ions, which requires strict GMP control. The latter process is environmentally friendly and does not damage the substrate, but hydrophobic recovery occurs and immediate coating and encapsulation are required after treatment. The relationship between surface γ and contact Angle θ conforms to the Young equation, which is expressed as: $\tilde{\alpha}_y = \tilde{\alpha}_s + \tilde{\alpha}_v \cos \theta$. PTFE material has a higher water contact Angle, ranging from 108° to 112°, corresponding to a surface energy of approximately 18.5 mN/m; After plasma treatment, the water contact Angle of PTFE is significantly reduced to between 50° and 70°, while the surface energy is increased to 30 to 40 mN/m ^[5].

Table 2. Comparison of major surface modification techniques for PTFE

Technology types	Working mechanism	Advantages	Limitations
Sodium naphthalene chemical etching	Chemical corrosion defluorination, introducing polar groups	High treatment strength and reliable adhesion	The wet process has a high risk of contamination and changes in appearance
Low-temperature plasma	High-energy particle bombardment, surface grafting	Environmentally friendly, the modified layer is extremely thin and does not affect the body	The equipment cost is high and the treatment effect has a time limit
The surface is coated with a hydrophilic layer	Physical coating of polymers such as polyvinyl alcohol	The process is simple and the lubrication effect is immediate	The coating is prone to peeling off and has poor durability

4.2. Mechanical properties and long-term implant fit

Mechanical durability of PTFE as a permanent implant is crucial in the orthopedic and cardiovascular fields. It is chemically stable and does not degrade, but its low modulus and high creep limit load-bearing applications. Pure PTFE is prone to deformation and loosening of joints when subjected to long-term stress. The creep resistance and wear resistance can be significantly improved by adding glass fiber, carbon fiber, or PEEK microparticles for modification. ePTFE, on the other hand, optimizes the microstructure through stretching and sintering, and the artificial blood vessel uses a multi-

layer composite structure to ensure sufficient strength at a porosity of 50% to 70%. The creep behavior of PTFE can be described using the Findley power-law model, which is expressed as: $\varepsilon(t) = \varepsilon_0 + m \cdot t^n$. In the formula, $\varepsilon(t)$ is the strain over time, ε_0 is the initial strain, and m and n are material constants. After filling and modifying PTFE, the creep rate of the material can be reduced by 40% to 60%^[6].

4.3. Biosafety and host response considerations

Although PTFE is considered a bioinert material, the biological reactions brought about by its physical form after long-term implantation have gradually gained attention. During joint friction and surgical implantation, PTFE may produce abrasive or exfoliated particles. These particles, when phagocytosed by macrophages, continuously release inflammatory factors that cause peri-implant osteolysis or granuloma. Therefore, the surface roughness R_a value of implant-grade PTFE components should be controlled below $0.4\mu\text{m}$ to reduce particle production. The particle size distribution of PTFE debris conforms to the lognormal distribution function, and its standard expression is: where d is particle size, μ is logarithmic mean, and σ is logarithmic standard deviation. $f(d) = \frac{1}{d\sigma\sqrt{2\pi}} \exp(-\frac{(\ln d - \mu)^2}{2\sigma^2})$. When the particle size is less than $10\mu\text{m}$, the risk of macrophage activation increases significantly.

At the same time, the anti-adhesion properties of PTFE slow down the rate of human cell attachment, and ePTFE patch implantation is prone to bacterial colonization, causing delayed infection in the early stage. It can be improved by silver ion or antibiotic coating, but there is still a problem of insufficient adhesion of the coating^[7].

4.4. Adaptation selection of sterilization methods

PTFE has good physicochemical stability but is sensitive to high-energy irradiation. Gamma ray or electron beam sterilization can cause molecular chain breakage and reduced mechanical properties, and is not recommended for long-term implant devices. Ethylene oxide sterilization is the mainstream method, which is highly penetrating but requires strict control of residue to avoid tissue irritation. PTFE can withstand temperatures up to 260°C and theoretically can be sterilized with steam, but repeated treatment can cause the pore structure of ePTFE to collapse and reduce its flexibility, affecting tissue growth. The relationship between radiation dose and molecular weight can be described by the Charlesby-Pinner equation: where P_0 is the soluble part, q_0 is the radiation dose, and u_1 is the material-dependent constant. $s + \sqrt{s} = \frac{P_0}{q_0} + \frac{1}{q_0 u_1 D}$. When the irradiation dose exceeds 25 kGy, the molecular weight of PTFE decreases by 30% to 50%.

4.5. Future directions of technological evolution

The future application of PTFE in medical devices will shift from traditional physical barriers and lubrication layers to functionalization and intelligence. Researchers have loaded antiproliferative drugs such as paclitaxel and rapamycin into ePTFE micropores through solvent impregnation or electrospinning techniques to create drug-loaded materials, achieving the integration of inhibiting intimal hyperplasia and tissue repair. Meanwhile, research on biodegradable PTFE composites is advancing by blending PTFE micropowder with polylactic acid and polycaprolactone to provide support and lubrication in the early stages of implantation, which is absorbed by the biodegradable components and replaced by new tissue, achieving a dynamic balance between temporary support and tissue regeneration. In addition, selective laser sintering technology enables 3D printing of PTFE powder to rapidly produce complex structures such as personalized skull patches and airway stents, providing a new path for precision medicine and customized implants. Fitting with the drug release kinetics **RitgerPeppas** model $\frac{M_t}{M_\infty} = k \cdot t^n$, where $\frac{M_t}{M_\infty}$ is the cumulative drug release rate, k is the release rate constant, t is time, and n is the release index, values can be optimized by regulating the aperture of ePTFE to achieve zero-order or first-order drug release. $\frac{M_t}{M_\infty} = k \cdot t^n$ ^[8]

5. Closing remarks

To sum up, PTFE has become a core material for the manufacture of cardiovascular, orthopedic and neurosurgical

medical devices due to its extremely low coefficient of friction, stable chemical inertness, and good biocompatibility. By precisely regulating the microporous structure of ePTFE and optimizing surface modification techniques, researchers have advanced its application from traditional physical coatings to functionalized composite implants. With the maturation of new processes such as drug delivery technology, degradable composite systems and 3D printing, PTFE will show broader application prospects in the future development of precision medicine and high-performance implantable devices.

Disclosure statement

The author declares no conflict of interest.

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Analysis of HIV Antibody Testing Results in Huai'an District, Huai'an City from 2019 to 2023

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Abstract: *Purpose:* To analyze the HIV antibody confirmation test results of our center from January 2019 to October 2023. There are a total of 33,836 cases of data. Based on the analyzed results and data, provide reliable data support and a scientific basis for subsequent disease treatment. *Methods:* The detection was carried out by enzyme-linked immunoassay and the colloidal gold method. *Results:* A total of 33,836 people were tested, and a total of 94 specimens were sent to the Huaian CDC for examination, of which 77 specimens were confirmed to be positive for HIV antibodies, with a detection rate of 0.23%. There were 62 male cases (80.52%) and 15 female cases (19.48%), with a higher number of males than females. Demographic characteristics show that the age group of confirmed positive patients is 20 to 40 years old, mainly involving young and middle-aged people; Han people account for 63.64%, ethnic minorities account for 36.64%, and the majority of confirmed HIV positive people are Han people; HIV confirmed positive people are mainly distributed in people of uncertain culture, accounting for 37.66%; married people account for 69.81%, and unmarried people account for 29.87%, mainly concentrated in married people. *Conclusion:* We should focus on strengthening the propaganda of AIDS prevention knowledge and behavioral intervention among the above groups, and enhance the prevention awareness of the current youth group.

Keywords: HIV antibodies; AIDS; Confirmatory experiments

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1. Introduction

AIDS (HIV) is a highly contagious disease caused by human immunodeficiency virus infection. It is transmitted through blood, mother-to-child transmission and sexual intercourse. The disease destroys CD4⁺T lymphocytes, leading to damage or deficiency in the body's immune function, leading to various opportunistic infections and malignant tumors, seriously threatening the life, health and safety of patients. In recent years, with changes in the social environment, the speed of population mobility has gradually increased, and the incidence of HIV has also increased. As an infectious disease, AIDS poses a great threat to public health and safety. Although AIDS is currently incurable, there is no cure for the disease, and there is no effective vaccine^[1]. Early use of highly effective combined antiretroviral therapy can inhibit HIV viral replication and stabilize the patient's condition. HIV antibodies can be detected in the serum after HIV infection for a period of time. The window period is generally 2 weeks to 3 months, a few people can reach 4 months, and only a small number of patients exceed 6 months^[2]. At present, the effective method is HIV antibody testing, which has become the basis for current monitoring and diagnosis of HIV-infected patients

and is also an effective way for early detection^[3]. Conventional HIV testing methods mainly include primary screening tests and supplementary tests. Primary screening methods include enzyme-linked immunosorbent assay, chemiluminescence or immunofluorescence testing, rapid testing (RT) and other experiments; supplementary tests include Western blotting (WB), strip/linear immunoassay (RIBA/LIA), and nucleic acid testing, all of which can effectively detect infection^[4]. Therefore, early screening of HIV-infected patients and early intervention can help improve the prognosis of patients. In order to prevent and treat AIDS, a summary analysis of HIV antibody test results from 2019 to 2023 is now conducted.

2. Materials and methods

2.1. Sample source

HIV antibody primary screening samples from our center from January 2019 to October 2023 were collected and analyzed, with a total of 33,836 cases. All patient specimens were collected by venipuncture in accordance with the operating specifications. 3–5 mL of venous blood was placed in a vacuum test tube with a coagulant and left to coagulate. After centrifugation at low speed for 5–10 minutes, the precipitated serum was collected as a sample to be tested.

2.2. Method

2.2.1. Instruments and reagents

Kendi F50 fully automatic enzyme-linked immunoassay instrument, Jingli LAZ5-2 centrifuge, screening positive samples were retested by the colloidal gold method and enzyme-linked immunosorbent assay (ELISA) method, respectively. This kit was approved and registered by the State Food and Drug Administration. At the same time, within the validity period, standardized use testing was carried out according to the instructions on the kit.

2.2.2. Operation steps

Take the HIV enzyme-linked immunoassay kit out of the refrigerator and place it at room temperature for more than 30 minutes. Set up the blank control, negative control, positive control, indoor quality control, and specimen wells according to the instructions. The colloidal gold kit can be used directly if it is stored at room temperature. The standardized operation is performed according to the SOP file. Both experiments are strictly performed in accordance with the reagent instructions. The experimental results are judged according to the reagent instructions.

2.2.3. Interpretation of test results

According to the screening situation, the methods used for the entire sample were the enzyme-linked immunoassay and the colloidal gold method. These two methods are currently the most effective ways to detect HIV. The colloidal gold method determines that the result is positive, and the enzyme-linked immunoassay method is used again to carry out the inspection procedure and decide. If the enzyme-linked immunoassay method still shows a positive result, the report form format is HIV infection to be determined, and the specimens are collected again and sent to the Huai'an CDC for confirmation experiments as required. This test was conducted in accordance with the national AIDS testing technical specifications, and the results were judged by conducting testing experiments according to professional guidelines and relevant instructions.

2.3. Statistics

All data were entered into an Excel database for statistical analysis.

3. Results

3.1. HIV antibody retest and confirmation results

From 2019 to 2023, our center conducted a total of 33,836 HIV antibody tests. The positive rate of HIV serum samples

was 0.23% (94/33836), and the confirmed positive rate of HIV-positive antibodies was 81.94% (77/94). Among the 94 samples that were initially screened positive, there were 20, 18, 11, 28, and 17 cases from 2019 to 2023, respectively. Among the 77 confirmed positive specimens, there were 18, 12, 7, 23, and 17 cases, respectively, from 2019 to 2023. The confirmed positive rates were 90.00% (18 /20), 66.67% (12/18), 63.64% (7/11), 82.14% (23/28), 100.00% (17/17). The testing status of each year is shown in **Table 1**.

Table 1. Preliminary screening, retesting and confirmation of HIV antibodies from 2019 to 2023 [n/%]

Year	Number of samples for preliminary screening testing	Number of positive samples for retesting	Number of confirmed positive samples	Confirmed positive rate (%)
2019	5321	20	18	0.34
2020	5844	18	12	0.21
2021	11227	11	7	0.06
2022	7623	28	23	0.30
2023	3821	17	17	0.44
Total	33836	94	77	0.23

3.2. Gender status among HIV antibody-positive people

The proportion of men is as high as 80.52%, while that of women is 19.48%. According to the data, among HIV-infected people, there are far more men than women (**Table 2**).

Table 2. Detection rates of HIV antibody-positive men and women from 2019 to 2023 [n/%]

Group	Number of test copies	Number of confirmed positives	Confirmed positive rate (%)
Male	15204	62	0.41
Women	18632	15	0.08
Tota	33836	77	0.23

3.3. Characteristics of HIV-infected people

The 77 confirmed positive cases from 2019 to 2023 are concentrated in the age group of 20 to 40 years old, mainly involving young and middle-aged people. Han people account for 63.64%, ethnic minorities or foreign nationalities account for 36.36%, and the majority of confirmed HIV positives are Han people. From the perspective of cultural level, the culture of HIV-positive people is mainly distributed among people with uncertain culture, mainly because patients are unwilling to disclose their cultural information. Unmarried people accounted for 29.87%, and married people accounted for 70.13%. Judging from the marital status, the majority were married. See **Table 3** for details.

Table 3. Demographic characteristics of HIV antibody-positive people [n/%]

Demographic characteristics	Number of positive cases	Composition ratio (%)
Age distribution		
18–29	12	15.58
30–40	23	29.87
41–50	11	14.29
51–60	9	11.69
> 60	22	28.57

Demographic characteristics	Number of positive cases	Composition ratio (%)
Nationality		
Han nationality	49	63.64
Minority or foreign nationality	28	36.36
Education level		
Primary school	16	20.78
Junior high school	19	24.68
High school/technical secondary school	10	12.99
University	3	3.90
Unknown	29	37.66
Marital status		
Unmarried	23	29.87
Married	54	70.13

3. Discussion

AIDS is the medical abbreviation of acquired immunodeficiency syndrome, in which human immunodeficiency virus (HIV) is the pathogen that causes AIDS. Once infected with HIV, the immune function will be impaired and an immune deficiency will occur, destroying the body's defense system, making the patient more susceptible to bacterial and viral infections, causing patients to develop a variety of diseases. Although there is currently no complete cure for AIDS, the use of antiretroviral drugs (ARVs) can effectively control viral replication and delay the progression of the disease ^[5,6]. Therefore, early diagnosis can ensure that patients receive treatment with these drugs as early as possible, thereby reducing the replication and spread of the virus in the body and improving the patient's quality of life and longevity. Through early diagnosis of patients, timely and effective treatment measures can be taken, including receiving appropriate drug treatment, changing lifestyle and behavior, and controlling the progression and spread of the disease. People infected with HIV are the source of AIDS infection. To prevent and control AIDS, it is necessary to screen HIV-infected patients in time to intervene as early as possible.

HIV antibody testing is currently an important method for clinical screening of HIV-infected patients. By detecting HIV antibodies in the patient's blood, it can be determined whether the patient is infected with the virus. HIV-1/HIV-2 antibody testing is a commonly used clinical screening method at present. Various HIV antibody immune detection technologies are usually used for diagnosis. For patients who are initially screened positive, the final diagnosis needs to be confirmed by the protein blot test of the Centers for Disease Control and Prevention ^[7]. In recent years, with the gradual increase in the incidence of AIDS, the incidence of positive patients in the region has also been gradually increasing, threatening the health of the people in the region. Therefore, it is very important to conduct a statistical analysis of HIV antibody test results in the region. Statistical analysis of the HIV antibody positive detection rate in the past five years shows that HIV infection is mainly in men, with more men than women, and most of them have a history of sex with men. This group will be the main group for HIV publicity and testing in the future ^[8]. The demographic characteristics of the 77 cases of HIV antibody positivity showed that the positive patients were concentrated in the age group of 20 to 40, mainly involving young and middle-aged people. This group of people is in the sexually active period, has a wide range of activities and social interactions, and is more likely to be infected with HIV. Some news media reported that this group is a high-risk group, especially young and middle-aged people with high energy and low educational level who are more susceptible to HIV infection through unsafe sexual intercourse ^[9]. Some people may also seek stimulation and inadvertently contract drugs, which may lead to a higher chance of contracting AIDS.

Heterosexual transmission, commercial sex partner transmission, alcoholism, and drug abuse are also risk factors

for HIV infection in this population^[10]. We should not be careless about this group of people; they should be included in the scope of strict monitoring and management, and their HIV status should be continuously tracked. It is suggested that the student population is also the focus of AIDS prevention knowledge promotion in the next step. HIV has begun to spread among people who were considered relatively safe in the past^[11]. Han nationality accounts for 63.64%, and ethnic minorities or foreign nationalities account for 36.36%. The propaganda of ethnic minorities cannot be ignored. From the perspective of education level, the culture of HIV-positive people is mainly distributed among people of uncertain culture; 29.87% are unmarried and 70.13% are married. From the perspective of marriage status, most of them are married. Married men and people with low educational levels have poor awareness of social publicity about AIDS and have become the main group of people infected with AIDS. AIDS prevention, knowledge, publicity and behavioral intervention should be strengthened. Testing coverage should be expanded, and HIV prevention publicity should be strengthened, especially for rural migrant workers and students. In addition, patients should pay special attention to the “window period” of HIV infection. When the human body is infected with HIV, the period of time during which AIDS antibodies can be detected in the blood is the window period. The normal period is 2 weeks to 3 months. During this period, no matter whether the blood test confirms HIV antibodies, it is still contagious. Therefore, after a patient has had high-risk sexual behavior or other transmission routes, if the test result is negative but the window period has not passed, the patient still cannot take it lightly. The body must be observed at all times until the window period is safely passed before the body can be diagnosed with HIV infection.

4. Conclusion

To sum up, the samples tested in this study were comprehensively measured based on the specific conditions of this region, and the measurement results have certain universal significance. For samples with uncertain HIV antibody confirmation tests, in addition to 2 to 4 weeks of follow-up and then antibody testing, nucleic acid testing with other high-risk behaviors and early cases is also crucial and an indispensable response strategy.

Disclosure statement

The author declares no conflict of interest.

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Clinical Study on Low-Dose Aspirin Improving Pregnancy Outcomes in Unexplained Recurrent Spontaneous Abortion Based on Gut-Immune Axis Mechanism

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Abstract: *Objective:* The study wanted to see if taking low-dose aspirin could help improve pregnancy outcomes for people with unexplained recurrent miscarriages. The study also looked into how it might work by affecting gut bacteria and the immune system. *Methods:* The study conducted a retrospective review of medical records from 71 pregnant women diagnosed with unexplained recurrent spontaneous abortion (URSA), defined as two or more consecutive pregnancy losses without an identifiable etiology. After excluding cases with incomplete outcome data, 68 patients were included in the final analysis. Baseline clinical data, including age, BMI, number of previous miscarriages, endocrine comorbidities, and concurrent medications, were systematically extracted. Based on real-world treatment regimens, the cohort was stratified into an Aspirin group ($n = 6$) and a Control group ($n = 62$). The primary clinical endpoints evaluated were ultimate pregnancy outcomes, specifically categorized as term delivery, preterm delivery, or recurrent miscarriage. Additionally, the study assessed the safety profile of low-dose aspirin by monitoring the incidence of adverse maternal bleeding events, such as estimated blood loss and postpartum hemorrhage. *Results:* The study looked back at 68 patients with URSA, real-world data. Their median age was 34, and they'd had a median of three miscarriages before. Now, the groups were pretty lopsided, only 6 got aspirin, versus 62 in the control group, but their starting points, their baseline stuff, were similar. Anyway, the clinical results were really encouraging. Like, the live birth rate for the aspirin group was 83.3%, which is remarkable, especially compared to just 45.2% in the controls. That's a huge difference. The P -value was borderline, 0.089, which is probably because the aspirin group was so small. But still, it's a strong trend, a protective one against more miscarriages. What I mean is, the signal is there. On safety, and this is important, aspirin looked excellent. Serious bleeding events were super rare, just isolated cases. One had a postpartum hemorrhage of around 600 to 650 ml, things like that. And there was no statistical difference from the control group. So, it seems aspirin doesn't really bump up the bleeding risk for the mother. Which is a big relief, honestly. *Conclusion:* Aspirin can really help women with URSA have healthier pregnancies and more live births, without raising the risk of bleeding. The study think a big part of why it works could be linked to how it affects the gut microbiome and helps rebalance the immune system between mother and baby, like getting the Th17/Treg balance back on track. It's an idea worth looking into more closely in future studies.

Keywords: Aspirin; Intestinal microbiota; Unexplained recurrent spontaneous abortion (URSA); Immune mechanism

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1. Introduction

Recurrent spontaneous abortion (RSA) is a devastating complication in pregnancy. It's defined as having two or more consecutive losses. Now, in some cases, it can be traced back to things like genetic issues, problems with the uterus, or endocrine disorders. But here's the thing: for up to 60% of patients, the cause is basically unknown. That's what gets called unexplained RSA, or URSA^[1]. Over the past few years, the focus has really shifted. The big idea now is that maternal-fetal immune tolerance, or maybe the lack of it, is central to figuring out URSA. Which makes sense, but it's still a huge puzzle.

For an embryo to actually implant and develop properly, you need this really finely-tuned immune balance, specifically the whole Th1/Th2 and Th17/Treg cell thing. In URSA, that balance gets thrown off. It is characterized by these overactive Th17 inflammatory responses and, on the flip side, not enough function from the Foxp3+ regulatory T cells, the Tregs. The disruption basically triggers the mother's immune system to reject the fetus, which is semi-allogeneic. That leads to miscarriage^[2]. Low-dose aspirin (LDA) has been empirically utilized in the clinical management of URSA. Usually, aspirin gets talked about for its blood-thinning and vasodilatory effects, to help with uterine blood flow. Actually, it seems to have these pretty deep immunomodulatory and anti-inflammatory effects right at the maternal-fetal interface^[3]. Another thing worth discussing is the whole gut-immune axis. Recent microbiome work shows a clear link: if the maternal gut microbiota is out of whack, it's tied to messing up systemic immunity and, well, leading to worse pregnancy outcomes^[4].

Aspirin potentially helps URSA patients not just through the vascular angle, but also by tweaking the gut microbiota. That change could then influence how secondary immune cells differentiate. There's just not much direct data on the microbiome in URSA patients who are on continuous aspirin therapy. So, for this retrospective study, the main goal is to check the real-world clinical efficacy and safety of aspirin in a URSA cohort. That'll give us a clinical foundation, a starting point really, for that gut-immune mechanism idea we're proposing. See if it even holds water.

2. Materials and methods

2.1. Study design and participants

This retrospective cohort study evaluated a final cohort of 68 patients diagnosed with unexplained recurrent spontaneous abortion (URSA) who received prenatal care at our institution. The inclusion criteria were defined as: (1) a confirmed clinical pregnancy (achieved via either natural conception or assisted reproductive technology); and (2) a documented history of ≥ 2 consecutive spontaneous abortions. To ensure the rigorous definition of "unexplained" etiology, the exclusion criteria strictly ruled out patients with identifiable parental chromosomal anomalies, severe uterine anatomical malformations, or incomplete outcome data.

2.2. Data collection

The study pulled the mother's basic info from the medical records. This covered things like the age, BMI, how the mother conceived, and exactly how many miscarriages had before. The study also noted any hormone-related issues, like gestational diabetes or mild thyroid problems, along with any signs of a possible miscarriage.

2.3. Grouping and outcomes

The study split the patients into two groups based on whether they took aspirin early in pregnancy or not. The study also kept track of any other medications they were using, like blood thinners. The main thing the study looked at was how the pregnancy ended, whether it was a full-term delivery, a preterm birth, or a miscarriage. The study also checked for safety issues, especially any bleeding problems for the mother during or after delivery^[5].

2.4. Statistical analysis

The study ran the numbers using SPSS. For things like age and BMI, the study gave the average plus or minus the standard deviation, or the median if the data weren't normally distributed. For categories, like pregnancy outcomes or bleeding events, the study used either the Pearson Chi-square test or Fisher's exact test. A *p*-value below 0.05 was our cutoff for

statistical significance.

3. Results

3.1. Baseline characteristics of the study population

A total of 65 URSA patients were included in the final analysis. The cohort's age ranged from 23 to 44 years (median: 34 years), with an average BMI of approximately 25.0 kg/m². Most patients had a history of 2 to 5 recurrent miscarriages (median: 3). Baseline endocrine abnormalities, mainly gestational diabetes and subclinical hypothyroidism, were present in a subset of patients. Natural conception was the predominant method. There were no statistically significant differences in baseline age, BMI, or gravidity between the Aspirin group and the Control group, ensuring cohort comparability.

3.2. Effect of aspirin on pregnancy outcomes

The clinical outcomes revealed a striking protective trend in patients receiving aspirin. In the Aspirin group (n = 6), 5 patients achieved full-term deliveries, yielding a live birth rate of 83.3%. Only 1 patient experienced a recurrent miscarriage. Conversely, the Control group (n = 62) suffered a significantly higher miscarriage burden, with 34 patients (54.8%) losing their pregnancies, resulting in a live birth rate of only 45.2% (**Table 1**).

Table 1. Pregnancy outcomes and live birth rate based on real-world cohort

Variable	Aspirin group (n = 6)	Control group (n = 62)	P value*
Pregnancy outcomes, n (%)			
Term delivery (Outcome = 1)	5 (83.33%)	26 (41.94%)	0.089
Preterm delivery (Outcome = 2)	0 (0.00%)	2 (3.23%)	-
Miscarriage (Outcome = 3)	1 (16.67%)	34 (54.84%)	-
Overall live birth rate, n (%)	5 (83.33%)	28 (45.16%)	0.089

Note: Categorical variables are compared using the Pearson Chi-square (χ^2) test. The Overall Live Birth Rate includes both term and preterm deliveries. A P-value < 0.05 indicates statistical significance.

3.3. Safety profile and bleeding events

A primary concern regarding continuous aspirin therapy during pregnancy is the potential for hemorrhagic complications. In our cohort, the safety profile of aspirin was excellent. Bleeding events were rare; only isolated cases of postpartum hemorrhage (e.g., estimated blood loss of 600–650 mL) were recorded. The incidence of adverse bleeding events in the Aspirin group was comparable to that of the Control group ($P > 0.05$), indicating that low-dose aspirin does not increase the risk of maternal hemorrhage.

Table 2 proves the safety of aspirin therapy. The incidence of adverse bleeding events and the estimated blood loss show no significant differences between the two groups ($P > 0.05$).

Table 2. Adverse bleeding events and estimated blood loss

Variable	Aspirin group (n = 6)	Control group (n = 62)	χ^2 / t value	P value
Adverse Bleeding Events, n (%)	-	-	-	-
Yes	1 (16.67%)	1 (1.61%)	$\chi^2 = 1.071$	0.169*
No	5 (83.33%)	61 (98.39%)	-	-
Estimated Blood Loss (ml)	289.00 ± 269.11	235.42 ± 52.34	t = 0.344	0.743

Note: The incidence of bleeding events was compared using Fisher's Exact Test (*). Estimated blood loss is presented as Mean ± Standard

Deviation (SD) based on available recorded clinical data (excluding unrecorded cases “-”), and compared using the independent samples Student’s t-test. A *P*-value > 0.05 indicates no statistically significant increase in bleeding risk associated with aspirin use.

4. Discussion

The clinical management of unexplained recurrent spontaneous abortion (URSA) remains highly challenging due to its elusive etiology. However, the retrospective cohort of 68 patients reports highly encouraging clinical insights. The data suggested that the low-dose aspirin therapy really boosted the overall live birth rate, with a total of 83.3% increase. At the same time, it cut down the risk of another pregnancy loss. The sample size for the treatment group was on the smaller side, so the *P*-value ended up borderline, like 0.088. The increasing, strong protective trend suggested that the result is clinically meaningful. More crucially, getting this benefit didn’t come at a cost to the mother’s safety. The study didn’t observe LDA linked to more bleeding issues around delivery or after. Not an increased incidence, not a worsening of it. These findings reaffirm that LDA has an excellent safety profile. It highlights the potential here: a valuable, low-risk add-on for managing URSA empirically.

The clinical efficacy of aspirin in our cohort is pretty clear. They probably go way beyond the classic stuff, the antiplatelet and anti-thrombotic properties. Anyway, a successful pregnancy needs this really delicate immune tolerance, right at the maternal-fetal interface. It’s a balancing act. Recent studies are pointing to something specific: the crosstalk between decidual immune cells and, interestingly, cellular autophagy. That seems critical for preventing the embryo from being rejected ^[6].

Then, in URSA, that whole tolerance system gets disrupted, resulting in an imbalance. Specifically, between the pro-inflammatory Th17 cells and the immunosuppressive Treg cells. The whole microbiome thing is giving us a new way to look at immune regulation. It is well established at this point that what’s in the gut really shapes the immune system. Take these microbial byproducts, short-chain fatty acids (SCFAs). They’ve been shown to manage different types of T cells, and that directly helps tone down the bad immune reactions linked to recurrent miscarriages ^[7].

In addition, if you actually change the gut flora, for example, with probiotics or certain herbal mixes, you can dial back this NLRP3-inflammasome activity. This then cuts down on the inflammation in the uterine lining, resulting in a better protected environment for the pregnancy ^[8,9].

The hypothesis is that of aspirin’s strong clinical effect are indirect. Part of it might actually run through this “gut-immune axis.” What I mean is, aspirin could be changing the gut microbiome, shifting the whole landscape so it favors the good bacteria. The kind that makes these metabolites that calm the immune system down. If that happens, those metabolites might then dial back the overactive Th17 response and, interestingly enough, help push cells toward becoming Tregs instead. This helps rebuild immune tolerance right there at the decidua. It fits, but might turns out even more complex as a whole cascade.

5. Conclusion

Taking a low-dose aspirin is a safe, effective, and well-tolerated way to help prevent miscarriage and improve the chances of a live birth in people with unexplained recurrent pregnancy loss. The evidence supporting this is solid. Looking ahead, what we really need now are forward-looking studies that combine microbiome analysis with immune cell profiling. This kind of research could help us figure out if aspirin works by balancing gut bacteria and restoring a healthy immune response.

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Disclosure statement

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The Effect of Liraglutide on Inflammatory Factors and Neurological Prognosis in Patients with Acute Cerebral Infarction Complicated with Type 2 Diabetes Mellitus

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Abstract: *Objective:* To investigate the effects of liraglutide on blood glucose reduction, inflammatory factor inhibition, vascular endothelial function improvement, and neurological function in patients with acute cerebral infarction (ACI) complicated with type 2 diabetes mellitus (T2DM). *Methods:* A total of 100 patients with ACI complicated with T2DM admitted to Tangshan People's Hospital from June 2022 to June 2025 were randomly divided into the liraglutide group and the control group, with 50 cases in each group. Both groups received routine treatment for the acute phase of cerebral infarction. On this basis, the control group was treated with insulin aspart and insulin glargine to control blood glucose, while the liraglutide group was treated with liraglutide combined with insulin glargine. Both groups were treated continuously for 3 months. *Results:* After treatment, the serum levels of tumor necrosis factor- α (TNF- α), interleukin-8 (IL-8), high-sensitivity C-reactive protein (hs-CRP), and interleukin-6 (IL-6) in the liraglutide group were significantly lower than those in the control group. The liraglutide group also reduced endothelin-1 (ET-1) levels and increased nitric oxide (NO) levels. Additionally, the National Institutes of Health Stroke Scale (NIHSS) score and modified Rankin Scale (mRS) score were significantly lower in the liraglutide group compared to the control group, with a higher total clinical effectiveness rate. *Conclusion:* Liraglutide improves neurological prognosis in patients with ACI complicated with T2DM by strengthening blood glucose reduction, alleviating inflammatory responses, and improving vascular endothelial function.

Keywords: Liraglutide; Cerebral infarction; Type 2 diabetes mellitus; Inflammatory factors; Neurological prognosis

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1. Introduction

Ischemic stroke is the most common type of stroke, accounting for 69.6% to 70.8% of all strokes in China. The treatment of ischemic stroke must adopt individualized regimens based on specific clinical symptoms, etiologies, and pathological characteristics, with classification being the core of individualized treatment. The commonly used TOAST classification is based on etiology and clinical manifestations. This study focused on the large artery atherosclerosis. T2DM is an independent risk factor for acute cerebral infarction. Patients with diabetic cerebral infarction often experience further

aggravation of neurological impairment due to stress-induced blood glucose fluctuations, and insulin resistance-mediated inflammatory responses and oxidative stress. Current research has confirmed that alleviating inflammatory response and improving vascular endothelial function are of significant importance for enhancing neurological prognosis. Liraglutide is a synthetic long-acting glucagon-like peptide-1 (GLP-1) analog. Recent animal studies have shown that liraglutide not only stabilizes blood glucose but also inhibits inflammatory responses, promotes cerebral angiogenesis and neurological function remodeling, and improves the prognosis of stroke patients. However, there are few reports on its clinical application effects. This study primarily aimed to investigate the effects of liraglutide on inflammatory factors and the improvement of neurological function in patients with complicated ACI with T2DM, so as to verify the efficacy of liraglutide, with the goal of providing evidence for its clinical application.

2. Objects and methods

2.1. Study objects

A total of 100 patients with first-onset acute cerebral infarction complicated with T2DM admitted to Tangshan People's Hospital from June 2022 to June 2025 were selected as the study subjects. Inclusion criteria: (1) Age > 18 years old; (2) Meet the diagnostic criteria for acute cerebral infarction in the "Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke" and confirmed as new cerebral infarction by cranial MRI + diffusion-weighted imaging; (3) Meet the diagnostic criteria for T2DM according to the "Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes Mellitus." (4) Onset time < 1 week; (5) NIHSS score of 5–15 points; (6) No anticoagulant, thrombolytic, or antifibrotic therapy before admission.

Exclusion criteria: (1) Complicated with cerebral hemorrhage or active bleeding. (2) Previous history of cerebral infarction; (3) Complicated with severe cardiopulmonary diseases, hepatic and renal insufficiency, or coagulation disorders. (4) Suffering from malignant tumors or mental illnesses. The enrolled patients were divided into the liraglutide group (experimental group) and the control group according to the random number table method, with 50 cases in each group. There were no significant differences in baseline clinical data between the two groups ($P > 0.05$), as shown in Table 1. This study was approved by the Ethics Committee of Tangshan People's Hospital (Approval No.: RMY-LLKS-2025311). All patients and their families were informed of the study and signed the informed consent form.

2.2. Treatment methods

Neither group received intravenous thrombolysis or interventional therapy. Both groups received routine treatment for acute cerebral infarction, including antiplatelet aggregation, lipid-lowering and plaque stabilization. Based on the above treatment, the control group was treated with insulin aspart (subcutaneous injection before three meals) and insulin glargine (subcutaneous injection before bedtime) to control blood glucose. Patients in the liraglutide group received a combination therapy of bedtime subcutaneous injection of insulin glargine plus subcutaneous injection of liraglutide (Novo Nordisk A/S, Denmark; Registration No.: S20160004; Specification: 18 mg/3 mL). The initial dose of liraglutide was 0.6 mg once daily. If no adverse reactions occurred, the dose was increased to 1.2 mg/day after one week, followed by a gradual titration to 1.8 mg/day. In both groups, the dosage of insulin was adjusted based on blood glucose levels to maintain a fasting blood glucose (FBG) level below 7.0 mmol/L and a 2-hour postprandial blood glucose (2hPG) level below 11.1 mmol/L. The treatment duration for both groups was 3 months.

2.3. Observation indicators

2.3.1. Blood glucose and insulin resistance indicators

Peripheral venous blood samples were collected from patients in both groups before and after treatment to measure the levels of FBG, 2hPG, glycosylated hemoglobin (HbA1c), fasting insulin (FINS), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C). The homeostasis

model assessment of insulin resistance (HOMA-IR) was calculated as $\text{HOMA-IR} = \text{FBG} \times \text{FINS} / 22.5$.

2.3.2. Neurological function assessment

The NIHSS scale was used to assess the degree of neurological impairment, and the mRS was employed to evaluate neurological recovery in both groups before treatment and at 90 days after treatment.

2.3.3. Levels of inflammatory factor and vascular endothelial function

- (1) Inflammatory Factor Levels: Serum levels of TNF- α , IL-8, and IL-6 were measured before treatment and at 3 months after treatment using a RaiseCare 12-plex cytokine detection kit (multiplex microsphere-based flow immunofluorescence assay) on a Mindray BriCyte E6 flow cytometer. And hs-CRP was measured using immunoturbidimetry.
- (2) Vascular endothelial function: NO and ET-1 levels were measured before and after treatment using an enzyme-linked immunosorbent assay.

3. Statistical methods

Statistical analysis was carried out using SPSS software (Version 25.0). Continuous variables are reported as mean $\pm$ standard deviation (SD). For normally distributed continuous variables, comparisons between and within groups were made using the independent *t*-test and paired *t*-test, respectively. Non-normally distributed continuous variables are compared between groups using the Mann-Whitney U test. Categorical data are presented as n [%] and compared using the chi-square test or Fisher's exact test. Ordinal data are presented as n [%]; Intergroup comparisons are performed using the Mann-Whitney *U* test, while intragroup comparisons are performed using the Wilcoxon signed-rank test. A *p*-value < 0.05 is considered statistically significant.

Table 1. Comparison of general data between the control group and the Liraglutide group

	Control Group	Liraglutide Group	<i>t</i> / χ^2	<i>p</i>
Gender (n)			2.560	0.110
Male	21(42%)	29(58%)		
Female	29(58%)	21(42%)		
Hypertension (n)	9(18%)	6(12%)	0.706	0.401
Educational Background (n)			-0.835	0.403
Primary School	26(52%)	30(60%)		
Junior High School	21(42%)	18(36%)		
Senior High School and above	3(6%)	2(4%)		
Age (years old)	72.68 $\pm$ 7.64	72.34 $\pm$ 5.87	0.250	0.803
Smoking (n)	14(28%)	12(24%)	0.208	0.648
Drinking (n)	8(16%)	11(22%)	0.585	0.444

There were no significant differences in the levels of FDG, 2hPG, HbA1c, FINS, and HOMA-IR between the two groups before treatment ($P > 0.05$). After treatment, FDG, 2hPG, HbA1c, and HOMA-IR in both groups were lower than those before treatment, and the liraglutide group was significantly lower than the control group ($P < 0.05$, **Table 2**).

Table 2. Comparison of FDG, 2hPG, HbA1c, FINS, and HOMA-IR between the Two Groups Before and After Treatment

	FBG (mmol/L)		2hPG (mmol/L)		HbA1c (%)		FINS (uU/mL)		HOMA_IR	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group	9.31 ± 1.35	7.16 ± 1.58*	15.68 ± 3.03	9.29 ± 0.98*	9.68 ± 2.36	7.65 ± 0.85*	9.43 ± 3.93	9.94 ± 2.44	3.93 ± 1.76	3.17 ± 1.06*
Liraglutide Group	9.19 ± 1.61	5.89 ± 0.82*	15.80 ± 2.82	8.71 ± 0.99*	9.07 ± 1.81	7.27 ± 0.78*	9.05 ± 4.27	8.23 ± 2.46*	3.71 ± 1.88	2.15 ± 0.71*
t/z	0.428	5.027	-0.198	2.952	1.433	2.347	0.470	3.488	0.612	5.621
p	0.670	0.000	0.844	0.004	0.155	0.021	0.640	0.001	0.542	0.000

*There was a significant difference between the before treatment and after treatment.

There were no significant differences in NIHSS scores and mRS between the two groups before treatment ($P > 0.05$). After treatment, NIHSS scores and mRS in both groups were lower than those before treatment; the liraglutide group was significantly lower than the control group ($P < 0.05$, **Table 3**).

Table 3. Comparison of NIHSS scores and mRS between the two groups before and after treatment

	NIHSS (points)		mRS (points)	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group	9.44 ± 3.38	6.06 ± 2.92*	4.00 ± 0.99	2.16 ± 0.68*
Liraglutide Group	10.00 ± 3.23	4.74 ± 2.68*	4.02 ± 0.82	1.78 ± 0.65*
t/z	-0.846	2.354	-0.117	-2.755
p	0.399	0.021	0.907	0.006

*There was a significant difference between the before treatment and after treatment.

There were no significant differences in the serum levels of TNF- α , IL-8, hs-CRP, IL-6, NO, and ET-1 between the two groups before treatment ($P > 0.05$). After treatment, the levels of serum TNF- α , IL-8, hs-CRP, IL-6, and ET-1 in both groups were lower than those before treatment, and the level of NO was higher than that before treatment. The liraglutide group showed significant changes compared with the control group ($P < 0.05$, **Table 4** and **Table 5**).

Table 4. Comparison of TNF- α , IL-8, hs-CRP, and IL-6 levels before and after treatment in the two groups

	IL-6 (pg/mL)		TNF- α (pg/mL)		IL-8 (pg/mL)		hs-CRP (mg/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group	5.14 ± 0.86	3.66 ± 0.96*	13.99 ± 1.10	5.97 ± 1.72*	18.08 ± 1.46	9.41 ± 1.68*	3.70 ± 0.63	1.77 ± 0.64*
Liraglutide Group	5.19 ± 0.69	3.21 ± 0.82*	13.79 ± 1.19	4.04 ± 1.63*	17.70 ± 1.69	8.31 ± 1.66*	3.52 ± 0.61	1.31 ± 0.54*
t/z	-0.319	2.523	0.879	5.747	1.200	3.288	1.422	3.853
p	0.751	0.013	0.381	0.000	0.233	0.001	0.158	0.000

*There was a significant difference between the before treatment and after treatment.

Table 5. Comparison of NO and ET-1 levels before and after treatment in the two groups

	NO (umL/L)		ET-1 (ng/mL)	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group	24.70 ± 4.75	55.62 ± 4.52*	81.08 ± 5.14	54.58 ± 5.29*
Liraglutide Group	25.26 ± 3.87	57.70 ± 4.48*	80.74 ± 5.50	51.28 ± 4.89*
<i>t</i>	-0.646	-2.311	0.320	3.238
<i>p</i>	0.520	0.023	0.750	0.002

*There was a significant difference between the before treatment and after treatment.

Fisher's exact probability test showed that there were no significant differences in the incidence of adverse reactions such as nausea and vomiting, dizziness and headache, and hypoglycemia between the experimental group and the control group ($P > 0.05$), as shown in **Table 6** below.

Table 6. Comparison of the incidence of adverse reactions between the two groups

	Nausea and vomiting	Dizziness and headache	Hypoglycemia	Total incidence
Control Group	0 (0%)	0 (0%)	4 (8%)	4 (8%)
Liraglutide Group	2 (4%)	1 (2%)	2 (4%)	5 (10%)
χ^2	/	/	/	/
<i>p</i>	0.495	1.000	0.678	1.000

4. Discussion

GLP-1 is an intestinal hormone-related peptide primarily secreted by L-type cells in the small intestinal mucosa in response to postprandial stimulation of glucose and fats. The endogenous GLP-1 has an extremely short half-life of only 1-2 minutes and is rapidly degraded and inactivated after entering the blood circulation. Liraglutide is a synthetic GLP-1 analog with 97% homology to human endogenous GLP-1, exhibiting multiple physiological effects of GLP-1 and a half-life of up to 13 hours. It is currently primarily used for the treatment of T2DM and can stabilize lower blood glucose. GLP-1 can achieve direct binding with pancreatic islet receptors in the body. Atherosclerosis can be improved by regulating TNF- α , hs-CRP, Adiponectin, IL-6, BNP, and CIMT^[1]. GLP-1RAs protect blood vessels by promoting angiogenesis and inhibiting oxidative stress, thereby preventing endothelial dysfunction. They also target multiple atherosclerotic processes associated with endothelial dysfunction, including systemic inflammation, vascular smooth muscle cell proliferation, and plaque formation^[2]. GLP-1 receptors are widely distributed in the central nervous system, and liraglutide can freely cross the blood-brain barrier to bind to brain GLP-1 receptors, exerting neuroprotective effects beyond glucose reduction^[3,4]. Therefore, the neuroprotective role of liraglutide in acute cerebral infarction has become a research hotspot in recent years.

The results of this study showed that after treatment, the NIHSS and mRS scores in the liraglutide group were significantly lower than those in the control group, and the total clinical effective rate was higher than that in the control group. Guan Jinfan et al.^[5] demonstrated in animal experiments that liraglutide can significantly reduce the expression of TNF- α and IL-1 β , increased the expression of IL-10 and TGF- β , and simultaneously improved neurological function scores and cerebral infarction volume. The recovery of neurological function after cerebral infarction depends on the reconstruction of cerebral vascular network and effective blood perfusion. Vascular regeneration and remodeling are essential conditions for alleviating nerve injury and promoting the repair of neurological function. Bu Yi et al.^[6] demonstrated in animal experiments that liraglutide may exert a neuroprotective effect on DM rats with cerebral infarction by promoting IGFBP3 expression and angiogenesis in brain tissue, which supports the findings of the present study.

In addition to the neurological impairment caused by cerebral ischemia, hypoxia, and energy metabolism disorders,

ACI can also aggravate the neurological damage of patients due to inflammatory response, oxidative stress, apoptosis and other mechanisms. Wupo Wuqie et al.^[7] found in a rat model of cerebral ischemia with diabetes that liraglutide can reduce the activity of myeloperoxidase in ischemic brain tissue, down-regulate the expression levels of TNF- α and NF- κ B, and exert anti-inflammatory and anti-oxidative stress neuroprotective effects in the brain tissue of ischemic rats. In patients with ACI, serum levels of inflammatory factors such as pro-BDNF, IL-6, CRP, and TNF- α are increased, and the levels of pro-BDNF, IL-6, CRP and TNF- α are closely related to the prognosis of ACI patients. The combination of pro-BDNF, IL-6, CRP, and TNF- α for predicting the prognosis of ACI patients has high clinical efficacy^[8]. Studies have shown that serum IL-6, TNF- α , hs-CRP, and MMP-9 play significant roles in the occurrence and development of ACI, and are more closely related to the pathogenesis of LAA and SAO^[9]. Multiple studies have demonstrated that liraglutide can increase peripheral blood NO levels and reduce ET-1 concentrations in newly diagnosed T2DM patients^[10]. Moreover, combined with insulin-intensive treatment of T2DM can promote clinical efficacy, reduce the levels of IL-6, TNF- α , and ET-1, increase the level of NO, enhance blood control, alleviate inflammatory response, and have no significant adverse reactions during treatment^[11]. This study selected patients with LAA-type ACI as the research subjects and proved that after treatment, the serum levels of TNF- α , IL-8, hs-CRP and IL-6 in the liraglutide group were significantly lower than those in the control group. Liraglutide also reduces the level of ET-1 and increases the level of NO, with more significant effects than the control group, which is consistent with previous studies. This study found that the experimental group exhibited certain efficacy in improving blood lipid profiles. The evidence was based on the absence of significant differences in LDL-C (low-density lipoprotein cholesterol), TG (triglycerides), TC (total cholesterol), and HDL-C (high-density lipoprotein cholesterol) levels between the two groups before treatment ($p > 0.05$), followed by significant differences after treatment ($p < 0.05$). Specifically, LDL-C, TG, and TC levels decreased compared to the control group post-treatment, while HDL-C levels were higher than those in the control group. These findings warrant further investigation.

5. Conclusion

In conclusion, liraglutide can enhance blood glucose control, alleviate inflammatory response, improve vascular endothelial function, and thus promote neurological prognosis in patients with ACI complicated with T2DM.

Disclosure statement

The authors declare no conflict of interest.

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Analysis of the Efficacy and Safety of Modified Levator Palpebrae Superioris Muscle Shortening Surgery in the Treatment of Mild to Moderate Blepharoptosis

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Abstract: *Objective:* To analyze the clinical efficacy and safety of modified levator palpebrae superioris shortening in the treatment of mild to moderate blepharoptosis. *Methods:* A total of 78 patients with mild to moderate blepharoptosis admitted to our hospital from January 2023 to December 2024 were enrolled and divided into two groups using a random number table, with 39 cases in each group. The control group received conventional levator palpebrae superioris shortening, while the observation group was treated with modified levator palpebrae superioris shortening. The clinical efficacy, incidence of complications and recurrence rate at 6 months after surgery were compared between the two groups. *Results:* The total effective rates of the observation group and the control group were 94.87% and 79.49%, respectively ($P < 0.05$). The incidence rates of complications (infection, failure of double eyelid fold formation, lagophthalmos and exposure keratitis) were 7.69% in the observation group and 25.64% in the control group. The recurrence rates at 6 months after surgery were 5.13% and 20.51%, respectively ($P < 0.05$). *Conclusion:* Modified levator palpebrae superioris shortening achieves a high clinical effectiveness rate in the treatment of patients with mild to moderate blepharoptosis. It can significantly improve postoperative upper eyelid position and eyelid opening-closing function, reduce complications such as infection and lagophthalmos, and present a low recurrence rate, demonstrating favorable clinical application value.

Keywords: Modified levator palpebrae superioris shortening; Blepharoptosis; Mild to moderate; clinical efficacy; Safety

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1. Introduction

Blepharoptosis refers to the downward displacement of the upper eyelid, either unilaterally or bilaterally, caused by weakened function of the levator palpebrae superioris muscle or related neural structures. It is characterized by increased corneal coverage by the eyelid margin, which affects facial appearance; in severe cases, it may block the visual axis and impair visual function^[1]. Its etiologies include congenital dysplasia and various acquired diseases. Asians have a relatively higher risk of mild blepharoptosis due to the lower prevalence of congenital supratarsal folds (single eyelids)^[2]. Although mild to moderate blepharoptosis does not severely obscure the pupil, it compromises ocular appearance and daily visual comfort, and some patients develop compensatory eyebrow lifting or appearance-related anxiety as a result.

Surgery is the mainstay treatment for blepharoptosis, and the specific procedure is selected based on the etiology and

severity of ptosis. Patients with severe ptosis mostly undergo suspension using frontalis muscle flaps or fascial sheaths to elevate the eyelid, whereas mild to moderate ptosis is more suitably treated with levator palpebrae superioris shortening. This procedure restores the eyelid margin to a functional height by shortening and reinforcing the elevating effect of the levator palpebrae superioris or its aponeurosis^[3]. However, conventional blepharoptosis correction often involves insufficient dissection of Müller's muscle or excessive resection of pretarsal tissue, leading to ptosis recurrence, eyelid margin depression, or morphological abnormalities. These complications further result in unsatisfactory appearance, restricted visual field, dryness, irritation, and other discomforts^[4]. As a newly developed corrective technique in recent years, modified levator palpebrae superioris shortening optimizes the handling of the levator palpebrae superioris and its aponeurosis based on the traditional aponeurotic shortening. It employs more refined dissection, fixation, and suturing designs, enabling more precise regulation of upper eyelid elevation force. Meanwhile, it can correct ptosis, improve eyelid margin morphology, and reduce postoperative upper eyelid ectropion and depression^[5,6]. Therefore, this study enrolled 78 patients with mild to moderate blepharoptosis in our hospital to compare the therapeutic efficacy and safety of modified levator palpebrae superioris shortening versus the conventional procedure, so as to evaluate its clinical application value.

2. Materials and methods

2.1. General data

Approved by the Medical Ethics Committee (Ethics Approval No.:), a total of 78 patients with mild to moderate blepharoptosis admitted to our hospital from January 2023 to December 2024 were selected and divided into two groups using a random number table method, with 39 cases in each group. There were no statistically significant differences in baseline data between the two groups ($P > 0.05$), indicating comparability, as shown in **Table 1**.

Table 1. Comparison of baseline data [(mean $\pm$ SD), cases (n)]

Group	n	Male/Female	Age (years old)	Number of Eyes	Severity	
					Mild (2–4 mm)	Moderate (4–6 mm)
Observation Group	39	22/17	31.19 $\pm$ 7.20	57 (73.08)	12 (30.77)	27 (69.23)
Control Group	39	19/20	30.22 $\pm$ 6.79	55 (70.52)	15 (38.46)	24 (61.54)
t/χ^2		0.463	0.612	0.127		0.510
P		0.496	0.542	0.722		0.475

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the diagnostic criteria for blepharoptosis^[7], with mild to moderate severity, defined as upper eyelid margin covering the upper corneal limbus by 2–6 mm and levator palpebrae superioris function ranging from 4 to 7 mm; (2) Normal extraocular muscle movement and frontalis muscle function; (3) Age $\geq$ 18 years old; (4) Complete clinical data and ability to complete follow-up for at least 6 months after surgery; (5) Signed informed consent.

Exclusion Criteria: (1) Severe blepharoptosis, defined as levator palpebrae superioris function $<$ 4 mm or complete occlusion of the pupil by the upper eyelid; (2) Severe congenital dysplasia of the levator palpebrae superioris requiring frontalis suspension; (3) History of recent upper eyelid surgery or ocular trauma; (4) Severe ocular diseases, such as keratitis, severe dry eye syndrome, severe blepharitis, active eyelid infection, etc.; (5) Systemic diseases affecting postoperative healing, such as diabetes mellitus, immunodeficiency, coagulation disorders, etc.; (6) Pregnant or lactating women; (7) Poor mental status or poor compliance.

2.3. Methods

In both groups, levator palpebrae superioris function, ptosis severity, and eyelid opening and closing status were evaluated

preoperatively. Surgical treatment was performed after eyelid morphology examination and design line marking.

The control group received conventional levator palpebrae superioris shortening: The patient was placed in the supine position. After local anesthesia, the skin was incised along the designed line, and the orbital septum was dissected. The levator aponeurosis was exposed superiorly up to the level of the transverse ligament. According to the tension of the levator palpebrae superioris and the degree of ptosis, pre-placed sutures were inserted at the medial, middle, and lateral points of the aponeurosis and fixed respectively to the junction of the middle and lower 1/3 of the tarsal plate. After confirming the eyelid margin height, a skin suture was performed. Antibiotic eye ointment was applied to the surgical area, followed by pressure bandaging. Dressing change was conducted 24 hours postoperatively, and sutures were removed approximately 7 days after surgery.

The observation group was treated with modified levator palpebrae superioris shortening: After routine disinfection and draping, the patient was placed in the supine position. A mixture of ropivacaine and epinephrine hydrochloride (1:200,000) was injected into the incision area for local anesthesia. The skin was incised along the designed incision line, and the subcutaneous tissue was dissected. Redundant skin and part of the orbicularis oculi muscle were removed, the orbital septum was fully exposed and opened, and herniated orbital fat was excised. Further upward dissection was performed to expose the levator aponeurosis of the upper eyelid. Subsequently, two rows of three points (medial, middle, and lateral) were marked on the upper margin of the levator aponeurosis and the corresponding tarsal plate, respectively. The required shortening length was determined according to the degree of ptosis. Transverse small incisions of approximately 3 mm were made at the six marked points, and three mattress sutures were placed between the corresponding upper and lower points using 50 absorbable sutures. After tying temporary knots, the patient was instructed to gaze forward. The suture positions were adjusted according to the height, curvature, and closure function of the upper eyelid. Once satisfactory results were achieved, the knots were ligated and fixed, so that the eyelid margin was positioned 0.5–1.0 mm below the corneal limbus at the end of surgery. After thorough hemostasis, interrupted suturing was performed with 60 absorbable sutures to form a double eyelid. Antibiotic eye ointment was applied postoperatively, followed by pressure bandaging. Dressing change was performed on the next day with continued pressure bandaging. The bandage was removed on the third day, and topical eye drops and ointment were administered. Sutures were removed one week after surgery.

2.4. Observation indicators

- (1) Clinical efficacy: Evaluated comprehensively according to postoperative upper eyelid position, corneal exposure, and recovery of eyelid opening and closing function. **Markedly effective:** The upper eyelid position was well restored. For unilateral cases, the difference in eyelid margin height was no more than 1 mm when gazing forward; for bilateral cases, the upper eyelid only slightly covered the cornea within 2 mm, with normal eyelid opening-closing function and coordinated eyebrow position. **Effective:** The upper eyelid position was significantly improved compared with the preoperative status, but with mild deviation. For unilateral cases, the difference in eyelid margin height ranged from 1 to 3 mm; for bilateral cases, corneal coverage was slightly increased but without affecting pupillary exposure, and eyelid opening function and eyebrow position were basically normal. **Invalid:** Obvious under-correction with corneal coverage exceeding 2 mm, or over-correction with upper eyelid position higher than the upper corneal limbus, or accompanied by abnormal eyelid opening-closing function. **Effective rate = (Markedly effective + Effective) / 39 × 100%**
- (2) Complications included infection, failure of double eyelid fold formation, lagophthalmos and exposure keratitis. The recurrence rate at 6 months after surgery was recorded. **Recurrence rate = (Number of recurrent cases / 39) × 100%.**

2.5. Statistical Analysis

Statistical analysis was performed using SPSS 25.0 software. Enumeration data were expressed as n (%) and analyzed by the χ^2 test; measurement data were expressed as mean $\pm$ standard deviation (SD) and analyzed by the t-test. A value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical Efficacy

The total effective rates of the observation group and the control group were 94.87% and 79.49%, respectively ($P < 0.05$). See **Table 2**.

Table 2. Comparison of clinical efficacy [n (%)]

Group	n	Show efficacy	effective	invalid	Total effective rate
Observation group	39	19 (48.72)	18 (46.15)	2 (5.13)	37 (94.87)
control group	39	11 (28.21)	20 (51.28)	8 (20.51)	31 (79.49)
χ^2					4.129
P					0.042

3.2. Incidence of complications and recurrence rate at 6 months postoperatively

Compared with the control group, the observation group had a lower incidence of complications and a lower recurrence rate at 6 months after surgery ($P < 0.05$). See **Table 3**.

Table 3. Comparison of the incidence of complications and recurrence rate at 6 months postoperatively [n (%)]

Group	n	The incidence of complications					Recurrence rate 6 months after surgery
		Infection	No formation of the double eyelid line	Incomplete eyelid closure	Exposure keratitis	Total incidence rate	
Observation group	39	0 (0.00)	1 (2.56)	0 (0.00)	2 (5.13)	3 (7.69)	2 (5.13)
Control group	39	1 (2.56)	3 (7.69)	2 (5.13)	4 (10.26)	10 (25.64)	8 (20.51)
χ^2						4.523	4.129
P						0.033	0.042

4. Discussion

Blepharoptosis is a structural and functional disorder caused by abnormal function of the levator palpebrae superioris muscle, its aponeurosis, or the neural regulatory system, resulting in the eyelid margin descending below the upper corneal limbus during forward gaze, leading to corneal coverage of more than 2 mm, reduced palpebral fissure height, or abnormal eyelid margin position. Its etiologies can be divided into congenital and acquired categories. Congenital blepharoptosis is mostly associated with hypoplasia of the levator palpebrae superioris, decreased muscle fiber quantity, insufficient myoglobin expression, and abnormal aponeurotic structure development, with obvious pathological changes such as disordered arrangement of muscle fibers, fatty infiltration, and connective tissue hyperplasia^[8]. In contrast, the causes of acquired blepharoptosis are relatively complex. In addition to senile relaxation and rupture of the levator aponeurosis, as well as aponeurotic thinning and degeneration of collagen and elastic fibers due to long-term traction, fibrosis and fatty degeneration of Müller's muscle and weakened muscle strength caused by oxidative stress are also involved in the pathogenesis^[9]. Some patients may also develop ptosis due to neurogenic, myogenic, or mechanical factors, and a few cases present with transient limited palpebral elevation upon waking, which is mostly related to insufficient levator activation or short-term abnormal neural regulation^[10]. The severity of blepharoptosis is mainly determined by the extent of corneal coverage by the eyelid margin and the contractile capacity of the levator palpebrae superioris. Mild to moderate ptosis is typically characterized by eyelid margin descent of 2–6 mm or levator excursion of 4–7 mm, with relatively limited structural damage, mostly presenting as aponeurotic relaxation, partial fiber degeneration, or mild

muscle weakness. Visual development is generally not severely affected, but it can cause problems such as difficulty in eye opening, visual fatigue, appearance changes, and compensatory eyebrow lifting, impairing quality of life^[11].

The present study showed that the total effective rate was 94.87% in the observation group and 79.49% in the control group ($P < 0.05$). Chen Yuan et al.^[12] reported that the total cure rate of modified levator palpebrae superioris shortening for mild to moderate blepharoptosis was 97.78%, which was similar to the results of this study, indicating that modified levator palpebrae superioris shortening can effectively improve mild to moderate blepharoptosis. The modified procedure conforms more closely to the original anatomical mechanics of the levator palpebrae superioris in terms of exposure, dissection and fixation of the levator aponeurosis, allowing for more precise control of the shortening length under adequate exposure of the aponeurosis. Marking six points (medial, middle and lateral) in upper and lower rows and applying mattress sutures stably connect the levator aponeurosis to the tarsal plate at multiple stress points. This not only strengthens the traction force of the levator muscle but also maintains a natural transition of the eyelid margin curvature, reducing the risk of uneven local stress and undercorrection caused by single suture fixation. Relevant literature has reported that such multipoint fixation can significantly reduce aponeurotic retraction and maintain longterm lifting efficiency of the levator muscle postoperatively^[13]. In addition, moderate excision of herniated orbital fat, removal of loose orbicularis oculi muscle, and reconstruction of the pretarsal fascia during surgery help the levator palpebrae superioris exert a fuller lifting effect during contraction, while reducing resistance against aponeurotic advancement from pretarsal tissue, thereby improving the range of upper eyelid movement. Furthermore, the modified procedure emphasizes preserving the functional length at the junction of Müller's muscle and the aponeurosis, avoiding decreased levator tension caused by excessive dissection. This helps reduce the incidence of undercorrection and exerts a positive effect on levator function recovery in patients with mild to moderate ptosis. In this study, both the complication rate and the 6month postoperative recurrence rate were significantly lower in the observation group ($P < 0.05$), which is consistent with the above mechanisms and reflects favorable safety.

5. Conclusion

In conclusion, modified levator palpebrae superioris shortening achieves a high clinical effectiveness rate in the correction of mild to moderate blepharoptosis. It can reduce complications such as infection, failure of double eyelid fold formation and lagophthalmos, as well as lower the recurrence rate at 6 months postoperatively, indicating that this procedure demonstrates favorable clinical value in both efficacy and safety.

Disclosure statement

The author declares no conflict of interest.

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Methods for Establishing Critical Value Standards for Psychiatric Patients and Their Clinical Application Effects

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Abstract: *Objective:* To explore the method of formulating critical value (CLV) standards for psychiatric patients and analyze the effect of its clinical application. *Methods:* Research time: January 2024 to December 2025, the research subjects were 62 psychiatric patients admitted to the psychiatric department of our hospital. According to the different criteria for determining the critical value of the test, they were divided into a research group and a control group, with 31 cases in each group. The research group used the specially formulated critical value standards for psychiatric patients to carry out inspection management, while the control group used conventional clinical inspection risk assessment methods for management. Explore the application effects of the 2 groups. *Results:* A total of 31 cases of critical value testing occurred in the study group, and 30 cases were correctly identified; a total of 31 cases of critical value testing occurred in the control group, and 23 cases were correctly identified, with a comparison $P < 0.05$. The incidence of adverse events in the study group was lower (3.23% vs 19.35%), with a comparison $P < 0.05$. The test report turnaround time and hospitalization time of the study group were shorter than those of the control group, $P < 0.05$. *Conclusion:* Combining the clinical characteristics of patients with mental illness, the critical value standard developed through the three-step method of literature review, expert consultation, and clinical verification can effectively improve the accuracy of critical value identification, shorten the turnaround time of test reports, avoid the occurrence of adverse events, and thus improve the prognosis of patients.

Keywords: Mental illness; Testing critical value; Formulating methods; Clinical application

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1. Introduction

The critical test value refers to the test result that indicates that the patient may be in a life-critical state. Once a critical value occurs, corresponding clinical intervention measures must be taken immediately, the patient's condition may worsen, and even life safety may be endangered^[1]. Due to the influence of the disease itself, mentally ill patients have characteristics such as poor ability to complain, mental symptoms masking physical discomfort, a narrow drug treatment window, high risk of poisoning, and difficulty in identifying physical comorbidities, making it significantly more difficult to identify and handle patients' critical values than ordinary patients^[2]. Currently, there is no unified clinical standard for critical value testing for psychiatric patients. Most medical institutions still use the critical value testing standards for

ordinary patients, or use conventional risk assessment methods to carry out testing and management. Problems such as missed critical value determination, misjudgment, or untimely treatment may occur, which increases the risk of clinical diagnosis and treatment of patients^[3]. To this end, this study analyzes the application effect of the critical value standard, which is summarized as follows.

2. Materials and methods

2.1. General information

(1) Research time

January 2024 to December 2025, the research subjects were 62 psychiatric patients admitted to the psychiatric department of our hospital. According to the different criteria for determining the critical value of the test, they were divided into a research group and a control group, with 31 cases in each group. There were 17 males and 14 females in the study group; the age range was 21 to 64 years old, with an average age of (38.25 ± 10.12) years old; the disease duration was 1.5 to 12.0 years, with an average disease duration of (5.68 ± 2.34) years; the disease types included 19 cases of schizophrenia, 7 cases of bipolar disorder, 3 cases of paranoid psychosis, and 2 cases of other types; 23 patients were taking antipsychotic drugs for a long time, and 8 patients had basic diseases such as mild hypertension and diabetes. There were 16 males and 15 females in the control group; they were 20 to 65 years old, with an average age of (37.98 ± 10.35) years old; the disease duration was 1.2 to 12.5 years, with an average disease duration of (5.52 ± 2.41) years; the disease types included 18 cases of schizophrenia, 8 cases of bipolar disorder, 4 cases of paranoid psychosis, and 1 case of other types; 22 patients were taking antipsychotic drugs for a long time, and 9 patients had basic diseases such as mild hypertension and diabetes. Comparison of baseline data between the 2 groups $P > 0.05$.

(2) Inclusion criteria

- (a) Clearly diagnosed with mental illness according to DSM-5 diagnostic criteria;
- (b) Stable mental symptoms, no severe mania, depression or impulsive aggressive behavior;
- (c) Regular routine blood tests, biochemistry, blood drug concentration and other tests;
- (d) Voluntarily participate in this study;
- (e) Able to cooperate in completing tests and follow-up work.

(3) Exclusion criteria

- (a) Serious blood system diseases, immune system diseases or infectious diseases;
- (b) Associated with mental retardation, organic mental disorder, alcohol or drug dependence, etc.;
- (c) Use of anticoagulants, hormones, immunosuppressants and other drugs that may affect test results in the past month;
- (d) Failure to cooperate with test operations, follow-up or incomplete clinical data.

2.2. Method

2.2.1. Method for formulating the standards for testing critical values

Combined with the clinical characteristics of patients with mental illness, a three-step method of literature review, expert consultation, and clinical verification was used to develop the standard for critical value testing.

- (1) Literature review: Systematic search of databases such as PubMed, China National Knowledge Infrastructure, and Wanfang to collect relevant research, clinical guidelines, and testing management specifications on critical value testing for mental patients at home and abroad. Focus on sorting out the critical value limits, formulation basis, and clinical application experience of common test items for patients with mental illness to provide theoretical support for the formulation of standards.
- (2) Expert consultation: Invite 2 chief physicians of the psychiatry department, 1 deputy chief physician of the laboratory department, and 1 clinical pharmacist to form an expert group. All experts have more than 10 years of relevant clinical or laboratory work experience and are familiar with the characteristics of diagnosis and treatment of mental patients

and the management process of critical laboratory test values. Based on the results of the literature review, the expert group conducted a demonstration on the critical value limits of common test items for patients with mental illness, focusing on the impact of antipsychotic drugs on test results, the masking characteristics of physical symptoms of patients with mental illness and other factors, and proposed revisions. After three rounds of consultation, a consensus was reached and a draft standard for testing critical values was formed.

- (3) Clinical verification: Select 10 patients with mental illness to conduct a pre-test, use the draft standard to carry out critical value identification and treatment, record the critical value identification situation, treatment effects and existing problems, and fine-tune the critical value boundaries in the draft standard based on clinical intervention feedback, optimize the identification process, and finally determine the critical value standard that meets the clinical characteristics of patients with mental illness, and clarify the upper and lower limits of critical values, identification processes and treatment principles for each test item.

2.2.2. Research group

The above-mentioned critical value standards for testing of mentally ill patients are used to carry out inspection management. The inspectors strictly follow the critical value limits in the standard to screen the patient's blood routine, biochemistry, blood drug concentration and other test results. Once a critical value is found, the specimen quality and testing process are immediately checked. After confirmation, the test results are notified via phone and system message within 5 minutes. Psychiatric medical staff also record the results of the critical value, the time of discovery, notification time and the recipient; after receiving the notification, the medical staff will evaluate the patient within 10 minutes and take targeted intervention measures. Within 30 minutes, the intervention measures and the patient's condition changes will be recorded in the course of the disease, and the test results will be followed up and reviewed until the critical value returns to normal.

2.2.3. Control group

Conventional clinical testing risk assessment methods are used for management. Testing personnel make manual judgments on obviously abnormal test results in accordance with the testing standards for ordinary patients. After abnormal results are discovered, medical staff are notified, and the risk assessment of the patient is conducted based on clinical experience, and corresponding intervention measures are taken. Both groups of patients received continuous intervention for 4 weeks.

2.3. Observation indicators

- (1) Test the accuracy of critical value identification: The test personnel will fill in the critical value identification record form to record the patient's test results, whether it is a critical value, identification results and other information.
- (2) Adverse event incidence rate: filled in by medical staff to record the time, type, cause and treatment results of adverse events.
- (3) Test report turnaround time: filled in by the tester, recording the patient test specimen collection time, test start time, report issuance time, and calculating the turnaround time.

At the same time, the time from the issuance of test results to the time when medical staff takes intervention measures is recorded in detail; the patient's prognosis is assessed using the Brief Psychiatric Rating Scale (BPRS), with a total score of 18 to 126 points. 18 to 35 points are a good prognosis, with mild mental symptoms and can lead a normal life; 36 to 70 points are a moderate prognosis, with obvious mental symptoms and require further intervention; 71 to 126 points are a poor prognosis, severe mental symptoms, and inability to take care of themselves.

2.4. Statistical methods

The SPSS 26.0 software was used to process the data involved in the study. Measurement data were expressed as "mean $\pm$ standard deviation (SD)" and tested by "t"; count data were expressed as "[n(%)]" and tested by " χ^2 ". $P < 0.05$ indicated

that the difference was significant.

3. Results

3.1. Comparison of test critical value identification accuracy

A total of 31 cases of critical value testing occurred in the study group, and 30 cases were correctly identified; a total of 31 cases of critical value testing occurred in the control group, and 23 cases were correctly identified, with a comparison $P < 0.05$ (Table 1).

Table 1. Comparison of critical value identification accuracy rates between two groups [n (%)]

Group	n	Actual critical value examples	Correctly identify instances	Recognition accuracy (%)
Research group	31	31	30	96.77
Control group	31	31	23	74.19
χ^2	—	—	—	6.369
P	—	—	—	0.012

3.2. Comparison of adverse event incidence rates

The incidence of adverse events in the study group was lower (3.23% vs 19.35%), with a comparison $P < 0.05$ (Table 2).

Table 2. Comparison of the incidence of adverse events between the two groups [n (%)]

Group	n	Electrolyte imbalance	Hypoglycemia	Drug poisoning	Worsening of the condition	Incidence rate (%)
Research group	31	1 (3.23)	0	0	0	1 (3.23)
Control group	31	2 (6.45)	2 (6.45)	1 (3.23)	1 (3.23)	6 (19.35)
χ^2	—	—	—	—	—	4.026
P	—	—	—	—	—	0.045

3.3. Comparison of inspection report turnaround time, nursing intervention timeliness and BPRS score

The test report turnaround time and hospitalization time of the study group were shorter than those of the control group, $P < 0.05$ (Table 3).

Table 3. Comparison of test report turnaround time, nursing intervention timeliness and BPRS score (mean $\pm$ SD) between the two groups

Group	n	Inspection report turnaround time (min)	Nursing intervention time (min)	BPRS score (points)
Research group	31	28.56 $\pm$ 4.32	18.56 $\pm$ 4.23	35.67 $\pm$ 5.89
Control group	31	45.23 $\pm$ 5.16	32.74 $\pm$ 5.61	48.92 $\pm$ 6.78
t	-	13.792	11.237	8.214
P	-	0.000	0.000	0.000

4. Discussions

In the clinical diagnosis and treatment of mentally ill patients, test results are an important basis for judging the patient's

physical condition and adjusting treatment plans, and the timely identification and handling of critical test values are directly related to the patient's life safety^[4]. Due to the special clinical characteristics of patients with mental illness, ordinary standards for testing critical values are difficult to adapt to the needs of clinical diagnosis and treatment. Conventional risk assessment methods lack standardized processes, which may lead to untimely identification of critical values and irregular handling, thereby increasing the risk of clinical adverse events for patients. Therefore, formulating targeted critical value standards for testing of mentally ill patients is of great significance to optimizing testing management and ensuring patient safety^[5].

This study adopted a three-step method of literature review, expert consultation, and clinical verification to formulate the critical value standard. The literature review provided solid theoretical support for the formulation of the standard and ensured the scientific nature of the critical value standard. Expert consultation combined with the opinions of psychiatry, laboratory medicine, clinical pharmacy and other disciplines, focusing on the impact of antipsychotic drugs on test results, avoiding the limitations of ordinary standards. Clinical verification passed pre-tests to further optimize the details of the standard to ensure that the critical value standard can adapt to actual clinical needs and improve operability of the critical value standard. Clinical application results show that the research team's critical value identification accuracy rate is 96.77%, indicating that the critical value standard can clarify the boundaries of critical values, standardize the identification process, and reduce missed judgments and misjudgments, thereby helping inspectors to quickly and accurately identify critical values^[6].

The incidence rate of adverse events in the study group was 3.23%, and the turnaround time of inspection reports was significantly shortened. The key is that the critical value standard clarifies the notification time limit and intervention time limit after the critical value is discovered, and establishes a closed-loop management process of "inspection-notification-intervention-review". Inspection personnel and medical staff cooperate with each other to quickly deal with critical values, promptly correct the patient's physical abnormalities, and avoid further deterioration of the condition. At the same time, the critical value standard also clarifies the handling principles of each test item, provides clear clinical guidance for medical staff, and reduces the blindness of intervention^[7].

The nursing intervention time of the study group was shortened and the BPRS score was reduced, indicating that by testing the critical value standard, the critical value can be quickly identified, the direction of intervention can be clarified, and the medical staff can take effective intervention measures in a short time, to obtain the best treatment opportunity for the patient, improve the patient's mental symptoms, alleviate physical discomfort, and thereby improve the patient's prognosis quality^[8].

The study also has certain limitations. The sample size of the study was small, including only 62 patients, and the study period was short. It was not possible to observe and test the application effect of the critical value standard for a long time; the study only selected patients from a single hospital, and the generalizability of the results may be affected. Follow-up studies can expand the sample size, extend the research period, and include patients from multiple centers to further verify the scientificity and practicality of the critical value test standards. At the same time, the critical value threshold can be optimized based on the individual differences of patients to achieve individualized test management.

5. Conclusion

In summary, combined with the clinical characteristics of patients with mental illness, the critical value standard for testing developed through the three-step method of literature review, expert consultation, and clinical verification can effectively improve the accuracy of identifying critical values for testing, shorten the turnaround time of test reports, avoid the occurrence of adverse events, and thus improve the prognosis of patients.

Disclosure statement

The author declares no conflict of interest.

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Clinical Effects of Cognitive Behavioral Therapy Combined with Mindfulness Training on Emotional Regulation and Sleep Quality in Adolescents with Depressive Disorders

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Abstract: *Objective:* This study aimed to investigate the intervention effects of cognitive behavioral therapy (CBT) combined with mindfulness training on emotional regulation ability and sleep quality in adolescents with depressive disorders, providing evidence for optimizing non-pharmacological intervention strategies for adolescent depression in clinical settings. *Methods:* A total of 200 adolescent patients with depressive disorders admitted to the psychiatric outpatient and inpatient departments of our hospital from February 2025 to February 2026 were selected and randomly divided into a control group (100 cases) and an observation group (100 cases). The control group received conventional antidepressant medication plus routine psychological care, while the observation group received CBT combined with mindfulness training in addition to the control group's treatment. Both groups underwent an 8-week intervention period. Emotional state, emotional regulation ability, and sleep quality were assessed before and after the intervention, and adverse reactions were recorded. *Results:* After 8 weeks of intervention, compared with the control group, the observation group showed significantly lower scores on the Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), Pittsburgh Sleep Quality Index (PSQI), and all dimensions and total scores of the Treatment Emergent Symptom Scale (TESS) (all $P < 0.001$). Scores on all dimensions of emotional regulation ability were significantly higher in the observation group (all $P < 0.001$). *Conclusion:* CBT combined with mindfulness training significantly improves depressive and anxious moods, enhances emotional regulation ability, and optimizes sleep quality in adolescents with depressive disorders, with good safety and clinical applicability.

Keywords: Cognitive behavioral therapy; Mindfulness training; Adolescent depressive disorders; Emotional regulation; Sleep quality

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1. Introduction

Adolescence is a critical period of rapid physical and psychological development and a high-risk phase for depressive disorders^[1]. Epidemiological data indicate a rising prevalence of depressive disorders among Chinese adolescents,

with detection rates reaching 15%–20% among those aged 12–18 years old, severely impacting academic performance, social functioning, and physical and mental health, while increasing the risk of self-harm and suicide^[2]. Currently, pharmacological treatment remains the primary approach for adolescent depressive disorders in clinical settings; however, monotherapy faces challenges such as slow onset, high recurrence rates, and poor adherence in some patients, with long-term medication use potentially affecting neurological development in adolescents. Cognitive behavioral therapy (CBT) is a widely used psychological intervention that improves depressive-related negative emotions by correcting distorted cognitions and reshaping adaptive behavioral patterns^[3]. Mindfulness training, centered on “present-moment awareness and non-judgmental acceptance,” helps individuals alleviate emotional distress and enhance psychological resilience. Combining these two approaches enables multidimensional intervention in depressive disorders through cognition, behavior, and emotional awareness. This study selected 200 adolescent patients with depressive disorders to explore the intervention effects of CBT combined with mindfulness training, with results reported as follows.

2. Materials and Methods

2.1. General Information

This study enrolled 200 adolescent patients with depressive disorders admitted to the psychiatric outpatient and inpatient departments of our hospital from February 2025 to February 2026. Inclusion criteria were as follows: (1) meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for depressive disorders; (2) aged 12–18 years old; (3) SDS standard score ≥ 53 ; (4) informed consent from patients and their families; and (5) absence of severe physical diseases or other psychiatric disorders such as schizophrenia. Exclusion criteria included: (1) severe liver or kidney dysfunction or cardiovascular/cerebrovascular diseases; (2) receipt of systematic psychological intervention within the past 3 months; (3) documented history of drug allergies; and (4) intellectual or communication disabilities precluding cooperation with intervention and assessment.

Patients were randomly assigned to a control group and an observation group using a random number table method, with 100 cases in each group. In the control group, there were 42 males and 58 females, aged 12–17 years old (mean: 14.62 ± 1.35 years old), with a disease duration of 3–18 months (mean: 8.25 ± 2.16 months). In the observation group, there were 45 males and 55 females, aged 13–18 years old (mean: 14.78 ± 1.29 years old), with a disease duration of 4–19 months (mean: 8.41 ± 2.08 months). No statistically significant differences in general characteristics were observed between the two groups ($P > 0.05$), indicating comparability.

2.2. Intervention methods

The control group received conventional antidepressant medication combined with routine psychological care: (1) Pharmacotherapy: Sertraline was administered based on the patient’s age, weight, and condition (initial dose: 25 mg/day, gradually adjusted to 50–100 mg/day), taken orally once daily. Liver and kidney function and blood routine tests were monitored regularly during treatment, with medication regimens adjusted as needed. (2) Routine psychological care: Weekly 30-minute one-on-one psychological counseling sessions were conducted, covering disease education, medication guidance, emotional support, and family support to enhance treatment adherence.

In addition to the control group’s interventions, the observation group received CBT combined with mindfulness training. Both groups underwent an 8-week intervention period, with weekly 30-minute sessions led by two professional physicians with over 5 years of clinical psychological intervention experience.

2.2.1. CBT intervention steps

- (1) Cognitive restructuring phase (Weeks 1–3): Patients were guided to identify negative cognitions during depressive episodes, such as self-denial and loss of confidence in the future. Cognitive biases, including absolutist thinking, catastrophizing, and overgeneralization, were addressed through heuristic questioning and case comparisons to foster

rational and objective thinking.

- (2) Behavioral activation phase (Weeks 4–6): Individualized behavioral rehabilitation plans were developed based on each patient's circumstances, encouraging participation in mild social activities and regular exercise (e.g., walking, jogging) to break the cycle of “low mood → social withdrawal → worsening depression.” Patients were instructed to record daily behavioral patterns and emotional changes to reinforce positive behaviors.
- (3) Consolidation and relapse prevention phase (Weeks 7–8): The entire intervention process was reviewed, and techniques for managing negative emotions were summarized. Patients were guided to apply cognitive restructuring methods flexibly in daily life to reduce the risk of depressive symptom recurrence.

2.2.2. Mindfulness training steps

- (1) Mindful breathing: Patients assumed a comfortable seated position and focused on the physical sensations of nasal breathing, gently redirecting their attention back to breathing if their minds wandered. Each session lasted 15 minutes^[4].
- (2) Body scan: Patients systematically scanned their bodies from toes to head, observing physical sensations with an accepting and non-judgmental attitude toward tension or discomfort. Each session lasted 20 minutes.
- (3) Present-moment awareness: Patients were guided to observe their immediate emotions and thoughts without resistance, adopting an observer's perspective to rationally view emotional fluctuations. Each session lasted 25 minutes. Professional guided audio was provided for all mindfulness exercises, and patients were instructed to practice independently at home for 20 minutes daily to reinforce intervention effects.

2.3. Observation Indicators

- (1) Emotional state assessment: The SDS and SAS were used to evaluate emotional states before and after the 8-week intervention. Each scale consists of 20 items rated on a 4-point scale. An SDS standard score ≥ 53 indicates depressive symptoms, while an SAS standard score ≥ 50 indicates anxiety symptoms. Higher scores reflect more severe emotional disturbances.
- (2) Emotional regulation ability assessment: The Emotion Regulation Scale (ERS), comprising 10 items across two dimensions (cognitive reappraisal and expressive suppression), was used with a 5-point rating scale. Higher total scores indicate stronger emotional regulation ability. Cognitive reappraisal, an adaptive strategy, correlates positively with emotional regulation ability, whereas expressive suppression, a maladaptive strategy, correlates negatively.
- (3) Sleep quality assessment: The Pittsburgh Sleep Quality Index (PSQI), which evaluates seven dimensions (sleep quality, sleep latency, total sleep time, sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction) with a total score ranging from 0 to 21, was used. A PSQI score > 7 indicates poor sleep quality, with higher scores reflecting greater deterioration.
- (4) Adverse reactions: The Treatment Emergent Symptom Scale (TESS), covering 37 items across multiple dimensions (e.g., somatic symptoms, behavioral abnormalities, laboratory abnormalities), was used to assess adverse reactions during the intervention. Each item was rated on a 0–4 scale (0: absent; 1: mild; 2: moderate; 3: severe; 4: life-threatening). Higher total scores indicate greater adverse reaction burden.

2.4. Statistical Methods

Data were analyzed using SPSS 27.0. Continuous variables are presented as means $\pm$ standard deviations (SD), with between-group comparisons conducted using t-tests. A P -value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of Emotional State Scores Before and After Intervention

Compared with the control group, the observation group had significantly lower SDS and SAS scores (both $P < 0.001$)

(Table 1).

Table 1. Comparison of SDS and SAS scores before and after intervention between the two groups

Group	SDS Score		SAS Score	
	Before Intervention	After 8 Weeks of Intervention	Before Intervention	After 8 Weeks of Intervention
Control Group (n = 100)	62.34 ± 5.27	51.26 ± 4.82	56.78 ± 4.95	47.35 ± 4.21
Observation Group (n = 100)	62.51 ± 5.19	42.18 ± 4.36	56.92 ± 4.88	39.67 ± 3.95
<i>t</i>	0.216	13.970	0.201	13.319
<i>P</i>	0.829	< 0.001	0.841	< 0.001

3.2. Comparison of emotional regulation ability scores before and after intervention between the two groups

Compared with the control group, the observation group demonstrated significantly higher scores in both the cognitive reappraisal dimension and the expressive suppression dimension (both $P < 0.001$), as shown in **Table 2**.

Table 2. Comparison of ERS scores before and after intervention between the two groups

Group	Cognitive Reappraisal		Expressive Suppression	
	Pre-intervention	After 8 weeks of intervention	Pre-intervention	After 8 weeks of intervention
Control Group (n = 100)	22.45 ± 3.16	28.67 ± 3.52	18.32 ± 2.85	22.54 ± 3.01
Observation Group (n = 100)	22.58 ± 3.09	35.79 ± 3.68	18.41 ± 2.79	27.86 ± 3.12
<i>t</i>	0.272	14.001	0.228	12.268
<i>P</i>	0.786	< 0.001	0.820	< 0.001

3.3. Comparison of sleep quality scores before and after intervention between the two groups

Compared with the control group, the observation group had a lower PSQI score ($P < 0.001$), as shown in **Table 3**.

Table 3. Comparison of PSQI scores before and after intervention between the two groups

Group	Before Intervention	After 8 Weeks of Intervention
Control Group (n = 100)	13.56 ± 2.47	9.87 ± 1.68
Observation Group (n = 100)	13.72 ± 2.51	6.24 ± 1.35
<i>t</i>	0.454	16.883
<i>P</i>	0.650	< 0.001

3.4. Comparison of the incidence of adverse reactions between the two groups

Compared with the control group, the observation group demonstrated significantly lower scores across all dimensions and the total score of the TESS scale (all $P < 0.001$). See **Table 4**.

Table 4. Comparison of TESS scale scores between the two groups during the intervention period

Group	Behavioral Symptoms	Neurological Symptoms	Autonomic Nervous System Symptoms	Gastrointestinal Symptoms	Skin Symptoms	Laboratory Abnormalities	Total Score
Control Group (n = 100)	1.23 ± 0.35	1.35 ± 0.42	1.18 ± 0.38	1.05 ± 0.32	0.21 ± 0.15	0.18 ± 0.12	5.20 ± 1.26
Observation Group (n = 100)	0.56 ± 0.22	0.62 ± 0.25	0.48 ± 0.19	0.42 ± 0.18	0.09 ± 0.08	0.07 ± 0.06	2.24 ± 0.78
<i>t</i>	15.907	14.873	16.736	17.071	7.346	8.613	20.013
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

4. Discussion

The pathogenic mechanism of adolescent depression is characterized by multivariate complexity. Clinical research and practical diagnosis and treatment both indicate that the onset and progression of this disease are closely related to three major factors: cognitive thinking biases, emotional regulation disorders, and sleep rhythm imbalances. These three factors do not act independently but interact and influence each other, forming a vicious cycle that is difficult to alleviate spontaneously. Adolescents are in a special developmental stage of cognitive growth and emotional and mental maturation, where negative cognitive beliefs can easily trigger adverse psychological experiences such as depression and anxiety. When an individual has deficiencies in emotional regulation ability, these negative emotions are difficult to effectively channel and release, subsequently disrupting normal sleep patterns and causing various sleep problems such as difficulty falling asleep, light sleep, and frequent nightmares^[5]. At the same time, long-term poor sleep quality further increases cognitive load on the brain, resulting in cognitive impairment, a more pronounced tendency towards negative thinking, and a continuous decline in emotional state, ultimately leading to the aggravation of depressive clinical manifestations and the formation of an intractable vicious cycle^[6]. Therefore, the key to clinical intervention in adolescent depressive disorders lies in breaking the vicious cycle among cognition, emotion, and sleep, and implementing comprehensive measures from multiple dimensions, such as cognitive correction, emotional regulation, and sleep intervention, to comprehensively improve the physical and mental health of patients.

The results of this study show that after 8 weeks of intervention, the scores of the Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS) in the observation group were significantly lower than those in the control group, suggesting that Cognitive Behavioral Therapy (CBT) combined with mindfulness training can more effectively alleviate depression and anxiety in adolescent patients with depressive disorders. CBT helps patients establish rational cognition and reduce the impact of negative thinking on emotions by identifying and correcting cognitive distortions such as absolutization and catastrophization^[7]; mindfulness training guides patients to observe their emotions with an accepting and non-judgmental attitude, avoiding emotional confrontation and reducing the intensity of emotional responses^[8]. The synergistic effect of the two improves negative emotions from the aspects of cognitive adjustment and emotional awareness, showing better results than single-drug therapy combined with routine care.

Emotional regulation ability is a core competence for adolescents to resist psychological stress and maintain physical and mental health. Depressed individuals often exhibit psychological characteristics such as weakened cognitive reappraisal ability and deliberate suppression of emotional expression^[9]. This study shows that after intervention, the score of the Cognitive Reappraisal Scale in the observation group was significantly better than that in the control group, confirming that comprehensive intervention can effectively improve patients' cognitive reappraisal level. This effect stems from the cognitive correction and behavioral activation of CBT, combined with the emotional perception effect of mindfulness training, helping patients master emotional regulation methods and improve emotional tolerance.

The synchronous increase in the score of the expression suppression dimension in the observation group suggests that intervention may exacerbate the tendency to suppress emotions and induce psychological repression. Some patients misinterpret the non-judgmental acceptance concept of mindfulness and deliberately suppress their emotional expression. Clinical intervention should pay attention to this issue, provide special guidance on reasonable emotional expression, correct misconceptions, and avoid psychological problems caused by excessive emotional suppression.

Sleep abnormalities are very common comorbid symptoms in adolescent patients with depression and are also a key factor restricting the recovery process of the disease^[10]. The data from this study show that the overall score and scores of each dimension of the Pittsburgh Sleep Quality Index (PSQI) in the observation group were significantly lower than those in the control group, confirming that the combined intervention program can effectively improve patients' sleep status. Negative emotions such as depression and anxiety are the main inducements for sleep dysfunction. CBT combined with mindfulness training can effectively channel adverse emotions. Among them, the relaxation intervention method of mindfulness training can regulate the body's autonomic nervous system state, reduce sympathetic nervous system excitement, help patients relieve pre-sleep anxiety, reduce the time taken to fall asleep, and improve overall sleep stability; and after sleep status improves, it can also effectively relieve brain fatigue and optimize cognitive ability, ultimately forming a virtuous cycle of physical and mental recovery.

Throughout the clinical intervention process, close attention should be paid to the monitoring and control of adverse events. The adolescent group is particularly special, as individuals in this age group have not yet fully developed physically and mentally and have relatively weak drug tolerance. Once drug-related adverse reactions occur, they will not only reduce patients' treatment compliance but also pose potential risks to clinical diagnosis and treatment safety. This study used the Treatment Emergent Symptom Scale (TESS) to conduct standardized evaluations of adverse reactions in the two groups of subjects. The results show that the scores of each dimension and the overall total score of the scale in the observation group were significantly lower than those in the control group, and there was also a significant advantage in the probability of adverse reactions. This confirms that the intervention model combining CBT with mindfulness training can effectively avoid the occurrence of adverse events and improve the safety guarantee of clinical diagnosis and treatment. Mindfulness training can effectively relieve physical discomfort symptoms and improve the body's tolerance state, which may also be an important reason for the significantly lower incidence of adverse reactions in the observation group. In this study, the adverse reactions that occurred in the two groups of subjects were all of mild to moderate severity, and the symptoms were successfully relieved after clinical symptomatic intervention. No severe adverse events occurred throughout the process, fully confirming that CBT combined with mindfulness training has reliable clinical application safety.

This study has certain limitations: the study sample was only from a single hospital, so the sample representativeness is limited; the intervention period was 8 weeks, and no long-term follow-up was conducted, making it impossible to evaluate the long-term impact of the combined intervention on depression recurrence; and the differences in intervention among adolescents of different ages and genders were not explored in depth. In the future, the sample size can be expanded, multi-center studies can be carried out, and the follow-up period can be extended to further optimize the intervention program.

5. Conclusion

In conclusion, the application of CBT combined with mindfulness training in adolescent patients with depressive disorders can significantly improve depression and anxiety, enhance emotional regulation ability, optimize sleep quality, and has a low incidence of adverse reactions and good safety. It is an efficient and feasible non-drug combined intervention program worthy of clinical promotion and application.

Disclosure statement

The author declares no conflict of interest.

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Effect of Targeted High-Quality Operating Room Nursing on Psychological Status and Pain in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract: *Objective:* To investigate the effect of targeted high-quality operating room nursing intervention on psychological status and pain in patients undergoing laparoscopic cholecystectomy. *Methods:* A total of 86 patients undergoing laparoscopic cholecystectomy were enrolled from March 2024 to March 2025. They were divided into two groups by a double-blind method: the observation group received targeted high-quality operating room nursing, while the reference group received routine nursing. The overall intervention effects were analyzed. *Results:* There were statistically significant differences between the two groups in anxiety and depression scores ($P < 0.05$); in restlessness and VAS scores ($P < 0.05$); in surgical and rehabilitation indicators ($P < 0.05$); and in complications and satisfaction rate ($P < 0.05$). *Conclusion:* In the nursing care of patients undergoing laparoscopic cholecystectomy, the nursing method used in this study has practical application value. It can effectively improve psychological status, relieve postoperative pain, reduce complications, and enhance overall patient satisfaction.

Keywords: Targeted nursing; Operating room nursing; Laparoscopy; Cholecystectomy; Pain degree

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1. Introduction

The incidence of gallstones remains high, with biliary colic as the main symptom, often manifesting as acute or chronic cholecystitis, which affects patients' physical and mental health. Scholars have found that the incidence of gallstones accounts for more than 10% of gallbladder diseases. In recent years, the onset age has tended to be younger, while the incidence remains elevated, and surgical treatment is commonly adopted clinically. The pathogenesis of this disease is complex, and disease progression can lead to adhesion and atrophy of tissues surrounding the gallbladder, making treatment rather challenging^[1]. Laparoscopic cholecystectomy is widely applicable for gallstones, chronic cholecystitis and other related conditions, and also possesses diagnostic value. It achieves therapeutic effects by resecting part of the gallbladder. With the advancement of laparoscopic technology in recent years, this procedure has gained increasing clinical attention. However, patients inevitably experience physiological and psychological responses during surgery, which may interfere with the surgical process and affect prognosis. The success of surgery depends not only on surgeons' professional skills and experience but also on perioperative cooperation from nursing staff, which is one of the key influencing factors^[2]. In traditional nursing

care, interventions lack specificity and purposefulness, resulting in unsatisfactory comprehensive outcomes. Targeted high-quality operating room nursing advocates formulating nursing plans based on disease diagnosis and surgical conditions, providing patients with whole-course care, delaying disease progression, and achieving favorable prognosis ^[3]. Operating room nursing aims to design individualized schemes according to patients' conditions, enabling nurses to cooperate closely with surgeons, give play to their initiative, shorten operation time, reduce blood loss, and improve surgical safety. This nursing model adheres to the people-oriented principle, requiring nurses to integrate past experience and diagnostic findings, so as to reflect the scientificity, systematicness and integrity of nursing practice.

2. Materials and methods

2.1. General data

A total of 86 patients undergoing laparoscopic cholecystectomy were enrolled from March 2024 to March 2025. They were divided into two groups by double-blind method, with 43 cases in each group. **Inclusion criteria:** (1) Meeting the diagnostic criteria for gallstones; no surgical contraindications; good compliance. **Exclusion criteria:** (1) Pregnant and lactating women; (2) Patients with impaired organ function; (3) Patients with mental disorders; (4) Patients with immune system diseases. There was no statistically significant difference in the above data between the two groups ($P > 0.05$). See **Table 1** for details.

Table 1. Comparison of general data between the two groups [n, mean $\pm$ SD]

Group	Total patients	Patients		Age (years old)	Average age (years old)	Average diameter of stones (cm)
		Male	Female			
Reference group	43	23	20	25–68	46.28 $\pm$ 2.30	(2.31 $\pm$ 0.42)cm
Observation group	43	24	19	24–71	46.55 $\pm$ 2.81	(2.08 $\pm$ 0.33)cm

2.2. Methods

The reference group received routine nursing care. Vital signs were monitored, patients were assisted with preoperative examinations, psychological counseling and health education were provided, and postoperative precautions as well as possible complications were explained.

The observation group received targeted high-quality operating room nursing.

- (1) Preoperative visit: Visit patients preoperatively to clarify disease progression and guide them in position training; assist patients with preoperative examinations and prepare medications, instruments and other supplies required for surgery in advance. Communicate and interact with patients proactively, understand their actual needs, listen to their statements, answer questions in a timely manner, and provide encouragement and support to alleviate negative emotions. Meanwhile, help patients fully understand the importance and necessity of the operation. In addition, nurses should be proficient in surgical procedures, emergency response methods, and precautions to boost patients' confidence. On the night before surgery, patients should be instructed to follow a light and easily digestible diet, avoiding strong irritants and greasy foods ^[4]. Enemas should be administered before sleep to keep the intestines clean for postoperative flatus.
- (2) Intraoperative nursing: Adjust the temperature and humidity of the operating room in advance. Explain the operating room environment patiently, based on the patient's actual condition. Fix the patient's limbs before anesthesia, explain possible sensations during the procedure, help the patient assume an appropriate position to improve comfort, and fix the lower extremities. Monitor vital signs during the operation; nurses should deliver surgical instruments and supplies promptly, inform doctors of any abnormalities immediately and assist in management to ensure orderly progress of the surgery. Offer encouragement to patients intraoperatively to enhance their confidence and stabilize their emotions.

- (3) Postoperative nursing: Gently call the patient when they are still unconscious after anesthesia to accelerate recovery of consciousness. Clean residual blood stains with warm saline and provide warming care. If no complications occur, transfer the patient to the ward, hand over all procedures and matters with other nursing staff, inform family members of the surgical situation, and explain possible postoperative adverse reactions and precautions. Provide a liquid diet to promote the recovery of gastrointestinal function. For symptoms such as subcutaneous emphysema and back pain, inform patients that these conditions will resolve gradually without special intervention to relieve their worries and anxiety. Use encouragement and comfort to improve patient compliance, enabling them to cooperate with nursing work, alleviate pain and shorten the recovery period^[5]. Conduct timely follow-up visits, inquire about the patient's feelings, check their mental state and whether the incision is infected, and provide hygiene guidance to reduce accidents. In addition, early functional rehabilitation training can be carried out to enhance physical fitness and accelerate recovery.

2.3. Observation indicators

- (1) The Self-Rating Anxiety Scale (SAS) was used to assess the degree of anxiety, and the Self-Rating Depression Scale (SDS) was used to assess the degree of depression, with scores ranging from 0 to 100.
- (2) Agitation: Postoperative agitation was evaluated using the Riker Sedation-Agitation Scale, with scores ranging from 1 to 7; a higher score indicated more severe agitation.
- (3) Pain intensity was assessed using the Visual Analogue Scale (VAS), with scores ranging from 0 to 10.
- (4) Surgical and rehabilitation indicators of the two groups were observed, including operation time, intraoperative blood loss, time to first flatus, and length of hospital stay; the incidence of complications was recorded.
- (5) A self-designed satisfaction questionnaire was used to evaluate and record patient satisfaction.

2.4. Statistical analysis

Data analysis was performed using SPSS 25. 0 software. Enumeration data were expressed as n(%) and measurement data as mean $\pm$ standard deviation (SD). Intergroup comparisons were conducted using the χ^2 test and t-test. A value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of psychological status between the two groups

After intervention, the anxiety and depression scores in the observation group were lower than those in the reference group, with statistically significant differences ($P < 0.05$). See **Table 2** for details.

Table 2. Comparison of psychological status between the two groups [n (mean $\pm$ SD)]

Group	Number of cases	Anxiety		Depression	
		Before nursing	After nursing	Before nursing	After nursing
Reference group	43	65.34 $\pm$ 8.42	55.77 $\pm$ 7.69	63.25 $\pm$ 5.48	53.56 $\pm$ 7.28
Observation group	43	66.38 $\pm$ 8.07	36.12 $\pm$ 6.87	63.67 $\pm$ 8.55	33.64 $\pm$ 6.19
<i>t</i>		0.584	12.495	0.271	13.669
<i>P</i>		0.560	0.000	0.786	0.000

2.2. Comparison of agitation and pain between the two groups

The Riker Sedation-Agitation Scale score and VAS score in the reference group were higher than those in the observation group ($P < 0.05$). See **Table 3** for details.

Table 3. Comparison of agitation and pain between the two groups [n (mean $\pm$ SD)]

Group	Number of cases	Riker Sedation-Agitation Scale	VAS score
Reference group	43	3.89 $\pm$ 2.30	5.25 $\pm$ 1.43
Observation group	43	2.45 $\pm$ 2.01	3.62 $\pm$ 1.25
<i>t</i>		3.091	5.627
<i>P</i>		0.002	0.000

2.3. Analysis of surgical and rehabilitation indicators between the two groups

The results showed that the surgical indicators in the observation group were lower and the length of hospital stay was shorter than those in the reference group, with statistically significant differences ($P < 0.05$). See **Table 4** for details.

Table 4. Analysis of surgical and rehabilitation indicators between the two groups [n (mean $\pm$ SD)]

Group	Number of cases	Surgery time (min)	Intraoperative blood loss (mL)	The first exhaust time (h)	Hospitalization time (d)
Reference group	43	55.27 $\pm$ 11.70	43.30 $\pm$ 7.18	19.03 $\pm$ 3.33	7.51 $\pm$ 1.72
Observation group	43	46.45 $\pm$ 12.61	34.40 $\pm$ 8.55	15.81 $\pm$ 3.84	5.30 $\pm$ 1.40
<i>t</i>		3.362	5.227	4.154	6.534
<i>P</i>		0.001	0.000	0.000	0.000

2.4. Comparison of complications between the two groups

The incidence of complications was 25.58% in the reference group and 6.98% in the observation group ($P < 0.05$). See **Table 5** for details.

Table 5. Comparison of complications between the two groups [n(%)]

Group	Number of cases	Incision infection	Biliary fistula	Intra-abdominal hemorrhage	Obstructive jaundice
Reference group	43	4	3	4	25.58
Observation group	43	1	1	1	6.98
χ^2					5.460
<i>P</i>					0.019

2.5. Comparison of nursing satisfaction between the two groups

The overall satisfaction rate in the reference group was significantly lower than that in the observation group ($P < 0.05$). See **Table 6** for details.

Table 6. Comparison of satisfaction between the two groups [n(%)]

Group	Number of cases	Very satisfied	Fairly satisfied	Not satisfied	Satisfaction rate
Reference group	43	15	16	12	72.09
Observation group	43	23	17	3	93.02
χ^2					6.540
<i>P</i>					0.000

3. Discussion

Gallbladder diseases are common clinical disorders characterized by complex pathogenesis and rapid disease progression, which can affect patients' physical and mental health. Although open cholecystectomy can achieve obvious therapeutic effects, it is associated with numerous complications and slow recovery, leading to negative emotions and psychological disorders, prolonged rehabilitation time and poor prognosis^[6]. In recent years, minimally invasive techniques have attracted increasing attention, especially laparoscopy, which has been widely applied in clinical practice. Laparoscopic cholecystectomy offers advantages such as rapid recovery of visceral function, minimal trauma and a broad surgical view. Medical staff have gradually emphasized the application of this technique, making it one of the preferred methods for the treatment of gallbladder diseases^[7]. Some patients have a limited educational background and insufficient cognition, and may develop negative emotions in unfamiliar environments, which increases the difficulty of surgery^[8]. Although traditional nursing has certain advantages and obvious effects, it lacks systematicness and scientificity, limiting its clinical application. Therefore, it is necessary to explore other nursing strategies on this basis^[9]. Some surgical experts have pointed out that providing nursing intervention throughout the perioperative period can achieve remarkable outcomes, promote postoperative recovery and improve prognosis^[10].

Targeted high-quality operating room nursing advocates formulating nursing plans according to patients' conditions, actual needs and surgical situations, to reduce intraoperative stress, promote orderly implementation of various procedures, and minimize postoperative complications as much as possible^[11]. This study found that the surgical and rehabilitation indicators in the observation group were superior to those in the reference group, confirming that operating room nursing can shorten operation time, accelerate recovery, minimize the risk of complications, and thereby achieve improved prognosis. Under the background of the rapid development of medical technology, the safety of operating room nursing has attracted increasing attention, and how to ensure the safety of nursing work and improve therapeutic efficiency has gradually gained wide focus^[12]. In operating room nursing, developing care plans based on pathological conditions and surgical approaches enhances targeting. Interventions are carried out with patients as the core; patients are encouraged to express their feelings according to their physical and mental status, and proactive care is provided to improve comfort and satisfaction. Preoperative emotional counseling relieves tension and promotes cooperation with procedures; intraoperative position guidance and coordination with surgical operations help shorten operation time and alleviate patients' pain to the greatest extent. Postoperative monitoring of vital signs reduces complications, relieves pain, and improves surgical safety, thus lowering the incidence of complications, adverse reactions and accidents^[13]. The results of this study showed that there were significant differences in anxiety and depression scores between the two groups ($P < 0.05$); the Riker Sedation-Agitation Scale score and VAS score in the reference group were higher than those in the observation group ($P < 0.05$); differences in surgical and rehabilitation indicators between the two groups were statistically significant ($P < 0.05$); and comparisons of complications and satisfaction between the two groups also showed statistical significance ($P < 0.05$). This indicates that the nursing approach adopted in this study is valuable in the care of patients undergoing laparoscopic cholecystectomy. It can improve psychological status, relieve pain, reduce complications, and enhance overall patient satisfaction.

4. Conclusion

To sum up, compared with conventional nursing, targeted high-quality operating room nursing demonstrates greater value. It can achieve the goals of relieving pain, improving clinical indicators, shortening hospital stay, reducing complications and achieving a favorable prognosis, as well as enhancing nursing satisfaction. As a scientific and efficient nursing model, it is worthy of promotion and application in clinical operating room nursing.

Disclosure statement

The author declares no conflict of interest.

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Facilitators and Barriers Influencing Tertiary Medical Institutions Physicians' Willingness to Participate in mhGAP Training

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Abstract: *Background:* In response to the United Nations Sustainable Development Goal (SDG) 3.4 (mental health target), this study aimed to explore the facilitating and barrier factors influencing doctors' willingness to participate in the Mental Health Gap Action Programme (mhGAP) training in tertiary hospitals, using the Consolidated Framework for Implementation Research (CFIR). *Methods:* Semi-structured interviews were conducted with 20 physicians from tertiary hospitals. Content analysis was performed using NVivo 11, and results were reported in accordance with the Consolidated Criteria for Reporting Qualitative Research (COREQ). *Results:* A total of 23 facilitating factors and 13 barrier factors were identified, distributed across five CFIR dimensions: innovation, outer setting, inner setting, individuals, and implementation process. Results showed that the implementation process dimension contained the most facilitating factors ($n = 7$), while the outer setting dimension had the most barrier factors ($n = 4$). *Conclusions:* The study indicates that mhGAP training has strong promotion potential in tertiary hospitals. However, targeted optimization of external support systems and implementation details is required to enable mhGAP training in tertiary medical institutions to play a leading, supportive, and radiating role in alleviating mental health resource scarcity and optimizing mental health services.

Keywords: Mental health services; Mental Health Gap Action Programme (mhGAP) training; Implementation science; Consolidated framework for implementation research (CFIR); Facilitating and barrier factors

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1. Introduction

In 2015, countries worldwide adopted United Nations Sustainable Development Goal (SDG) 3, which aims to ensure healthy lives and promote well-being for people of all ages. Within this, Target 3.4 explicitly incorporates mental health for the first time, requiring the promotion of mental health and well-being through prevention and treatment. The World Health Organization's (WHO) Mental Health Gap Action Programme (mhGAP), which trains non-mental health professionals in mental health service competencies to deliver treatment and care to patients with mental, neurological, and substance use disorders, has become an effective tool for low- and middle-income countries to address shortages and uneven professional standards in mental health service human resources^[1]. mhGAP includes treatment guidelines for patients and training programs for non-mental health professionals.

Only three studies have focused on the pre-implementation phase of mhGAP, examining the facilitating and barrier factors for initiating the program. However, adequate pre-implementation research for mhGAP is necessary, as implementation plans developed based on facilitating and barrier factors are more conducive to the fidelity, acceptability, and sustainability of mhGAP implementation. Attention to the tertiary healthcare level is also critical: within the context of hierarchical medical system reform, tertiary hospitals typically play leading, supportive, and radiating roles. Thus, for the successful implementation and promotion of mhGAP, efforts should first start with tertiary hospitals, which can then gradually extend to secondary hospitals and primary care facilities, ultimately achieving full coverage. Nevertheless, research on factors influencing doctors' willingness to participate in mhGAP training within tertiary medical institutions prior to mhGAP implementation remains a gap.

This study will utilize the CFIR framework, aiming to focus on the pre-implementation phase of mhGAP and systematically explore the facilitating and barrier factors influencing doctors in tertiary medical institutions regarding their willingness to participate in mhGAP training. It seeks to provide optimization directions for the implementation and promotion of mhGAP training in countries and regions where hierarchical medical system reform is widely advancing.

2. Methods

2.1. Development of interview guide

The study designed the interview guide based on the CFIR ^[2]. First, an initial interview guide was drafted according to the research objectives through literature review and group discussions. Subsequently, three experts, with senior titles (associate senior or above), over 15 years of work experience, and from hospital management, department management, and senior medical leadership, respectively, were consulted to evaluate the guide. Revisions were made based on their feedback. Finally, pre-interviews were conducted with two physicians, and the guide was adjusted again based on the pre-interview results.

2.2. Data collection

Weicheng Qin (M.M.) and Wei Jiang conducted data collection using semi-structured interviews, having received professional training in qualitative interviewing. Prior to formal interviews, communication was held with respondents to explain the purpose of the interview, obtain their consent, and schedule the time and location. Face-to-face interviews were conducted in respondents' offices or rest areas, while online meeting interviews took place in their rest areas or homes, ensuring respondents were in a quiet and relaxed environment.

At the start of each interview, 10 minutes were spent using a PowerPoint presentation to introduce respondents to the Chinese-translated mhGAP guidelines and training program, including both outline and detailed content. Interviewers then used the interview guide as a framework, adjusting questioning strategies appropriately based on respondents' responses, and obtained detailed, in-depth information through questioning and active listening. Biased or leading questions were avoided during interviews to ensure the objectivity and authenticity of respondents' responses, and all interviews were audio-recorded. The study adhered to the principle of data saturation in qualitative research.

Using purposeful sampling, interviews were conducted with 20 physicians from Deyang People's Hospital. Physicians included in the study are those who have long-term engagement in frontline clinical diagnosis and treatment work with direct patient contact, specifically referring to physicians who routinely undertake direct clinical service tasks such as outpatient consultations, inpatient ward diagnosis and treatment, and patient follow-ups. The reason for selecting Deyang is that the city has established a mental health specialist alliance encompassing 31 member institutions, which is a form of medical consortium. Its construction achievements have been reported by authoritative official media in China. Deyang People's Hospital, as the leading tertiary medical institution in Deyang with the highest medical standards and greatest influence, serves as an ideal research site. Taking Deyang and Deyang People's Hospital as the research setting, this can provide a template for the implementation of mhGAP training led by tertiary medical institutions in the context of hierarchical medical system reform.

A total of 20 interviews were conducted from December 2024 to July 2025, including 13 face-to-face interviews and 7 online meeting interviews, with each interview lasting approximately 40 minutes. Interviews were concluded once data saturation was reached. Researchers adhered to the principle of confidentiality and properly stored all collected audio and text data.

2.3. Data analysis

Audio files were transcribed into text within 24 hours after each interview, and the text data were imported into NVivo11 qualitative analysis software for analysis. Weicheng Qin and Wei Jiang organized interview texts and conducted coding using NVivo11, applying content analysis to analyze interview content based on the CFIR-derived interview framework. Additionally, the two researchers cross-validated the coded content to ensure the reliability of results. Qualitative content reporting was conducted in accordance with the Consolidated criteria for Reporting Qualitative research (COREQ) guidelines.

3. Results

Table 1 presents the basic information of the respondents in this study. Among the 20 respondents, in terms of gender, 13 are male (accounting for 65%) and 7 are female (35%). For age, 8 are aged 26–30 (40%), 9 are 31–35 (45%), 1 is 36–40 (5%), and 2 are 41–45 (10%). Regarding educational qualifications, 15 have a master's degree (75%) and 5 have a doctor's degree (25%). In terms of title, 5 are beginners (25%), 13 are intermediate (65%), and 2 are advanced (10%). For professional years of service, 7 have 0–5 years (35%), 8 have 6–10 years (40%), 4 have 11–15 years (20%), and 1 has 16–20 years (5%). Overall, most respondents are male, relatively young, highly educated, with intermediate titles, and mainly have shorter-term professional experience.

Table 1. Basic information of the respondents

Characteristic	Number	Proportion
Gender		
Male	13	65%
Female	7	35%
Age		
26–30	8	40%
31–35	9	45%
36–40	1	5%
41–45	2	10%
Education		
Master's degree	15	75%
Doctoral degree	5	25%
Title		
Junior	5	25%
Intermediate	13	65%
Senior	2	10%
Professional Years		
0–5	7	35%
6–10	8	40%
11–15	4	20%
16–20	1	5%

Content analysis of the interview data based on the CFIR framework identified 23 facilitating factors and 13 barrier factors, which were specifically distributed across five dimensions: Innovation, Outer Setting, Inner Setting, Individuals,

and Implementation Process (**Table 2**). The five dimensions were numbered using uppercase English letters; facilitating factors were numbered with Arabic numerals; barrier factors were numbered with circled Arabic numerals; and each respondent was numbered using “R” (abbreviation for Respondent) followed by an Arabic number.

Table 2. Facilitating and barrier factors with exemplary textual materials

Dimension Categories	Facilitating Factors	Barrier Factors
A. Innovation	1. Clear core value <i>R01: “helps address patients’ physical and psychological issues through a dual approach... and also avoids some doctor-patient disputes, improving patient compliance.”</i>	
	2. High authority and credibility <i>R19: “It is developed by the WHO and supported by ample evidence-based research and practical experience.”</i>	① Rigidity in implementation: Lack of flexible adjustment space tailored to actual scenarios <i>R14: “Following the outline as it is should be fine, but in actual operation, adjustments still need to be made according to special circumstances.”</i>
	3. Systematic and detailed content <i>R17: “I find it covers a wide range of content, with detailed explanations of principles, and is divided into modules to address different scenarios/populations.”</i>	② Learning pathway obstacle: Excessive complexity of existing programs causes entry difficulties <i>R03: “It feels quite complex when first encountered. Could there be a more progressive learning plan? I think it seems quite complex initially, creating a psychological fear of difficulty... A guide for selecting key components to use would be helpful.”</i>
	4. Strong practicality <i>R01: “It provides specific operational steps. For example, when encountering relevant situations in clinical practice, one can refer to it for guidance.”</i>	
	5. Integration of multiple teaching formats <i>R06: “It includes both centralized learning and mentorship, making it easier to understand the knowledge.”</i>	① Inadequate policy incentives: Lack of performance evaluation guidance and promotion support <i>R07: “Without incorporating mental health service capabilities into hospital performance evaluations, it is impossible to promote bottom-up attention, making widespread implementation difficult”.</i>
B. Outer Setting	1. Strong external demand <i>R03: “With societal development, the public’s attention to mental health is increasing”.</i>	② Cognitive differences among service recipients; low acceptance of mental health knowledge in some groups <i>R15: “In fourth-tier cities, for young groups, their knowledge level is relatively better. However, middle-aged and elderly people have a much lower level of acceptance of such knowledge.”</i>
	2. Alignment with the concept of ecological model <i>R10: “Nowadays, there is an emphasis on practicing medicine based on the physiological-environmental-social ecological model, and participating in mhGAP training is in line with this trend.”</i>	③ Lack of organizational promotion <i>R08: “the absence of unified organization by government systems leads to fragmented training”.</i>
		④ Insufficient professional communication <i>R09: “There is a lack of a communication platform, making it difficult to have opportunities to communicate with a wide range of peers on mental health topics.”</i>

Dimension Categories	Facilitating Factors	Barrier Factors
C. Inner Setting	1. Established rapid linkage mechanism with psychiatric and psychological specialties <i>R02: "When encountering unresolved mental health issues in daily practice, we can quickly connect with psychiatric and psychological specialties, forming a positive cycle".</i>	① Limited time and energy among doctors: Heavy workloads leading to difficulties in learning participation <i>R03: "It is common to work from 7 a.m. to 7 p.m. at the hospital—writing medical records, issuing medical orders, performing surgeries, conducting preoperative consultations, processing discharges, and engaging in these tasks from morning to evening. After returning home, already exhausted, they may feel overwhelmed when it comes to learning mental health counseling, knowledge, or related training".</i>
	2. Guarantee of basic resources <i>R05: "The venue and personnel allocation can still meet our needs for participating in this training."</i>	② Scarcity of training resources <i>R01: "Basically, I rarely participate in courses in this area."</i>
	3. Long-term communication mechanism <i>R06: "Based on my past experience, participating in training is a good opportunity for mutual communication and learning."</i>	③ Lack of incentive mechanisms <i>R19: "There is a lack of incentive measures, such as financial incentives, certificates of honor, etc."</i>
	4. Driven by peer competition <i>R17: "The general mastery of knowledge by peers creates learning pressure on me."</i>	
D. Individuals	1. Dual promotion of doctors' capacity improvement, diagnostic and treatment level, and career development <i>R05: "For example, in communication or medication, through this training, we can obtain practical methods to guide patients, which will also be helpful for our own career development... It is more conducive to teaching students... Conducting necessary mental health assessments during diagnosis and treatment makes the diagnostic and treatment process more standardized."</i>	① low time priority <i>R06: "arrange training and learning after clinical work and academic conferences".</i>
	2. Enhanced professional sense of achievement <i>R20: "Providing better services to patients brings a sense of achievement."</i>	② Weak learning foundation <i>R08: "The prior reserve of relevant theories is insufficient, and I worry about being unable to keep up with the training progress."</i>
	3. Adequate intrinsic motivation <i>R18: "I am very interested in the field of mental health."</i>	
	4. Self-empowerment of doctors <i>R09: "Knowledge about psychological and health issues is definitely helpful for oneself; it can make one's own mental state healthier."</i>	
	5. Expanded social support and improved ability to care for relatives <i>R19: "In other aspects, including for relatives and family members, it can help them get out of some difficulties."</i>	

Dimension Categories	Facilitating Factors	Barrier Factors
E. Implementation Process	1. Standardized, systematic yet concise materials <i>R16: "has both a complete set of plans and materials for fragmented learning, and video materials for spare-time learning would be better".</i>	
	2. Teaching interaction support <i>R15: "There will definitely be doubts, and I hope there are channels to communicate and learn with trainers."</i>	
	3. Guarantee for centralized training <i>R05: "I hope for full-time training; it should be more helpful for quickly improving skills."</i>	
	4. Reasonable long-term training cycle: combining short-term intensive sessions with long-term continuity <i>R10: "Combining short-term and long-term sessions allows us to continue learning sustainably."</i>	①Lack of effect feedback <i>R12: "It's hard to persist without feedback".</i>
	5. Integration with clinical scenarios <i>R07: "Since our work already involves routine communication with patients, I hope the training content can be integrated into clinical work."</i>	
	6. Guarantee of high-quality teaching staff <i>R09: "I hope to have lectures by experts. Such rare opportunities may also encourage us to participate in training, because usually you may not have the chance to access these teachers."</i>	
	7. Standardized training management: clear mandatory content with supporting assessments <i>R11: "It is necessary to set some mandatory learning chapters along with assessments; this will promote everyone to study seriously."</i>	

The Innovation domain (A) comprises 5 facilitating factors and 2 barrier factors. Among the facilitating factors, a clear core value (A1) stands out as a prominent feature. Physicians reported that the training “R01- helps address patients’ physical and psychological issues through a dual approach,” while also “avoiding some doctor-patient disputes” and “improving patient compliance,” directly reflecting the practical value of mhGAP training for clinical practice. The primary barrier factor manifests as a learning pathway obstacle (A②). Some physicians noted, “R03- It feels quite complex when first encountered. Could there be a more progressive learning plan... It creates a psychological fear of difficulty... A guide for selecting key components to use would be helpful.”

The Outer Setting domain (B) includes 2 facilitating factors and 4 barrier factors. Among the facilitating factors, strong external demand emerged as a significant driver (B1). “R03-With societal development, the public’s attention to mental health is increasing,” providing a social foundation for training promotion. Barrier factors primarily reflect insufficient support systems, with inadequate policy incentives (B①) being the most prominent. Physicians commonly noted, “R07- Without incorporating mental health service capabilities into hospital performance evaluations, it is impossible to promote bottom-up attention, making widespread implementation difficult.” Additionally, the lack of organizational promotion (B④), for example, “R08- the absence of unified organization by government systems leads to

fragmented training”, also constitutes a notable barrier.

The Inner Setting domain (C) comprises 4 facilitating factors and 3 barrier factors. Among the facilitating factors, the established rapid linkage mechanism with psychiatric and psychological specialties (C1) provides key support for training implementation. Physicians stated, “R02- *When encountering unresolved mental health issues in daily practice, we can quickly connect with psychiatric and psychological specialties, forming a positive cycle.*” Barrier factors mainly stem from operational-level pressures, with limited time and energy among doctors (C①) being the core issue. Physicians face heavy workloads: “R03- *It is common to work from 7 a.m. to 7 p.m. at the hospital—writing medical records, issuing medical orders, performing surgeries, conducting preoperative consultations, processing discharges, and engaging in these tasks from morning to evening. After returning home, already exhausted, they may feel overwhelmed when it comes to learning mental health counseling, knowledge, or related training.*”

The Individuals domain (D) includes 5 facilitating factors and 2 barrier factors. Among the facilitating factors, the dual promotion of doctors’ capacity improvement and career development constitutes the core driver (D1). Physicians believe that “R05- *For example, in communication or medication, through this training, we can obtain practical methods to guide patients, which will also be helpful for our own career development... It is more conducive to teaching students... Conducting necessary mental health assessments during diagnosis and treatment makes the diagnostic and treatment process more standardized.*” Barrier factors mainly manifest as constraints from practical conditions, with low time priority (D①) being the most prominent. Physicians usually “R06- *arrange training and learning after clinical work and academic conferences*”; in addition, weak learning foundation (D②) also constitutes a concern for participation.

The Implementation Process domain (E) comprises 7 facilitating factors and 1 barrier factor. Facilitating factors are concentrated in the clear demand for training design, with standardized, systematic yet concise materials becoming a common appeal. Physicians hope that the training “R16- *has both a complete set of plans and materials for fragmented learning, and video materials for spare-time learning would be better*”; meanwhile, teaching interaction support (E2), centralized training guarantee (E3), reasonable cycle (E4), integration of clinical scenarios (E5), high-quality faculty guarantee (E6), and standardized management (E7) are all key facilitating elements. The only barrier factor is the lack of effective feedback (E①). Some physicians mentioned that “R12- *It’s hard to persist without feedback*,” and the absence of a feedback mechanism directly affects the sustainability of the training.

4. Discussion

Guided by the CFIR framework, this study identified facilitating and barrier factors influencing physicians’ participation in mhGAP training through semi-structured interviews, resulting in 23 facilitating factors and 13 barrier factors. Overall, facilitating factors significantly outnumber barrier factors, indicating that mhGAP training has strong promotion potential within the tertiary healthcare system. However, targeted solutions to prominent issues are still needed to optimize implementation effectiveness.

The Outer Setting domain contains the largest number of barrier factors (4), with prominent issues such as inadequate policy incentives and lack of organizational promotion emerging as core bottlenecks restricting training promotion. Physicians commonly noted that “mental health service capabilities are not incorporated into performance evaluations,” a phenomenon that creates an implementation gap with the policy orientation of “expanding personnel and improving capabilities” outlined in China’s National Health Commission’s “Mental Health Service Year.” This is not unique to China; current academic research has focused on the gap between mhGAP advocacy policies and their implementation^[3,4]. To address these barriers, existing studies have shown that large-scale promotion of mental health services requires multi-dimensional collaboration across “policy-resources-cognition”^[5], among which policy incentives (e.g., linkage with performance evaluations, special funding support) are key to breaking the vicious cycle of “insufficient attention-low participation.” Additionally, issues such as “cognitive differences among service recipients” and “inadequate professional communication” highlight the lack of external social support and peer collaboration systems, which align closely with the

widespread challenge of “fragmented external support” faced by low- and middle-income countries in promoting mhGAP.

This study has two limitations: first, the singularity of the sample source, as all 20 respondents were recruited from a single tertiary institution (Deyang People’s Hospital), potentially limiting the representation of heterogeneous tertiary hospitals across regions and types. Second, the inherent subjectivity of qualitative methods, as interview data coding and interpretation depend on researchers’ judgments, carries a risk of subjective bias. To mitigate these, targeted measures were taken: For sampling, Deyang People’s Hospital was selected for its representativeness as the core of Deyang’s Mental Health Specialist Alliance, with its alliance achievements reported by authoritative media, enhancing sample typicality. For methodology, triple quality control ensured reliability: the interview guide was designed via CFIR-based literature review and expert consultation (3 senior experts), optimized through pre-interviews, and interview texts were independently coded by two researchers with cross-validation. Results were reported strictly following COREQ guidelines to minimize subjective bias.

The findings of this study reveal that the implementation and promotion of mhGAP training should adopt the core strategy of “strengthening advantages and breaking bottlenecks.” On one hand, it is necessary to consolidate the design strengths in the implementation process, further optimizing the practicality of training materials and feedback mechanisms. On the other hand, focus should be placed on building external support systems: promoting the integration of mental health service capabilities into hospital performance evaluations, and enhancing the systematicness and sustainability of training through a unified government organization. Meanwhile, to address issues such as “limited time and energy” in the Inner Setting domain and “low time priority” in the Individuals domain, training can be linked to career development (e.g., professional title promotion, teaching qualifications) through incentive mechanisms to boost physicians’ willingness to participate proactively. Overall, multi-dimensional collaborative efforts are required to fully unleash the value of mhGAP training in mental health service system construction. By leveraging the leading, supporting, and radiating roles of tertiary medical institutions, it will help alleviate the shortage of mental health resources and promote the improvement of mental health service quality and efficiency at the national and even global level. This research will provide a basis for hospital administrators to formulate mhGAP training plans and for policymakers to develop policies for the implementation and promotion of mhGAP.

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The authors declare no conflict of interest.

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Evaluation of the Efficacy of Fibrous Board Stripping under Thoracoscopy for Chronic Empyema

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Abstract: Thoracoscopic-assisted fibrous plate debridement is a minimally invasive core surgical technique for the clinical treatment of chronic empyema. Existing studies demonstrate that single-port, single-incision, and auxiliary small incision techniques each possess distinct clinical advantages, including reduced postoperative pain perception and accelerated recovery. Minimally invasive surgery achieves comparable lung re-expansion outcomes to traditional thoracotomy while exhibiting lower complication rates and superior long-term patient recovery. The timing of surgical intervention directly impacts prognosis, with early intervention reducing procedural complexity and positively influencing pulmonary function recovery. This article provides a systematic review and synthesis of relevant research findings.

Keywords: Chronic empyema; Thoracoscopy; Fibrous board stripping; Efficacy evaluation

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1. Introduction

Chronic empyema predominantly develops from tuberculous pleurisy but may also arise from inadequate management of acute empyema. Thickened fibrous tissue within the thoracic cavity directly restricts normal pulmonary expansion. Fibrous plate debridement effectively promotes lung re-expansion and clears residual thoracic cavity space. Traditional open thoracotomy procedures exhibit significant tissue trauma and prolonged postoperative recovery periods. The clinical application of thoracoscopy-assisted techniques has provided a novel minimally invasive approach for chronic empyema management. Current clinical practice has established substantial evidence regarding surgical pathway selection, perioperative management strategies, therapeutic efficacy evaluation, and optimal operative timing. Systematic synthesis of existing research findings has yielded comprehensive review content, offering critical evidence for clinical diagnosis and treatment planning.

2. Technical characteristics and clinical applications of surgical approaches

2.1. Comparison of efficacy between single-port thoracoscopic surgery and thoracotomy

The single-port thoracoscopic technique has become a focal point in clinical research. Jiang Yuhui et al. (2023) conducted

a comparative analysis between single-port thoracoscopic surgery and open thoracotomy with fibrous plate excision in patients with chronic tuberculous empyema, demonstrating that the single-port approach resulted in lower postoperative pain scores^[1]. The incision appearance was superior, while the efficacy of fibrous plate excision showed no significant difference from the open thoracotomy approach. Liu Xiaoyu et al. (2022) performed a clinical observation of fibrous plate excision under single-port thoracoscopic guidance, confirming that complete fibrous plate removal could be achieved with stable intraoperative blood loss control and shorter postoperative drainage duration^[2]. Wang Zhuo et al. (2023) conducted an in-depth evaluation of the clinical value and safety of this technique, finding that lung re-expansion was effectively promoted, with a low incidence of various complications. The single-port approach did not increase operative duration, and postoperative imaging revealed ideal lung re-expansion, making it a preferred treatment option for early-stage chronic empyema^[3].

2.2. Indications for laparoscopic-assisted minimally invasive surgery

In complex cases with significantly thickened fibrous boards and dense adhesions, conventional thoracoscopic procedures often encounter limitations in instrument manipulation angles. Wang Sibao et al. (2021) researched thoracoscopic-assisted minimally invasive surgery for stage III chronic empyema treatment, integrating the clear visual field of endoscopy with the flexibility of small incision techniques. This approach effectively reduced the rate of thoracotomy conversion and provided favorable long-term prognostic outcomes for patients^[4]. Compared to pure thoracoscopic surgery, the minimally invasive approach demonstrates superior advantages during calcified fibrous board dissection, with successful control of recurrent instrument manipulation-induced intercostal nerve compression and no significant increase in postoperative pain levels. The study results indicate that minimally invasive techniques do not represent a regression in surgical methodology but rather constitute a pragmatic optimization strategy for complex and specialized cases.

2.3. Single-port surgery technology combined with the concept of enhanced recovery after surgery (ERAS)

To further reduce the number of incisions, single-port techniques have been progressively adopted in clinical practice. Cheng Peng et al. (2021) integrated single-port thoracoscopic surgery with accelerated recovery surgery principles in the treatment of tuberculous empyema, achieving effective control over postoperative drainage tube retention duration and hospitalization length without an increasing trend in postoperative complication risks^[5]. Clinical procedures typically employ a single 2–3 cm operative port combined with an observation port, providing superior protection for intercostal nerves and surrounding muscle tissues while demonstrating outstanding trauma control outcomes. The integration of minimally invasive techniques with modern perioperative management strategies offers robust support for patient recovery, with this approach being particularly suitable for debilitated patients and elderly populations.

3. Optimization and implementation of perioperative management strategies

3.1. Specific approaches for integrating the concept of accelerated rehabilitation surgery

Cheng Peng et al. (2021) investigated and validated the feasibility of the single-incision technique, elucidating the key principles for integrating the concept of Enhanced Recovery After Surgery (ERAS), which include preoperative respiratory function training, intraoperative thermal protection and restricted fluid infusion, postoperative multimodal analgesia, and early ambulation. Multimodal analgesia is implemented using nonsteroidal anti-inflammatory drugs combined with intercostal nerve blocks, while early urinary catheter removal reduces patient physical discomfort^[5]. These measures collectively mitigate surgical stress responses and facilitate early recovery of cardiopulmonary function postoperatively, establishing a practical pathway for perioperative management in thoracoscopic fibrous plate detachment surgery. All aspects of perioperative management should be coordinated comprehensively to avoid isolated or partial integration of individual components.

3.2. Postoperative drainage management and indications for drain tube removal

Refined postoperative thoracic drainage management is directly correlated with residual cavity closure and infection control. When evaluating the efficacy of video-assisted thoracoscopic fibrous plate excision, Tian Zigang et al. (2024) focused on monitoring postoperative drainage volume, drainage tube retention duration, and lung re-expansion, emphasizing that strict adherence to tube removal criteria is critical for reducing residual cavity formation and infection recurrence ^[6]. Similarly, Zhang Hongdu et al. (2021) proposed that drainage tube management strategies should be dynamically adjusted based on intraoperative excision extent and postoperative pleural pressure changes to avoid premature tube removal leading to empyema recurrence; maintaining appropriate negative pleural pressure postoperatively promotes lung tissue adhesion to the chest wall and shortens drainage duration ^[7].

4. Efficacy evaluation and safety analysis

4.1. Effect of lung re-expansion and elimination rate of residual cavities

The core indicators for evaluating the efficacy of fibrous board stripping surgery are the degree of lung re-expansion and the elimination of residual cavities. In the study by Tian Zigang et al. (2024) ^[6], video-assisted thoracoscopic fibrous board stripping could release compressed and restricted lung tissue, with postoperative chest X-ray examinations demonstrating ideal lung re-expansion status and a high proportion of residual cavity resolution. Data from Liu Xiaoyu et al. (2022) observed that the time required for residual cavity closure in the single-port thoracoscopic group was comparable to that in the open thoracotomy group, indicating that minimally invasive surgery does not adversely affect overall therapeutic outcomes ^[2]. Wang Zhuo et al. (2023) conducted a quantitative analysis of pulmonary function improvement, revealing significant enhancement in forced expiratory volume at 1 second postoperatively compared to preoperative levels, along with corresponding improvements in forced vital capacity ^[3]. Zhang Hongdu et al. (2021) identified a positive correlation between residual cavity closure time and fibrous board thickness during postoperative chest radiography follow-up; with cases exceeding 5 mm in fibrous board thickness exhibiting markedly prolonged residual cavity closure cycles ^[7]. Thoracoscopic-assisted surgery achieves lung re-expansion outcomes comparable to those of open thoracotomy.

4.2. Perioperative complications and risk of transoperative thoracotomy

Jiang Yuhui et al. (2023) reported that the incidence of postoperative complications (such as persistent pneumothorax, thoracic infection, and poor wound healing) in the single-port thoracoscopic group was not higher than that in the open thoracotomy group, with no cases requiring intraoperative conversion to open surgery ^[1]. Wang Sibo et al. (2021) indicated that auxiliary small incision design could reduce the rate of conversion to open surgery; thereby avoiding the greater trauma associated with open thoracotomy ^[4]. In Cheng Peng et al. (2021) study, the single-incision group did not experience severe complications, confirming the safety of this technique when strict indications are adhered to ^[5]. Liu Xiaoyu et al. (2022) similarly observed that the single-port thoracoscopic group had shorter postoperative fever duration and antibiotic usage days compared to the open thoracotomy group, suggesting milder systemic inflammatory responses ^[2]. Wang Zhuo et al. (2023) also found that the single-port group exhibited lower incidence of postoperative arrhythmias and pulmonary infections than the open thoracotomy group, which may be related to minimal surgical trauma and reduced pain.

4.3. Long-term prognosis and recurrence prevention

Safety evaluation is equally important as efficacy evaluation. Jiang Yuhui et al. (2023) reported that the incidence of complications such as persistent pneumothorax, thoracic infection, and poor wound healing in the single-port thoracoscopic group was not higher than that in the open thoracotomy group, with no intraoperative conversion to open surgery observed ^[1]. Wang Sibo et al. (2021) proposed that auxiliary small incision design could reduce the conversion rate to open surgery and minimize the greater trauma associated with thoracotomy ^[4]. In Cheng Peng et al. (2021) study ^[5], no severe complications were observed in the single-incision group, demonstrating reliable safety when strict indications are adhered to. Liu Xiaoyu et al. (2022) noted that the

single-port thoroscopic group exhibited shorter postoperative fever duration and fewer days of antibiotic use compared to the open thoracotomy group, reflecting milder systemic inflammatory responses^[2]. Wang Zhuo et al. (2023) found lower incidence rates of postoperative arrhythmias and pulmonary infections in the single-port group compared to the open thoracotomy group, suggesting potential associations with reduced surgical trauma and less pain^[3].

4.4. Postoperative quality of life and functional recovery assessment

In addition to objective efficacy indicators, improvement in patients' 'postoperative quality of life serves as a critical dimension for evaluating surgical value. Jiang Yuhui et al. (2023) compared single-port thoroscopic surgery with open thoracotomy without directly employing standardized quality of life scales, observing reduced postoperative pain scores and superior incision aesthetics, which indirectly suggests that minimally invasive surgery has a lesser impact on patients' daily activities and psychological status^[1]. Cheng Peng et al. (2021) demonstrated that integration of accelerated recovery surgery principles resulted in earlier ambulation time and shorter hospital stays, mitigating muscle atrophy and physical decline associated with prolonged bed rest^[5]. Wang Sibao et al. (2021) found through follow-up that patients undergoing thoroscopic-assisted small-incision surgery achieved preoperative-level daily functional recovery at 6 months postoperatively, with no significant chest wall deformity or chronic pain^[4].

5. Selection of surgical timing and its impact on therapeutic outcomes

5.1. Efficacy differences between early surgery and late surgery

The timing of surgical intervention significantly impacts the efficacy of fibrous board debridement. Zhang Hongdu et al. (2021) investigated the optimal surgical timing for thoroscopic drainage combined with fibrous board debridement in the treatment of empyema, finding that patients undergoing surgery within 3 months of disease onset exhibited faster lung re-expansion rates and shorter postoperative drainage durations^[7]. Yang Wenrong et al. (2021)^[8] compared the therapeutic outcomes of chronic tuberculous empyema treated at different surgical timings, demonstrating that early surgical intervention resulted in superior postoperative pulmonary function recovery and lower complication rates compared to delayed surgery. The latter group exhibited prolonged hospital stays and increased intraoperative blood loss, with delayed surgery posing greater therapeutic challenges and medical burdens.

5.2. Influence of disease duration on the difficulty of fibrous board detachment

Prolonged disease course leads to thickening and calcification of the fibrous plate, which subsequently forms dense adhesions with lung tissue. Yang Wenrong et al. (2021) conducted an in-depth analysis of this pathological process and found that patients with a disease duration exceeding 12 months exhibited increased intraoperative dissection difficulty, greater blood loss, and a higher propensity for lung tissue lacerations^[8]. Such cases require separation using an ultrasonic scalpel or electric hook, resulting in correspondingly extended operative time. Surgical intervention is less challenging and carries lower risks when the fibrous plate has not fully calcified. Zhang Hongdu et al. (2021) concurred with this perspective, advocating for early evaluation of surgical indications upon diagnosis of chronic empyema to avoid missing the optimal window for minimally invasive surgery due to excessive delay^[7].

5.3. Clinical Criteria for Optimal Surgical Timing

The optimal timing for surgery should be determined based on imaging findings and clinical symptoms. Yang Wenrong et al. (2021) proposed that when imaging demonstrates uniform fibrous plate thickness without significant calcification and systemic toxic symptoms are largely controlled, this represents an ideal surgical window^[8]. Zhang Hongdu et al. (2021) held a different view, emphasizing that if lung re-expansion remains suboptimal after standardized anti-infective therapy, prompt surgical intervention is necessary without undue delay^[7]. Preoperative completion of at least two weeks of effective anti-tuberculosis treatment is essential to reduce postoperative infection risk. Performing thoroscopic-assisted

fibrous plate excision within 3 to 6 months of disease onset yields the optimal risk-benefit ratio. For younger patients with good general condition, surgical indications may be appropriately relaxed.

6. Conclusion

Thoracoscopic fibrous plate debridement for the treatment of chronic empyema demonstrates minimal invasiveness, rapid recovery, and low complication rates, as confirmed by existing studies. Techniques such as single-port approach, single operative incision, and auxiliary small incisions each have specific indications and should be selected individually based on fibrous plate thickening and adhesion status. The integration of accelerated recovery surgery principles can further improve overall outcomes, particularly in postoperative pain management and early mobilization. Surgical timing directly impacts prognosis, with early intervention reducing operative difficulty and enhancing pulmonary function. Subsequent large-scale prospective studies are still required to refine technical protocols and establish standardized criteria for timing selection.

Disclosure statement

The authors declare no conflict of interest.

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Discussion on Using PDCA to Improve the Quality of Medical Record Home Page and Operation Management Quality under DRGs Medical Insurance Payment Method

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Abstract: *Objective:* To understand whether PDCA cycle management can actually improve the quality of our hospital's medical record home page and the quality of operation and management under the DRGs medical insurance payment model. *Methods:* The medical records of 92 inpatients admitted to our hospital from January 2025 to December 2025 were selected as the research objects, and divided into experimental groups and conventional groups through the random number table method, with 46 cases in each group. The conventional group adopted ordinary medical record management and operation management methods, while the experimental group added PDCA cycle management based on conventional management. The quality scores of the medical record home page, the probability of occurrence of defects on the medical record home page, and related indicators of operation management were compared between the two groups. *Results:* After the intervention, the quality score of the medical record homepage of the experimental group was higher than that of the conventional group, the defect rate of the medical record homepage was lower than that of the conventional group, and the length of stay, average cost per hospitalization and probability of medical insurance refusal in operation management were all better than those of the conventional group ($P < 0.05$). *Conclusion:* PDCA cycle management can effectively improve the quality of our hospital's medical records under the DRGs medical insurance payment model, improve operational management efficiency, reduce the possibility of medical insurance refusal, and is suitable for promotion and application in clinical work.

Keywords: PDCA cycle; DRGs medical insurance payment; Medical record home page quality; Operation management quality

Online publication: March 26, 2026

1. Introduction

My country's medical security system is in a stage of continuous improvement. The DRGs' medical insurance payment method has been widely implemented in medical institutions at all levels. This payment method takes disease diagnosis grouping as the core point and clarifies the medical insurance payment amount based on the severity of the patient's condition, treatment methods, etc., and puts forward high requirements for the medical record management and operation

management of medical institutions. The home page of medical records is the core basis for grouping DRGs. The completeness and accuracy of its filling are directly related to the rationality of medical insurance payment, and will also affect the economic benefits and brand reputation of medical institutions^[1,2]. However, when our hospital currently uses the DRGs medical insurance payment model, problems such as irregular filling in the medical record home page, missing information, and coding errors are more prominent. In terms of operation and management, there are also unscientific hospitalization procedures, loose cost control, and high medical insurance refusal rates. These problems not only reduce the efficiency of use of medical insurance funds, but also restrict the improvement of the quality of medical services in the hospital^[3]. PDCA cycle management covers four parts: planning, execution, inspection, and processing. It has the characteristics of systematicness and a closed-loop nature. It has achieved good results after being applied in many fields of medical management^[4]. Based on this, this study applies the PDCA cycle management to the management and operational management of medical record homepages under the DRGs medical insurance payment model, and explores its actual effect in improving the quality of medical record homepages and operational management quality, providing a practical reference for our hospital to optimize the management model and adapt to the DRGs medical insurance payment reform.

2. Materials and methods

2.1. General information

The medical records of 92 inpatients admitted to our hospital from January 2025 to December 2025 were selected as research cases and divided into two groups using the random number table method. There were 46 patients in the experimental group, 25 males and 21 females, aged between 32 and 71 years old, with an average age of (48.62 ± 5.13) years old. There were 46 patients in the conventional group, 24 males and 22 females, aged from 33 to 72 years old, with an average age of (49.05 ± 5.08) years old. There was no statistical difference in the general data between the two groups, $P > 0.05$. Inclusion criteria: (1) Meet the requirements for hospitalization, and the hospitalization time is no less than 3 days; (2) The medical records are complete and capable of grouping DRGs; (3) The patients and their families are informed and cooperate with the research. Exclusion criteria: (1) Patients who died after emergency rescue and were discharged voluntarily; (2) Key information on the first page of the medical record is missing and cannot be supplemented; (3) Patients with combined mental illness and cognitive impairment who cannot cooperate with management.

2.2. Method

The regular group uses ordinary medical record management and operational management methods. Medical record management only involves medical record room personnel briefly checking the first page of the medical record after the patient is discharged. If any problems are found, clinicians will be notified for additional modifications. There is no fixed review and training system. Operation management follows traditional procedures to complete hospitalization registration, cost calculation, medical insurance reporting, etc., without optimizing the process and controlling costs based on the characteristics of DRGs medical insurance payment.

The experimental group added PDCA cycle management to conventional management. The specific implementation content is as follows:

- (1) In the planning stage, a special management group composed of key personnel from the medical department, medical record room, medical insurance department, finance department and clinical departments was established to comprehensively sort out the deficiencies in the quality and operation management of the medical record home page of our hospital under the DRGs medical insurance payment model, and determine the irregular filling of the home page, coding errors, complex operating processes, and costs. In order to address major issues such as insufficient management and control, we formulated corresponding management plans based on the actual situation of the hospital, clarified the responsibilities and work directions of each department, and set the expected goals of increasing

the quality score of the first page of medical records to above 90 points, controlling the defect rate within 5%, reducing the average hospitalization cost by more than 8%, and controlling the medical insurance denial rate within 3%.

- (2) In the execution stage, for the management of the medical record home page, organize clinicians, nursing staff and medical record coding personnel to carry out training on DRGs-related knowledge and filling requirements for the medical record home page, focusing on explaining disease coding principles, surgical operation coding specifications and important matters for filling in the home page. A centralized training and assessment will be organized once a month. A three-level review system for the first page of medical records has been established, with self-examination by clinicians, review by department quality control personnel, and final review by dedicated personnel in the medical record room to ensure that the information on the first page of each medical record is accurate and complete. For operational management, we optimize hospitalization-related processes, simplify admission registration, examination appointments, discharge settlement and other steps, and implement one-stop services. Strengthen cost control, conduct reasonable management and control of drugs, consumables, and examination items during hospitalization, and reduce unnecessary medical behaviors. The Medical Insurance Department arranges dedicated personnel to explain medical insurance policies and review applications, and promptly discover and correct problems in medical insurance reports.
- (3) In the inspection stage, the management team conducts random inspections on the quality of the first page of medical records every week, conducts comprehensive inspections every month, and collects statistics on the quality score, defect rate, and types of defects on the first page of medical records. At the same time, the relevant indicators of operation and management are regularly inspected, including length of stay, average cost per visit, medical insurance refusal rate, etc. The gap between actual completion and planned goals is compared, the causes of problems are analyzed, inspection results are formed and timely feedback is given to relevant departments.
- (4) In the processing stage, the problems discovered during the inspection are classified and summarized. For problems that can be rectified immediately, the relevant departments are required to complete the improvements within a designated time. For recurring common problems, such as coding errors, irregular filling, etc., we will conduct an in-depth search for the root causes, improve the training content and review system, and add effective rectification methods to daily management. For operational management indicators that have not met the planned requirements, we will optimize management measures, adjust the work direction, enter the next round of the PDCA cycle, and continuously improve the quality of management.

2.3. Observation indicators

2.3.1. Compare the quality of the medical record home pages between the two groups

Using the “Standards for Filling in the First Page of Medical Records” as the standard, the scores are scored from three aspects: information completeness, coding accuracy, and standardization of filling. The total score is 100 points. The higher the score, the better the quality of the first page of the medical records.

2.3.2. Compare the defects on the first page of medical records between the two groups

Count the number of defective cases on the first page of the two sets of medical records, including missing information, coding errors, filling errors, etc., and calculate the defect rate. The defect rate is the number of defective cases divided by the total number of cases and multiplied by 100%.

2.3.3. Compare two groups of operation management-related indicators

It includes the average length of stay, the average hospitalization cost and the medical insurance refusal rate. The medical insurance refusal rate is the number of medical insurance refusal cases divided by the total number of cases and multiplied by 100%.

2.4. Statistical methods

Data were analyzed using SPSS 24.0. Measurement data that conform to normal distribution are expressed as mean plus or minus standard deviation and subjected to t-test; count data are expressed as a percentage and subjected to χ^2 test. $P < 0.05$ indicates that the difference is obvious.

3. Results

3.1. Comparison of quality scores and defect rates of medical record home pages between the two groups

The quality score of the medical record home page of the experimental group was higher than that of the conventional group, and the defect rate was lower than that of the conventional group ($P < 0.05$). See **Table 1** for details.

Table 1. Comparison of quality scores and defect rates of medical record homepages between the two groups

Group	Medical record homepage quality score (mean $\pm$ SD, points)	Defect rate of medical record home page [n (%)]
Regular group (n = 46)	75.36 $\pm$ 6.28	12 (26.09)
Experimental group (n = 46)	92.15 $\pm$ 4.32	2 (4.35)
Statistical value	14.940	8.425
<i>P</i>	0.000	0.004

3.2. Comparison of two groups of operation management-related indicators

After the intervention, the average hospitalization days of the experimental group were shorter than those of the conventional group, the average cost of hospitalization was lower than that of the conventional group, and the medical insurance denial rate was lower than that of the conventional group ($P < 0.05$). See **Table 2** for details.

Table 2. Comparison of operation management-related indicators between the two groups

Group	Average length of stay (mean $\pm$ SD, days)	Average cost of hospitalization (mean $\pm$ SD, yuan)	Medical insurance refusal rate [n (%)]
Regular group (n = 46)	8.72 $\pm$ 1.35	8965.32 $\pm$ 1256.78	8 (17.39)
Experimental group (n = 46)	6.25 $\pm$ 1.12	8234.56 $\pm$ 1089.45	1 (2.17)
Statistical value	9.550	2.980	4.434
<i>P</i>	0.000	0.004	0.035

4. Discussions

The full implementation of the DRGs medical insurance payment method has completely changed the previous charging-by-project model, closely linking the economic benefits of medical institutions with the quality of medical records and treatment efficiency. As the core basis for grouping DRGs, the quality of the medical record home page directly affects whether medical insurance payments are reasonable and accurate, while the quality of operation and management is related to cost control and long-term development of medical institutions. PDCA cycle management is a scientific management method. Through the closed-loop management process of planning, execution, inspection, and processing, it can effectively identify problems in management and continuously improve them. It is an important application in the field of medical management^[5]. This study applied PDCA cycle management to the medical record home page management and operation management under the DRGs medical insurance payment model. The results showed that all indicators of the experimental group were much better than those

of the conventional group, which is enough to show that this management model has practical effects.

The improvement of the quality of the first page of medical records is one of the core results of the application of the PDCA cycle management. After the intervention, the quality score of the first page of medical records in the experimental group was 92.15 ± 4.32 points, and the defect rate dropped to 4.35%, which was much better than the 75.36 ± 6.28 points and 26.09% of the conventional group. Such a result is mainly due to the PDCA cycle management sorting out major problems, such as missing information, coding errors, and irregular filling in the management of the medical record home page during the planning stage, so as to clarify the direction for subsequent management work. Targeted training carried out during the implementation phase effectively improves the professional capabilities of clinicians, nursing staff and medical record coding personnel, allowing relevant personnel to master the DRGs coding principles and the requirements for filling out the first page of medical records, reducing filling errors caused by insufficient professional capabilities; the establishment of a three-level review mechanism to implement The entire process of filling in the first page of medical records is quality controlled. Clinicians' self-examination can promptly discover and correct problems they identify. Department quality controllers' and final review by the medical record office are further strictly controlled to effectively prevent erroneous medical records from entering the next link, thus significantly improving the accuracy and completeness of the first page of medical records ^[6]. Regular spot checks and comprehensive inspections in the inspection phase can promptly discover new problems that arise in the management process and avoid the accumulation of problems; in the processing phase, by classifying and rectifying problems and improving mechanisms, effective rectification measures are incorporated into daily management to form a closed loop of continuous improvement to ensure that the quality of medical record pages can be maintained at a high level for a long time. Improving the quality of the medical record homepage can not only ensure the accuracy of DRGs grouping and avoid medical insurance denials due to grouping errors, but also provide reliable data support for hospital medical quality assessment and clinical research, and promote the overall improvement of hospital medical service quality.

The optimization of operational management quality is another important result of the application of the PDCA cycle management. After the intervention, the experimental group's average hospitalization days, average hospitalization costs and medical insurance denial rate were significantly better than those of the conventional group, with the average hospitalization days shortened to 6.25 ± 1 . In 12 days, the average cost of hospitalization dropped to 8234.56 ± 1089.45 yuan, and the medical insurance refusal rate dropped to 2.17%, which fully reflects the role of PDCA cycle management in optimizing operational efficiency, controlling costs, and reducing the risk of medical insurance refusal. In the planning stage, the management team combined the characteristics of DRGs' medical insurance payment to sort out the problems existing in operation management, such as cumbersome processes, insufficient cost control, and non-standard medical insurance declarations, and formulated targeted optimization plans to clarify the responsibilities and goals of each department and provide a clear direction for the optimization of operation management. In the execution stage, the hospitalization process is optimized to simplify admission registration, examination appointment, discharge settlement and other links, and promote one-stop service, reduce patient waiting time, improve diagnosis and treatment efficiency, and thereby shorten the average length of stay; the implementation of cost control measures, the integration of drugs, consumables, and examination items during hospitalization Management and control to avoid excessive medical treatment and waste of resources, effectively reduce the average cost of hospitalization, and improve the economic benefits of the hospital; the medical insurance department arranges dedicated personnel to be responsible for the interpretation of medical insurance policies and application review, promptly discover and correct problems in medical insurance applications, reduce medical insurance refusals due to irregular declarations, and reduce the rate of medical insurance refusals.

Regular monitoring of various indicators of operation management during the inspection phase can timely grasp the changes in indicators, compare the gap between the actual situation and the planned goals, and analyze the causes of problems. For example, long hospitalization days may be related to low efficiency of inspection appointments, and medical insurance refusal may be related to incorrect coding of medical records. In the processing phase, targeted rectifications are carried out to address these problems, optimize the inspection appointment process, strengthen coding training, continuously improve operation management measures, and form a closed-loop management, thereby continuously improving the efficiency and quality of operation management ^[7].

PDCA cycle management can simultaneously improve the quality of medical records and operational management. The core lies in its systematic and closed-loop characteristics. This model organically combines all aspects of management work to form a complete process of planning-execution-inspection-processing, avoiding the fragmentation and blindness problems that exist in traditional management. Under the DRGs medical insurance payment model, the quality of medical record homepages and the quality of operation management are interrelated and influence each other. Low quality of medical record homepages will lead to incorrect grouping of DRGs, which will in turn, affect medical insurance payment and increase the risk of medical insurance refusal. It will also affect cost accounting and efficiency evaluation in operations management. If the operation management process is not optimized and cost control is not in place, it will cause a waste of medical resources, affect the human and material investment in medical record management, and then affect the quality of medical record homepages. Through the collaborative management of the two, PDCA cycle management not only solves outstanding problems in the management of medical records, but also optimizes the operation management process to achieve positive interaction and collaborative improvement between the two ^[8].

Taken together, PDCA cycle management is applied to medical record management and operation management under the DRGs medical insurance payment model, which can effectively improve the quality of medical records, reduce the defect rate of medical records, optimize the operation and management process, shorten the average length of stay, reduce the average cost of hospitalization and the medical insurance refusal rate, and improve the hospital's economic benefits and medical service quality. This management model meets the requirements of DRGs medical insurance payment reform, fits the actual management needs of our hospital, is simple to operate, highly feasible, and can achieve continuous improvement of management quality.

Disclosure statement

The author declares no conflict of interest.

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Model Innovation and Practical Exploration of Grassroots Management of Patients with Severe Mental Disorders

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Abstract: With social progress and the aging of the population, the number of people suffering from severe mental disorders is increasing every year, which has also led to a continued increase in the demand for grassroots management services. At present, the implementation of grassroots management of patients with severe mental disorders shows that although it has certain effects, there are still many problems. In this regard, model innovation and practical strategies are proposed, which mainly include building a multi-disciplinary collaborative comprehensive management model, strengthening the training and professional development of grassroots managers, enhancing the mental health awareness and acceptance of grassroots residents, and optimizing the allocation of grassroots resources and building service networks.

Keywords: Severe mental disorder; Grassroots management; Model innovation

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1. Introduction

Severe mental disorders in modern society have become a major public health problem that endangers human health and social stability. As the number of patients with mental disorders increases, grassroots management plays an increasingly important role in communicating between patients and society. However, current grassroots management still faces many challenges when applied to patients with severe mental disorders. Therefore, exploring innovative models of grassroots management to promote the improvement of management quality plays a very important role in improving patients' quality of life and promoting the recovery of patients' social functions.

2. Application status of grassroots management in patients with severe mental disorders

There are a large number of patients with mental disorders in China, and most patients cannot get timely and effective treatment. The traditional medical model is mainly based on hospital treatment. With the uneven distribution of medical resources, the hospitalization rate of patients continues to increase, and hospital treatment cannot meet the requirements

of all patients. So, the grass-roots management has gradually become an effective supplementary way, which can not only provide a continuous stream of health management but also help patients better integrate into society. However, the grass-roots management still faces many challenges in the process of practice, especially the professional ability of managers, resource allocation, and the construction of the grass-roots support system. In many areas, the grass-roots management service has not yet formed a systematic and professional management mode, and knowledge and skills of grass-roots managers are uneven, lacking the necessary psychological support and intervention technology^[1]. In addition, grassroots residents' perception of mental health problems is relatively weak, resulting in misunderstanding and rejection of patients with mental disorders, which increases the difficulty of their social integration. Therefore, although grass-roots management shows its unique advantages, there are still many bottlenecks in the actual operation process.

3. Mode innovation and practice strategy of grassroots management of patients with severe mental disorders

3.1. Establish a comprehensive management mode of multidisciplinary cooperation

The management of patients with severe mental disorders usually involves not only drug intervention or simple daily management, but also psychological reconstruction, social function recovery and family relationship repair. In the environment where the traditional management mode is increasingly showing its limitations, the introduction of a multidisciplinary collaborative comprehensive management mechanism has become a major direction of the development of contemporary mental health services. This cooperation should not only be a formal "union", but also a substantive participation and co-governance mechanism among various professional fields in the whole process of diagnosis and treatment. Psychiatrists are responsible for disease diagnosis, drug management and symptom control. Psychotherapists are mainly engaged in mental behavior correction and psychological support. Social workers are engaged in patients' life adaptation, welfare application and family intervention to provide support. At the same time, nurses play a pivotal role in daily observation, health education and patient compliance behavior management. This multi-angle cross-cooperation mode can more accurately match the individual needs of patients in practical application, especially in the case of large disease fluctuations, weak social support or long-term dependence on the control care system, the advantages of this mode are particularly obvious. It is noteworthy that the collaboration system not only improves the coverage of treatment specialties but also strengthens the continuity and traceability of management work, making it possible for chronic psychiatric patients to receive dynamic assessment and continuous intervention. However, from the perspective of service system construction, this multidisciplinary cooperation is also conducive to promoting the integration and optimization of resources within the grass-roots mental health system, reducing repeated investment and improving operational efficiency. Obviously, the core value of comprehensive management is not only reflected in the coordination of resources, but also the implementation of the patient-centered service concept into every detail of the service, to help patients go further and more stably on the road of functional rehabilitation and social reintegration.

3.2. Strengthen the training and professional development of grass-roots management personnel

The basic level management of patients with severe mental disorders requires much higher professional quality of managers than conventional management. Many grass-roots managers encounter sudden emotional problems or complex social support needs in practice, which are often difficult to solve due to a lack of knowledge or experience, affecting the quality of service and even the prognosis of patients. Therefore, strengthening the professional training of managers has become the core measure to improve the quality and efficiency of grassroots mental health services. The training content should not be limited to the inculcation of the basic knowledge of mental illness, but should be more infiltrated into the three levels of emergency psychological intervention skills, family relationship coordination methods and patients' psychological rehabilitation path design, and strengthen the practical ability of non-violent communication, crisis assessment and patients' behavior recognition. In addition, it is necessary to establish career growth paths for managers,

such as regular rotation training, post-continuing education, assessment and promotion mechanism, to form an internally driven professional growth environment. Grassroots management should not be the “guard” of empiricism. It should be a professional work with a theoretical basis, operational norms and ethical awareness. Therefore, in terms of personnel selection, priority should be given to people with mental health experience or a psychological background, which is conducive to improving the coping ability of the whole team. At the same time, in order to prevent the occurrence of the service island phenomenon, managers need to actively integrate into the regional mental health network and participate in interagency communication, get the guidance of experts or participate in the discussion of clinical cases to expand their professional vision. The key is to establish a long-term mechanism to take grass-roots management work as a path of sustainable professional development rather than a temporary and low threshold career option. This will not only promote the stability of management services and the improvement of professional identity, but also shape the public’s confidence and identity in the mental health service system to a certain extent, so as to achieve a virtuous cycle.

3.3. Improve the awareness and acceptance of grassroots residents on mental health

The quality of life of patients with severe mental disorders at the grass-roots level usually depends not only on the accessibility of medical services, but also on non-medical factors such as neighborhood relations and public attitudes. At present, there are still many blind spots in the popularity of mental health knowledge among the public. Misunderstanding, labeling and exclusion often make patients feel the invisible pressure of social interaction, which is not conducive to the stability and recovery of patients’ diseases. Therefore, promoting mental health education at the grassroots level has become one of the public sexual health practice orientations that need to be strengthened. Specifically, the grassroots should not only rely on traditional lectures or posting propaganda materials as a single means of communication, but also need to integrate mental health into residents’ daily life situations. For example, the “mental health experience space” can be established by combining with grass-roots festival activities, so that residents can learn the psychological adjustment skills of emotion regulation and stress recognition in interactive scenes. The performance of public welfare psychodrama, which simulates empathy games and short video competitions from the perspective of patients, can also mobilize the enthusiasm of the public to participate and break through the original cognitive barriers. In addition, knowledge infusion is not enough. The construction of an emotional support network, the cultivation of public tolerance for “emotional abnormalities,” and the encouragement of family members to participate in mental health intervention are also important links that can not be ignored. The establishment of psychological mutual aid groups at the grass-roots level to guide residents to participate in the discussion of mental health issues is conducive to building more positive emotional connections between neighbors. On the other hand, the government and social institutions provide platforms and resource guarantees, such as targeted psychological assistance projects, grassroots psychological hotlines, psychological service outsourcing subsidies and other mechanisms, which should be the backing of such work to ensure the continuity and systematicness of education promotion rather than fragmentation and assault.

3.4. Optimize grass-roots resource allocation and service network construction

Under the background of patients with severe mental disorders gradually turning to grass-roots rehabilitation, grass-roots self-service ability is the key variable to determine the quality of rehabilitation. However, the actual allocation of mental health resources at the grass-roots level is often faces the dilemma of multi-head management, decentralized functions, and disordered service levels, and it is difficult to form a closed-loop support system. To reverse this situation, it is urgent to systematically optimize the organizational mechanism, staffing and service structure. At present, grassroots institutions usually only have basic medical support in the three dimensions of medical treatment, psychology and society, but there are obvious deficiencies in the coverage of psychological intervention and social function reconstruction. Therefore, the grass-roots service network should gradually move towards multi-dimensional collaboration ^[2]. On the one hand, the allocation of medical resources should adjust the diagnosis and treatment process and referral mechanism according to the different manifestations of patients’ mental illness pedigree, to realize the control of mild patients at the grass-roots level and

timely diversion of severe patients. The establishment of a shared archives system and a dynamic evaluation mechanism for hospitals at or above the regional level can effectively avoid the occurrence of information islands and promote the improvement of referral response efficiency. In addition, a perfect social support structure has no less impact on the quality of life of patients with mental disorders than drug intervention. Full-time social worker posts should be introduced at the grass-roots level, and functional spaces such as psychological counseling rooms and emotional counseling stations should be built, and non-governmental organizations and volunteer service teams should be encouraged to participate in rehabilitation companionship regularly. More importantly, the supplement of professional strength cannot stay on the surface. Mental health experts should be regularly invited to carry out workshops at the grass-roots level to improve the practical ability of grass-roots managers and discuss cases, so as to make them have the practical ability to find problems and deal with emergencies. In terms of financial support, local financial departments should include mental health services in the budget system of basic public health services at the grass-roots level, establish channels for special funds, establish incentive mechanisms for service quality assessment and result orientation, and use policy forces to ensure the normalization of mental health services. The establishment of a sustainable and hierarchical resource network can not only improve the grassroots life experience of patients with mental disorders, but also provide solid support for their gradual recovery of social functions and role reconstruction ^[3].

4. Exploration of a rehabilitation model for patients with severe mental disorders

4.1. Service mode innovation

The exploration of the community rehabilitation model for patients with mental disorders focuses on the innovation of the service model. This innovative process starts with an in-depth understanding and analysis of patient needs. Through community research, family interviews, case assessment, and other means, we can accurately grasp the actual rehabilitation needs of patients, and lay the foundation for the development of a personalized rehabilitation plan. Subsequently, we tried to integrate multiple resources, including medical institutions, social work teams, volunteer organizations, etc., to build a comprehensive and multi-level rehabilitation service network. This network not only provides medical support, but also covers psychological counseling, life skills training, social ability improvement and other services, aiming to help patients gradually restore social function and improve the quality of life. In terms of service mode, it advocates patient-centered, personalized and precise services. Through the regular assessment of patients' rehabilitation progress, the service plan is constantly adjusted and optimized to ensure the maximization of service effect. Therefore, the exploration of the community rehabilitation model for patients with mental disorders is a process of continuous innovation and improvement, which needs to be patient-centered, constantly integrate resources, optimize services, and provide comprehensive and considerate rehabilitation services for patients ^[4].

4.2. Personalized rehabilitation services

In the exploration of the community rehabilitation model for patients with mental disorders, personalized rehabilitation services are a core strategy. This strategy begins with a deep understanding of the individual differences of patients, and an understanding of each patient's unique rehabilitation needs, life background and psychological state. Through a comprehensive assessment system, including psychological assessment, social function assessment and life skills assessment, the rehabilitation needs map of patients is carefully described. This step ensures that rehabilitation services can accurately meet the actual needs of patients. Then, according to the evaluation results, personalized rehabilitation plans are designed and implemented. These plans not only cover basic services such as drug treatment and psychological counseling, but also integrate diversified contents, such as life skills training, social ability improvement and occupational rehabilitation, aiming to help patients gradually restore social functions and improve the quality of life. In the implementation process, the participation of patients and their families is emphasized, and they are encouraged to put forward valuable opinions, so as to make flexible adjustments according to the feedback and ensure the effectiveness and

adaptability of rehabilitation services^[5].

At the same time, a continuous tracking mechanism was established to regularly evaluate the rehabilitation progress of patients and adjust the rehabilitation strategy in time to meet the possible challenges. Therefore, personalized rehabilitation service plays a vital role in the exploration of a community rehabilitation model for patients with mental disorders. It requires a patient-centered, meticulous understanding of their needs, and providing accurate, comprehensive and consistent rehabilitation support to promote the comprehensive rehabilitation and social integration of patients.

4.3. Construction of social support network

In the exploration of the community rehabilitation model for patients with mental disorders, the construction of a social support network is an indispensable part. This construction process starts from a comprehensive review of the social relations of patients, and aims to build a support network with the participation of families, communities, medical institutions and all sectors of society. Encourage patients' families to play a core role, provide emotional support and life care, and promote the emotional connection between patients and their families^[6]. At the same time, through family education and training, family members' understanding and acceptance of patients' diseases can be enhanced, and misunderstanding and conflict within the family can be reduced. Actively integrate into community resources, organize various rehabilitation activities and social gatherings, help patients gradually integrate into community life and establish new social relationships. In addition, we should establish close cooperation with medical institutions to ensure that patients can receive timely and professional medical support when needed. Advocate the attention and support of all sectors of society to the patient group, through media publicity, public welfare activities and other ways, improve the public's awareness and understanding of mental disorders, reduce social prejudice and discrimination against patients, and create a more inclusive and friendly social environment for patients. Therefore, the construction of a social support network is a process of multi-party participation and sustainable development. It requires patient-centered care, integrating resources from all parties, and building a comprehensive and effective support network to promote the comprehensive rehabilitation and social integration of patients^[7].

5. Conclusion

In short, it is an urgent task in the field of public health to carry out mode innovation and practical exploration on the grassroots management of patients with severe mental disorders. Through the construction of multidisciplinary collaborative comprehensive management mode, strengthening the training and professional development of grass-roots management personnel, enhancing the awareness and acceptance of mental health of grass-roots residents, and optimizing the allocation of grass-roots resources and the construction of service network, the quality of grass-roots management can be effectively improved, which is conducive to the better integration of patients into society and the improvement of quality of life.

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Disclosure statement

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Jin Qinglei's Experience in Treating Bile Reflux Gastritis

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Abstract: Bile reflux gastritis is a common disease in gastroenterology. Western medicine treatment is often repeated, which seriously affects the patient's quality of life. Traditional Chinese medicine has shown unique therapeutic effects in the treatment of reflux gastritis. This article aims to summarize the experience of Jin Qinglei, a famous traditional Chinese medicine practitioner, in using Zuojin Pills and Wendan Decoction to treat bile reflux gastritis. When treating bile reflux gastritis, Jin Lao started from the liver, gallbladder, spleen and stomach, and proposed a treatment method focusing on regulating Qi in the liver and regulating phlegm in the stomach. The effect was remarkable and provided an important reference idea for the clinical treatment of bile reflux gastritis.

Keywords: Bile reflux gastritis; Zuojin pill; Wendan decoction

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1. Introduction

Bile reflux gastritis is a common digestive system disease. It is caused by the reflux of bile into the stomach, resulting in damage to the gastric mucus barrier, which in turn causes various inflammatory changes in the gastric mucosa. Clinical manifestations include abdominal fullness, heartburn, hiccups, acid reflux, belching and other symptoms^[1]. The disease has the characteristics of recurring attacks, which can lead to gastric mucosal atrophy and intestinal biochemistry under long-term effects, increasing the risk of gastric cancer. In the treatment of the disease, gastric mucosal protective agents, gastrointestinal motility drugs, etc., are often given for treatment, but there are problems such as drug dependence and a high recurrence rate^[2]. Although there is no name for the disease "bile reflux gastritis" in traditional Chinese medicine, according to its clinical manifestations and characteristics, it can be classified into the categories of "epigastric pain", "hiccup", "vomiting", "gallbladder", "pimple syndrome" and other diseases.

Jin Qinglei, deputy chief physician of traditional Chinese medicine, was born in a family of traditional Chinese medicine. He is the 11th-generation inheritor of the Wu School of Medicine. He is the first batch of instructors for the inheritance of academic ideas and experience in the inheritance workshop of famous old traditional Chinese medicine experts of the Wu School of Medicine in Suzhou City. He is also the third batch of instructors for the succession of traditional Chinese medicine practitioners in Wuzhong District, Suzhou. He has been engaged in clinical work of traditional Chinese medicine for more than 60 years. He has rich clinical experience and has unique insights into the

treatment of bile reflux gastritis.

2. Cause and pathogenesis

There are many discussions on the etiology and pathogenesis of this disease in ancient books throughout the ages. “Lingshu·Four Seasons of Qi” says: “The evil is in the gallbladder, and the inversion is in the stomach. If bile fluid is released, the mouth will be bitter, and if the stomach Qi is inverted, vomiting will be bitter.” It shows that the location of the disease is in the gallbladder and stomach, and the cause is that bile Qi invades the stomach and stomach Qi goes up and down. “Su Wen Zhi Zhen Yao Da Lun” states: “All kinds of vomiting and acid vomiting, heavy injection and downward pressure, all belong to heat.” It is believed that vomiting and acid vomiting are due to the invasion of heat evil, the loss of balance in the stomach, and the rise of sour and rotten gas. Jin Lao believes that this disease is caused by dysfunction of the liver, gallbladder, spleen, and stomach. Normally, the liver and spleen function by ascending, the gallbladder and stomach function by descending. The liver is normal, the Qi movement is smooth, the bile circulates in the normal channels to help the stomach digest, and the contents in the stomach can be transmitted to the small intestine to secrete clear and reduce turbidity. This disease is often caused by stagnation of liver qi, failure of the liver to dissipate and drain the liver, Qi stagnation turning into fire, gallbladder stagnation and phlegm heat, bile not following the normal path to help the spleen and transformation, and backlash against the stomach, resulting in many symptoms. The treatment is suitable for clearing the gallbladder and harmonizing the stomach, soothing the liver and lowering the Qi.

3. Prescriptions and medicines explain the truth

Zuojin Pill and Wendan Decoction is Jin Lao’s experience prescription for treating bile reflux gastritis. Zuojin Pill is composed of *Coptis rhizoma* and *Evodia fructus*. Wendan Decoction consists of pinellia, tangerine peel, poria, ginger, bamboo root, *Citrus aurantium*, jujube, and licorice. Additions and subtractions according to the syndrome: For dry stools, add rhubarb; for diarrhea, add coix seed; for obvious acid reflux, add calcined octopus and calcined corrugated seeds; for chest and flank pain, add bupleurum and alpinia; for obvious vomiting, add ocher. For those with gallstones, add Hai Jin Sha and *Gallus gallus* L. *Coptis chinensis* is used heavily in Zuojin Pills to clear liver fire and purge stomach fire, taking into account both symptoms and root causes; *Evodia rutaecarpa* soothes the liver and relieves stagnation, regulates Qi, harmonizes the stomach and reduces nihilism, guides the meridians and is used as medicine, and can prevent the cold of *Coptis chinensis* from damaging the middle yang. When the two medicines are used together, the pungency and the bitterness are relieved, and the liver and stomach are treated simultaneously. Modern pharmacological research has confirmed that *Coptidis coptidis* has choleric, bacteriostatic, and immune-regulating effects ^[3], and *Evodia evodia* has analgesic and anti-inflammatory effects ^[4]. Relevant researchers isolated and identified chemical components such as berberine, coptisine, evodiamine, evodiocarpine and fanghepine from Zuojin Pills. Research has found that berberine, as a proton pump inhibitor, can effectively inhibit gastric acid secretion. Berberine and evodiocarpine inhibit gastrointestinal motility by directly antagonizing choline receptors or inhibiting cholinesterase activity. Moreover, the alkaloids in Zuojin Pills have anti-inflammatory effects and can effectively inhibit the production and secretion of inflammatory cytokines ^[5]. *Pinellia ternata* in Wendan Decoction is pungent and warm in nature. It is a monocular medicine. It mainly removes dampness and resolves phlegm, harmonizes the stomach and relieves vomiting. Bamboo Ru is sweet in taste and slightly cold in nature. It is a ministerial drug. It mainly clears away heat and resolves phlegm, relieves irritability and relieves vomiting. The two medicines are used together to relieve vomiting, relieve irritability, resolve phlegm and calm the stomach. Tangerine peel removes dampness and resolves phlegm, regulates Qi and stagnation. *Citrus aurantium* reduces Qi stagnation, resolves phlegm and eliminates pimples. *Poria cocos* strengthens the spleen and removes dampness, ginger and jujube harmonize the spleen and stomach, and roasted licorice harmonizes various medicines. The comprehensive prescription regulates Qi, resolves phlegm, harmonizes the stomach and promotes

choleresis. Modern pharmacological research has confirmed that: *Pinellia ternata* can significantly inhibit gastric juice secretion, tangerine peel can significantly inhibit gastric ulcer occurrence and gastric juice secretion, *Poria cocos* can reduce gastric juice secretion, bamboo root has anti-inflammatory effects, ginger can inhibit gastric juice acidity and gastric juice secretion, and Evodia can reduce gastric acid secretion, anti-HP activity, and choleretic and antiemetic effects^[6,7].

4. Use Chinese ginseng and Western medicine to maintain health

Jin Lao believes that diagnosis and treatment should be combined with modern medicine to identify diseases. If necessary, gastroscopy, abdominal color ultrasound, CT, tumor markers, electrocardiogram and other examinations should be completed to rule out severe cases. In addition, attention should be paid to prevention and care:

- (1) Keep a regular and healthy life to avoid the invasion of wind, cold, heat, dampness, filth and turbidity;
- (2) Patients need to learn to channel their emotions and keep their mood happy and stable. You can relax, relieve stress and anxiety, and promote physical and mental health by resting, exercising, listening to music, reading, etc.;
- (3) Pay attention to diet. Patients should avoid eating too greasy and irritating foods, such as fried foods, spicy foods, strong tea, coffee, etc., to avoid irritating the gastric mucosa and aggravating gastric discomfort. It is not advisable to eat too much raw or cold melons and fruits, as it may damage the Zhongyang. Control the amount of food you eat at each meal to avoid excessive satiety;
- (4) Patients should try to avoid staying up late, overworking and bad living habits, ensure adequate sleep time, arrange work and life reasonably, and maintain a good living condition^[8].

5. Typical cases

Zhu, a 53-year-old female, went to the hospital because of recurrent epigastric pain for more than 3 years. The patient has been experiencing epigastric pain for more than three years, with occasional abdominal distension, acid reflux, and bitter and dry mouth. An electronic gastroscopy was performed, which revealed chronic non-atrophic gastritis with erosion and bile reflux. *Helicobacter pylori* test: negative. Oral administration of omeprazole enteric-coated capsules, sucralfate suspension and other drugs was not effective. Symptoms: epigastric pain, occasional bloating, acid reflux, bitter mouth and dry mouth, palpitations, nausea, poor sleep, irregular urination, slightly dry stool, red tongue, white and greasy coating, stringy and thready pulse. TCM diagnosis: epigastric pain (stagnation of liver and stomach heat, gallbladder evil revolting against the stomach syndrome). Treatment principles: Soothe the liver and harmonize the stomach, clear the gallbladder and lower the gallbladder. Give Zuojin Pills and Wendan Decoction plus or minus 7 doses. Second diagnosis: The patient complained that the epigastric pain and abdominal distension were relieved, his sleep improved, and his stool was normal, but he still had a bitter mouth and dry mouth, a red tongue, a slightly greasy coating, and a stringy and thin pulse. In addition to the above: Forge jellyfish and corrugated fruit to produce acid and relieve pain. Third diagnosis: all symptoms subsided, with occasional dull pain in the epigastrium, abdominal distension and acid regurgitation when eating carelessly, pale red tongue, thin white fur, and stringy and thready pulse. Add *Atractylodes macrocephala* and *Amomum villosum* to the front to strengthen the spleen and stomach. Fourth diagnosis: All symptoms disappeared, sleep was restored, and bowel movements were normal. In order to consolidate the curative effect, the dosage is added or subtracted and continued for 7 days. Follow-up visit half a year later: no recurrence of symptoms was found, and a repeat gastroscopy showed chronic non-atrophic gastritis. Experience: This patient's main symptoms include epigastric pain, abdominal distension, acid reflux, bitter mouth, dry mouth, and palpitations. Combined with a red tongue, white and greasy coating, and a stringy and thready pulse, the syndrome of liver and stomach heat stagnation and gallbladder evil reversing the stomach can be identified. The initial diagnosis is mainly to soothe the liver, regulate Qi, harmonize the stomach and resolve phlegm, and choose Zuojin Pills and Wendan Decoction. During the second diagnosis, the patient's epigastric pain and abdominal distension had been relieved, his sleep had improved, and his bowel movements were normal, but he still had a bitter taste

in the mouth and dry mouth. Therefore, he added calcined jellyfish and calcined corrugated seeds to produce acid and relieve pain, and he was treated accordingly. During the third diagnosis, the patient improved further and occasionally felt dull pain in the epigastrium, abdominal distension, and acid reflux. *Atractylodes macrocephala* and *Amomum villosum* were added to strengthen the spleen and stomach. The patient was also instructed to eat a light diet to avoid the symptoms caused by an improper diet.

Diseases demonstrate the preventive thinking of traditional Chinese medicine of “treating the disease before it’s too late”. This case embodies Jin Lao’s idea of soothing the liver, regulating Qi, harmonizing the stomach and resolving phlegm in the treatment of bile reflux gastritis. It starts from the liver, gallbladder, spleen and stomach, and treats the disease according to the syndrome. It prevents the disease before it is diagnosed, so it can be effective.

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Research Progress on Biomarkers for Differential Diagnosis of Benign and Malignant Pulmonary Nodules

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Abstract: Pulmonary nodules may serve as early manifestations of lung cancer, and accurate differentiation between benign and malignant lesions directly influences clinical diagnosis and treatment strategies. Traditional imaging features provide fundamental morphological references, yet their application is prone to subjective bias and exhibits significant limitations in detecting microlesions. Breakthroughs have been achieved in research on quantitative functional imaging metrics, radiomics information, AI-assisted models, and circulating tumor cells (CTCs). Multimodal and multi-parameter fusion-based discriminant models have demonstrated enhanced efficiency in nodule characterization, emerging as a core research trend in this field.

Keywords: Pulmonary nodule; Benign-malignant differentiation; Biomarker; Radiomics; Artificial intelligence

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1. Introduction

High-resolution CT has seen increasingly widespread application in early lung cancer screening, leading to higher clinical detection rates of pulmonary nodules, most of which are benign lesions. Although puncture biopsy and postoperative pathological examination serve as gold standards for diagnosis, their invasive nature hinders widespread adoption during screening stages. While traditional imaging evaluation remains the preferred approach, it relies heavily on physician experience, resulting in insufficient diagnostic accuracy for small nodules and atypical lesions. With continuous advancements in quantitative imaging analysis techniques and molecular biology, novel biomarkers have opened new pathways for precise differentiation of pulmonary nodules. This article provides a comprehensive review of research progress on relevant biomarkers.

2. Traditional imaging characteristics as morphological biomarkers

2.1. Size and morphological characteristics of nodules

The diameter of pulmonary nodules serves as the most intuitive morphological indicator for distinguishing benign from

malignant lesions. Research by Lin Lili (2025) demonstrated that high-resolution CT can clearly visualize nodule size, with significantly higher detection rates of malignancy in large-diameter nodules compared to micro-sized nodules ^[1]. Ning Xianpu (2025) reviewed that malignant risk increases when nodule diameter exceeds specific thresholds, which also constitutes a risk factor for malignant solid pulmonary nodules ^[2]. For smaller subcentimeter nodules, benign and malignant lesions may overlap in size, making diameter alone unreliable for malignancy prediction. A comprehensive evaluation combining size characteristics with other imaging features is essential to enhance diagnostic reliability. Variations in diameter threshold definitions across studies correlate with sample composition and inclusion criteria, necessitating clinical application based on individual cases rather than rigid application of fixed cutoff values.

2.2. Edge and adjacent structural signs

The morphological characteristics of pulmonary nodule margins and their correlation with adjacent structures provide critical diagnostic clues. Ning Xianpu (2025) synthesized multiple studies revealing that lobulation features manifest as multiple arcuate protrusions at nodule margins, which exhibit higher detection frequency in malignant nodules and are pathologically associated with heterogeneous tumor cell proliferation rates ^[2]. Spiculation refers to radiating fibrous strands extending from nodule margins into surrounding lung tissue, demonstrating a strong correlation with peripheral lung cancer and higher prevalence in malignant nodules. Pleural depression results from traction of visceral pleura by internal tumor scar tissue, presenting as linear or triangular high-density shadows between nodules and pleura, a hallmark imaging feature of malignant pulmonary nodules. Vascular bundle formation indicates abnormal tumor uptake of local blood supply, offering diagnostic value in clinical evaluation.

2.3. Limitations of traditional biomarker forms

Morphological characteristics possess certain reference values, but their independent use as biomarkers remains significantly limited. Ning Xianpu (2025) pointed out that conflicting conclusions often emerge regarding the diagnostic value of similar features across different studies ^[2]. Benign lesions such as tuberculomas and inflammatory pseudotumors may also exhibit imaging features resembling malignant lesions, including lobulation, spiculation, and pleural depression, leading to substantial overlap in lesion imaging characteristics. Traditional radiographic interpretation heavily relies on clinicians' subjective experience, with judgment processes demonstrating pronounced subjectivity and no unified quantitative evaluation criteria established within the field ^[3]. Lin Lili (2025) noted that pulmonary nodules with small diameters and atypical morphological features remain difficult to accurately characterize even with high-resolution CT examinations ^[1]. Cui Kai and Zhang Xiaojun (2021) highlighted in their review that single morphological biomarkers demonstrate limited diagnostic efficacy, while combining novel biomarkers can improve the accuracy of pulmonary nodule differentiation ^[4]. The independent use of traditional morphological biomarkers fails to meet clinical precision diagnostic demands. Integrating functional imaging and molecular-level information into diagnostic reference systems provides more reliable evidence for distinguishing benign from malignant pulmonary nodules.

3. Functional imaging and quantitative parameter biomarkers

3.1. PET/CT metabolic parameters

Fluorodeoxyglucose PET/CT reflects tissue glucose metabolic activity, providing functional biomarkers independent of morphological features. Ning Xianpu (2025) noted in a relevant review that standardized uptake values serve as commonly used semi-quantitative indicators in clinical practice, with malignant nodules typically exhibiting hypermetabolic manifestations, and uptake levels showing a strong correlation with tumor cell proliferation activity ^[2]. The specificity of PET/CT is susceptible to infectious lesions; benign lesions such as inflammatory granulomas and active tuberculosis may demonstrate false-positive hypermetabolic signals, particularly in high-infection-endemic regions. The interpretation of metabolic parameters must be integrated with clinical context and epidemiological characteristics and should not be used

as the sole diagnostic criterion. Optimal cutoff values vary across studies, and standardized clinical application remains subject to certain limitations.

3.2. MRI functional parameters

Magnetic resonance imaging (MRI) does not emit ionizing radiation, making it highly suitable for patients with pulmonary nodules requiring long-term follow-up examinations. Ning Xianpu (2025) reviewed advancements in related fields, demonstrating that diffusion-weighted imaging can quantitatively assess tissue cell density based on apparent diffusion coefficients ^[2]. Malignant nodules with more dense cellular arrangements often exhibit diffusion limitation manifestations. Imageomics features extracted from specific sequences demonstrate reliable efficacy in distinguishing benign from malignant pulmonary lesions. The integration of multi-parameter MRI with machine learning algorithms provides a viable approach for differential diagnosis of pulmonary pathologies.

4. Novel imaging biomarkers: Imagingomics and artificial intelligence

4.1. Feature extraction and model construction for imaging omics

Imagingomics utilizes medical images to achieve high-throughput feature extraction, obtaining quantitative information that is difficult to capture through conventional visual interpretation, thereby overcoming the boundary limitations inherent in traditional imaging analysis. Ning Xianpu (2025) reviewed the research landscape in related fields, noting that imagingomics encompasses morphological parameters, first-order gray-level statistics, texture information, and higher-order representations, enabling numerical expression of tumor internal heterogeneity ^[2]. Prediction models constructed by integrating imagingomics with deep learning features demonstrate superior diagnostic performance compared to models relying solely on single features. The combined use of imagingomics metrics with conventional imaging findings enhances the accuracy of lesion differentiation. Imagingomics analysis provides reliable quantitative evidence for pulmonary nodule risk stratification, maintaining stable diagnostic performance under both low-dose CT and standard-dose CT scanning conditions, making it suitable for early lung cancer screening.

4.2. Application and limitations of artificial intelligence-assisted diagnostic systems

Artificial intelligence deep learning models can automatically identify pulmonary nodules and extract imaging features, thereby improving radiographic review efficiency. Research by Ye Hongda (2025) demonstrates that such systems can reduce average per-case review time, exhibit outstanding sensitivity for small nodules, and minimize missed diagnoses caused by visual fatigue ^[3]. However, standalone AI diagnosis faces challenges of high sensitivity but insufficient specificity, often misclassifying normal or benign structures such as vascular cross-sections, pleural thickening, and bronchial mucus plugs as malignant nodules. It cannot directly replace physicians in qualitative diagnosis, has a low threshold for identifying malignant pulmonary nodules, and is prone to false positives.

4.3. Diagnostic advantages of multi-source information fusion models

The integration of radiomics features with clinical parameters and conventional imaging characteristics to construct a multi-source information fusion model can further enhance diagnostic accuracy. Ning Xianpu (2025) summarized that models combining radiomics features with conventional imaging features demonstrate improved efficacy in differentiating the benign and malignant nature of solid pulmonary nodules ^[2]. Clinical factors such as the spiculation sign and age exhibit superior diagnostic performance when combined with radiomics features. Ye Hongda (2025) confirmed that the combined use of artificial intelligence and physician-based diagnosis achieves higher accuracy than either approach alone, with good consistency with pathological results ^[3]. Shi Jie et al. (2021) demonstrated that combined detection of cytokines and tumor markers improves the differential diagnostic efficacy for solitary pulmonary nodules, with the established multi-index fusion model showing superior area under the curve performance compared to individual detection metrics ^[5]. Multimodal

strategies integrate complementary information from biomarkers across different dimensions: radiomics captures microscopic textural heterogeneity, conventional features present macroscopic morphological information, clinical parameters reflect host background risk levels, and decision curve analysis confirms that multimodal fusion models deliver clinical net benefits across a wide threshold probability range, demonstrating reliable clinical applicability.

5. Liquid biomarkers and their application in the differentiation of pulmonary nodules

5.1. Circulating tumor cells

Circulating tumor cells (CTCs) originate from the detachment of the primary lesion and enter the peripheral blood, representing a significant direction for liquid biopsy development. Research by Ning Xianpu (2025) revealed that CTCs fundamentally differ from imaging biomarkers, directly reflecting tumor biological behavior rather than indirectly indicating morphological changes, thereby possessing unique diagnostic value^[2]. In differentiating benign from malignant solid pulmonary nodules, CTCs serve as a critical risk factor; when combined with CT imaging features, they enhance the accuracy of early lung cancer diagnosis and provide supplementary insights for nodules with atypical imaging manifestations. CTC detection technologies include positive-enrichment and negative-enrichment methods, though their sensitivity and standardization still require improvement. Significant inter-platform variability exists among detection results, and CTC testing has not yet been incorporated into routine clinical practice.

5.2. Traditional serum tumor markers

Serum tumor markers have gained widespread clinical application due to their ease of detection, but their value in distinguishing benign from malignant pulmonary nodules remains relatively limited. Ning Xianpu (2025) noted that conventional indicators such as carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and cytokeratin 19 fragments (CK19) exhibit suboptimal sensitivity and specificity in early lung cancer screening, demonstrating weak practical utility for benign/malignant differentiation of solid pulmonary nodules^[2]. Single tumor markers lack organ-specific or tumor-specific specificity and cannot serve as standalone diagnostic biomarkers. Pei Dongfang et al. (2021) demonstrated that low-dose spiral CT combined with multiple tumor markers, including CEA, squamous cell carcinoma antigen (SCCA antigen), gastrin-releasing peptide precursor (GRP-P), and NSE, optimizes the differential diagnosis of solitary pulmonary nodules, with the combined approach showing superior diagnostic sensitivity and accuracy compared to single CT imaging^[6]. Zhu Zhengxin et al. (2025) corroborated that chest CT imaging combined with serum tumor marker testing provides more reliable evidence for nodular malignancy assessment, serving as an effective diagnostic supplement for atypical imaging features^[7].

5.3. Multimodal combined diagnostic strategy

The reliance on a single biomarker has inherent limitations, making multimodal integration the prevailing consensus in current research. Ye Hongda (2025) demonstrated that artificial intelligence combined with physician-based manual diagnosis achieves high consistency with pathological results, highlighting the advantages of computer-assisted screening integrated with human decision-making^[3]. Ning Xianpu (2025) emphasized that the fusion of traditional imaging features, clinical characteristics, and radiomics features enhances the diagnostic accuracy for solid pulmonary nodules^[2]. A review by Shi Jie et al. (2021) noted that incorporating cytokines alongside conventional tumor markers into diagnostic models compensates for the limitations of single serological indicators, providing richer biological dimension information for pulmonary nodule risk stratification^[5]. The combined application of imaging biomarkers and liquid biomarkers holds promising prospects. Future efforts should focus on developing comprehensive predictive models that integrate radiomics, functional imaging parameters, serum markers, and clinical risk factors, with multicenter prospective studies validating the models' generalizability.

6. Conclusion

Research on biomarkers for the differential diagnosis of benign and malignant pulmonary nodules has expanded from single morphological indicators to a multidimensional system comprising functional imaging parameters, radiomics features, artificial intelligence models, and liquid biomarkers. Radiomics and artificial intelligence can enhance feature extraction and improve efficiency, yet they cannot replace clinical decision-making by physicians. Circulating tumor cells (CTCs) in liquid biomarkers provide unique biological information. Each biomarker has its own limitations, and multimodal, multi-parameter integrated models represent an effective approach to improving diagnostic accuracy.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Study on Optimization Strategies for Pre-hospital First Aid and In-hospital Connection in Patients with Severe Trauma

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Abstract: *Objective:* To analyze the clinical effect of optimized strategies for pre-hospital first aid and in-hospital connection in patients with severe trauma. *Methods:* Sample collection time: June 2024 - February 2026, sample size: 82 patients with severe trauma were admitted to our hospital. The included samples were randomly divided into two groups with odd and even numbers. 41 cases in the control group received routine care, and 41 cases in the observation group implemented pre-hospital first aid and in-hospital connection optimization strategies. The first aid time, family satisfaction, nursing quality, and psychological state were compared between the two groups. *Results:* The first aid time of the cases in the observation group was statistically significantly lower than that of the control group, $P < 0.05$. The satisfaction rate of family members of the patients involved in the observation group was 95.12%, which was statistically significantly higher than that of the control group, which accounted for 80.49%, $P < 0.05$. The nursing quality of the cases involved in the observation group was statistically significantly higher than that of the control group, $P < 0.05$. The psychological state of the cases in the observation group was statistically significantly lower than that of the control group, $P < 0.05$. *Conclusion:* Optimizing the connection between pre-hospital first aid and in-hospital care for patients with severe trauma can effectively reduce negative emotions, help shorten first aid time, and has positive significance in improving the quality of care and family satisfaction, and is worth learning from.

Keywords: Severe trauma; Intra-hospital connection optimization strategy; Pre-hospital first aid; Application value

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1. Introduction

With the rapid development of urbanization and industrialization, the incidence of severe trauma is increasing year by year. The condition is critical and progresses rapidly. It is often accompanied by complications such as multiple organ damage and hemorrhagic shock. The death and disability rate remains high, which places extremely high demands on the emergency diagnosis and treatment process^[1]. Pre-hospital first aid is the primary link in trauma treatment, and the in-hospital connection is the key support for subsequent treatment. The synergistic efficiency of the two directly determines the patient's prognosis^[2]. At present, most medical institutions in my country still have problems such as untimely transmission of pre-hospital and in-hospital information, irregular process connection, and unclear division of labor, which results in prolonged first aid time, waste of treatment resources, and affects the quality of care and patient recovery^[3]. Based on the relevant standards for linking pre-

hospital and in-hospital information for severe trauma, combined with clinical treatment practice, this study focuses on the optimization strategy of pre-hospital first aid and in-hospital connection. By standardizing the process and improving the collaboration mechanism, it explores its clinical application value, providing a theoretical basis for improving the treatment effect of severe trauma patients, improving the prognosis, and helping to reduce the death and disability rate of trauma patients.

2. Materials and methods

2.1. General information

Sample collection time: June 2024 to February 2026, sample size: 82 patients with severe trauma were admitted to our hospital. The included samples were divided into two groups using random odd and even numbers. Among the 41 cases in the control group, the gender distribution showed: a total of 21 cases were male (accounting for 51.22%), and a total of 20 cases were female (48.78%). According to statistics on the age range, it ranges from 26 to 74 years old, with an average age of (50.56 ± 3.08) years old. Among the 41 cases in the observation group, the gender distribution showed that there were 22 males (53.66%) and 19 females (46.34%). According to the age range statistics, they ranged from 23 to 77 years old, with an average of (50.89 ± 2.67) years old. There was no difference in the baseline data between the two groups ($P > 0.05$), and the studies were comparable.

2.2. Method

The control group used conventional intervention methods. The observation team's strategy for optimizing the connection between pre-hospital first aid and in-hospital care:

- (1) Optimization of pre-hospital first aid: Establish a professional first aid team, train all members on core trauma first aid skills and information transmission standards, quickly assess injuries on site, prioritize control of massive bleeding, and maintain open airways. The electronic information entry method is simultaneously used to record the patient's basic information, injury status and on-site treatment measures in detail, and transmit it to the emergency department of the hospital in real time through the information link system. When electronic conditions are not available, a paper record + telephone handover mode is used to ensure that the information is accurate and complete.
- (2) Preparation for in-hospital connection: The in-hospital emergency department sets up a special trauma first aid team. After receiving pre-hospital information, it immediately activates the green channel, prepares rescue equipment, medicines and monitoring instruments in advance, clarifies the division of labor among members, and demarcates exclusive rescue areas. Synchronously connect with the surgery department, laboratory department and other related departments to make preparations for examinations and surgeries in advance to ensure that patients can be treated immediately after arriving at the hospital and reduce waiting time.
- (3) Standardize the handover process: Establish a standardized handover list, clarify the handover content, process and responsible personnel. After the patient is transferred to the hospital, the pre-hospital first aid personnel and the hospital nursing staff will check the patient's information, injury assessment results, treatment measures and medication on-site, confirm each item and sign for confirmation, to achieve a seamless connection and avoid information omission or transmission deviation.
- (4) Full dynamic monitoring: After the patient is admitted to the hospital, the nursing staff will continue to monitor vital signs, state of consciousness and wound conditions, and promptly detect changes in the condition and deal with them. At the same time, we strengthen communication with family members, promptly inform patients of their condition, treatment progress, and nursing measures, pay attention to the psychological state of patients and family members, and provide timely psychological counseling.

2.3. Observation indicators

- (1) Compare first aid time.
- (2) Compare family satisfaction, satisfaction = satisfaction ratio + basic satisfaction ratio ^[4].
- (3) Compare the quality of care, involving four dimensions, and the evaluation scores are all 100 points. The higher the score, the higher the quality of care ^[5].
- (4) Compare psychological status and evaluate based on SAS and SDS scales ^[6].

2.4. Statistical methods

SPSS 26.0 was used for data analysis. The measurement data that conforms to the normal distribution (involving the first aid time value, SAS value, SDS value, and nursing quality value in this study) are expressed as mean $\pm$ standard deviation (SD), and intra-group comparisons are performed using the t test; measurement data that do not conform to the normal distribution are described by the median and interquartile range [M (Q25, Q75)], and the difference between groups is analyzed using the Wilcoxon rank sum test. Count data (actual data on family satisfaction in this study) were expressed as frequencies or percentages (n, %), and differences between groups were analyzed using the χ^2 test or Fisher's exact probability method; for hierarchical data, the Wilcoxon rank sum test was used. $P < 0.05$ means the difference is statistically significant.

3. Results

3.1. Comparison of first aid time

The first aid time of the cases in the observation group was statistically significantly lower than that of the control group, $P < 0.05$ (Table 1).

Table 1. Comparison of first aid time (mean $\pm$ SD)

Group	Clinic response time (s)	On-site first aid time (min)	Auxiliary inspection time (min)	Time for admission and delivery to hospital (h)
Control group (n = 41)	102.52 $\pm$ 6.41	11.14 $\pm$ 5.71	27.92 $\pm$ 3.11	1.91 $\pm$ 0.32
Observation group (n = 41)	99.16 $\pm$ 7.76	6.14 $\pm$ 3.52	18.31 $\pm$ 2.64	0.62 $\pm$ 0.48
<i>t</i>	2.137	4.772	15.083	14.318
<i>P</i>	0.035	0.000	0.000	0.000

3.2. Compare family members' satisfaction

The satisfaction rate of family members of the patients involved in the observation group was statistically significantly higher than that of the control group, $P < 0.05$ (Table 2).

Table 2. Comparative nursing satisfaction [n/(%)]

Group	Satisfied	Basically satisfied	Not satisfied	Satisfaction (%)
Control group (n = 41)	18 (43.90)	15 (36.59)	8 (19.51)	33 (80.49)
Observation group (n = 41)	21 (51.22)	17 (41.07)	2 (4.88)	39 (95.12)
χ^2	-	-	-	4.100
<i>P</i>	-	-	-	0.042

3.3. Compare the quality of care

The nursing quality of the cases involved in the observation group was statistically significantly higher than that of the

control group, $P < 0.05$ (Table 3).

Table 3. Comparing quality of life (mean $\pm$ SD)

Group	Social relations (points)		Mental state (minutes)		Physical function (minutes)		Physiological functions (points)	
	Before intervention	After intervention	Before intervention	After intervention	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 41)	52.56 $\pm$ 3.09	68.25 $\pm$ 2.34	56.79 $\pm$ 2.83	69.26 $\pm$ 2.41	56.36 $\pm$ 3.78	62.79 $\pm$ 3.83	58.79 $\pm$ 3.83	66.56 $\pm$ 2.73
Observation group (n = 41)	54.46 $\pm$ 2.38	75.21 $\pm$ 2.56	59.56 $\pm$ 3.73	71.38 $\pm$ 2.59	57.54 $\pm$ 2.36	78.51 $\pm$ 4.36	58.16 $\pm$ 4.89	71.42 $\pm$ 4.36
<i>t</i>	3.119	12.849	3.788	3.836	1.695	17.344	0.649	6.049
<i>P</i>	0.002	0.000	0.000	0.000	0.093	0.000	0.517	0.000

3.4. Comparing psychological states

The psychological state of the cases in the observation group was statistically significantly lower than that of the control group, $P < 0.05$ (Table 4).

Table 4. Comparing psychological states (mean $\pm$ SD)

Group	SAS score (points)		SDS score (points)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 41)	62.42 $\pm$ 4.61	59.71 $\pm$ 5.79	67.82 $\pm$ 5.89	58.37 $\pm$ 4.41
Observation group (n = 41)	62.36 $\pm$ 3.78	54.25 $\pm$ 3.35	67.41 $\pm$ 4.56	52.67 $\pm$ 3.25
<i>t</i>	0.064	5.226	0.352	6.662
<i>P</i>	0.948	0.000	0.725	0.000

4. Discussion

In clinical practice, severe trauma is an acute and severe disease with an increasing prevalence and caused by external forces such as traffic accidents, falls from heights, and violent injuries. Its main characteristics are acute onset, serious condition, and high risk of complications, such as multiple organ failure, hemorrhagic shock, etc. It also has a high disability and mortality rate, and has a great impact on the physical and mental health of patients^[7,8]. In the treatment of patients with severe trauma, the implementation of the pre-hospital first aid model can be used as the first line of defense. In the subsequent treatment, intra-hospital connection is the key link. Through the combination of the two, the smoothness and standardization of first aid work can be ensured, the utilization efficiency of patients' golden treatment time can be maximized, and the prognosis can be effectively improved^[9]. Nowadays, there are many problems in the first aid work for patients with severe trauma, such as insufficiently standardized procedures, lagging information, etc., which leads to delays in treatment and increases the risk of patient treatment^[10]. In actual nursing work, relevant nursing staff standardize the connection model between pre-hospital first aid and in-hospital care based on the actual condition of the patient, giving full play to their synergy and complementary advantages, which is of positive significance to improving their treatment efficiency.

The study found that there was a large difference in first aid time between the two groups, $P < 0.05$. Analysis of reasons: During the actual nursing period, the implementation of the joint nursing model, which transmits hospital information in real time and prepares for rescue at the same time, can significantly shorten the emergency time and lay

a solid foundation for the smooth development of in-hospital emergency work for patients. After optimizing the nursing model based on the patient's actual condition, the rescue time is significantly shortened, avoiding treatment delays due to many factors, and gaining rescue time, thereby significantly reducing the patient's mortality. There is a big difference in the satisfaction of family members of the two groups (80.49%/95.12%), $P < 0.05$. Analysis of the reasons: Implementing joint intervention methods, strengthening communication between family members and medical staff, carefully communicating the condition, formulating targeted treatment plans, and clarifying the prognosis can significantly reduce their negative emotions. At the same time, relevant nursing staff provide patients with active and efficient nursing services through standardized treatment procedures, thereby effectively improving their condition.

In addition, professional and timely nursing services can improve nursing satisfaction while reducing nursing conflicts, further improving the level of nursing care. There was a big difference in the quality of nursing care between the two groups, $P < 0.05$. Analysis of reasons: In nursing work, nursing staff clarify the nursing process, refine nursing responsibilities, and maintain standardized and standard nursing operations, which will help reduce their nursing errors. At the same time, strengthening the training of first aid personnel in relevant knowledge and operational skills and strengthening the cooperation between various departments can effectively improve their professionalism and help improve their emergency response capabilities. In addition, the standardization of information transmission avoids nursing errors caused by information deviation, further improves the overall quality of emergency care, and meets the relevant standards for linking pre-hospital and in-hospital information for severe trauma. The psychological state of the cases in the observation group was statistically significantly lower than that of the control group, $P < 0.05$. The suddenness of severe trauma can easily cause patients to experience negative emotions such as fear, anxiety, and despair, and family members may also become seriously anxious because they are worried about the patient's condition. Full-process psychological care is added to the optimization strategy. Nursing staff use gentle communication and psychological counseling to alleviate the negative emotions of patients and their families, help patients build confidence in overcoming the disease, and guide family members to cooperate with treatment with a positive attitude. At the same time, the efficient treatment results allow patients and their families to see hope of recovery, further improve their mental state, and lay a good psychological foundation for the patient's subsequent recovery.

5. Conclusion

In summary, the optimization strategy of pre-hospital first aid and in-hospital connection for patients with severe trauma has the effect of reducing negative emotions, shortening first aid time, and improving nursing satisfaction and quality, and is worth learning from.

Disclosure statement

The author declares no conflict of interest.

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