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Research Progress on the Prevention of Infection in Operating Rooms Using the HFMEA Model Combined with Evidence-Based Medicine

Wen Xu¹, Xiaofu Ji^{2*}

¹Department of Anesthesiology and Operation II, Olympic Center, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan 250021, Shandong, China

²Department of Anesthesiology and Operation I, Olympic Center, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan 250021, Shandong, China

**Author to whom correspondence should be addressed.*

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Abstract: The Healthcare Failure Mode and Effect Analysis (HFMEA) model, as a proactive risk assessment tool, systematically identifies potential infection risk points during surgical procedures and evaluates the failure modes and their effects that may result from these risks. Evidence-based medicine, on the other hand, emphasizes making medical decisions based on the best available evidence. Combining these two approaches can provide more scientific and effective strategies for preventing infection in operating rooms. This paper delves into the application of the HFMEA model and evidence-based medicine in the field of infection prevention in operating rooms, aiming to offer new perspectives and methods for this critical aspect of healthcare.

Keywords: Healthcare failure mode and effect analysis; Evidence-based medicine; Operating room infection; Prevention; Progress

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1. Introduction

As the core area for infection prevention and control in hospitals, the incidence of infection in operating rooms directly affects patient prognosis and the quality of medical care. Statistics indicate that approximately 5% of surgical patients worldwide develop postoperative infections, with 20–30% being surgical site infections (SSIs), leading to prolonged hospital stays, increased medical costs, and higher mortality rates^[1]. Traditional postoperative infection control has largely relied on retrospective tracing and empirical interventions, making it difficult to identify high-risk areas and implement proactive control measures. In recent years, foreign research has focused on refined prevention and control strategies that combine HFMEA with evidence-based medicine, while domestic research has emphasized the optimization of localized processes and the evaluation of empirical intervention effects. Together, these efforts have driven the scientific and systematic development of infection prevention and

control in operating rooms^[2]. The HFMEA is based on team analysis, systematic process review, and evaluation of the risk levels of failure modes, providing a decision-making basis for postoperative infection control. Evidence-based Medicine (EBM) centers on evidence and aims to formulate optimal decisions based on the interests of patients and hospitals. The integration of HFMEA with EBM has emerged as a focal point of research in recent years for infection prevention and control in operating rooms. By leveraging failure mode analysis and incorporating evidence-based interventions, it facilitates a closed-loop operation from “identifying risks” to scientific prevention and control. This paper aims to systematically review the research progress of the HFMEA model combined with EBM in preventing infections in operating rooms, analyze its theoretical advantages, practical effects, and future development directions, and provide references for enhancing infection prevention and control standards in operating rooms.

2. Overview of the HFMEA model and evidence-based medicine

2.1. HFMEA model

HFMEA is a systematic and forward-looking risk management tool, with its core concept derived from Failure Mode and Effects Analysis (FMEA) in the industrial sector. It was later optimized and introduced into the medical field by the Veterans Health Administration in the United States. HFMEA systematically identifies and proactively prevents various potential risk factors in medical processes by establishing an organized procedure. Unlike traditional post-event remedial approaches, HFMEA emphasizes “prevention over correction”. It organizes multidisciplinary personnel to collaborate, divides processes into stages, and conducts failure mode analysis for each process (e.g., operational errors, equipment failures, communication breakdowns), analyzes the impact of failures (e.g., infections, treatment delays), and calculates the Risk Priority Number ($RPN = O \times S \times D$) based on the likelihood of occurrence (O), severity (S), and detectability (D) of failures. This enables precise identification of high-risk areas and the formulation of targeted improvement measures^[3]. In 2002, the Joint Commission on Accreditation of Healthcare Organizations incorporated HFMEA into its patient safety standards, further promoting its widespread application in operating rooms, medication management, blood transfusion safety, and other fields. Its advantage lies in combining qualitative analysis with quantitative assessment, providing an actionable risk management framework for medical quality improvement.

2.2. Evidence-based medicine

EBM is a clinical thinking process that formulates optimal medical decisions based on existing scientific research evidence. It was proposed in the 1990s by a team led by Professor David Sackett from McMaster University in Canada. Its core principle is “to formulate the best medical decisions based on the current best research evidence, combined with the clinical expertise of healthcare professionals and the individual needs of patients”. Unlike traditional empirical medicine, EBM emphasizes hierarchical integration: it integrates evidence from multicenter, randomized, controlled clinical trials obtained through systematic reviews and meta-analyses in a hierarchical manner, and combines it with clinical practice guidelines and patient values to achieve a balance between scientific decision-making and humanization^[4]. Currently, in the prevention and control of infectious diseases, evidence-based hierarchical integration is widely used to determine optimal intervention measures. For example, the effectiveness of interventions such as hand hygiene, aseptic techniques, and rational use of antimicrobial agents is determined through evidence grading, providing standardized references for clinical practice. With the

advent of the information age, evidence management has gradually incorporated artificial intelligence and big data technologies, forming a dynamic “evidence repository” that further enhances the accuracy and timeliness of clinical decision-making.

3. Application progress of the HFMEA model in the prevention of infections in hospital operating rooms

3.1. Detailed decomposition of surgical processes and risk quantification

The HFMEA model provides a detailed decomposition of infection prevention processes in operating rooms, covering all stages from preoperative preparation to intraoperative procedures and postoperative care. Research by Ma Xiaojun et al. indicates that during the preoperative preparation phase, the team identified potential failure modes such as “incomplete cleaning and disinfection of surgical instruments” and “low hand hygiene compliance among surgical personnel” through process mapping^[5]. During the intraoperative phase, high-risk areas such as “improper storage of sterile items” and “inadequate protective measures for surgical incisions” were identified. By calculating the Risk Priority Number (RPN) for each failure mode, the team can quantitatively assess risk levels. Research by Yao Yao et al. applied HFMEA to the infection prevention process for laparoscopic surgery and found that the RPN value for “incorrect sterilization parameter settings for surgical instruments” was as high as 240 (severity S = 8, probability of occurrence O = 6, detectability D = 5), making it the primary target for intervention^[6]. By optimizing sterilization equipment operation protocols and adding a double-check process, the RPN value for this failure mode was reduced to 80, significantly lowering the risk of infection.

3.2. Multidisciplinary collaboration and development of standardized intervention measures

The HFMEA model emphasizes interdisciplinary teamwork, integrating perspectives from infection control experts, surgeons, nurses, anesthesiologists, and other stakeholders to ensure the scientific validity and operability of intervention measures^[7]. In a hospital operating room infection prevention project, Fu Tingting and her team identified “air pollution caused by frequent movement of personnel during surgery” as a high-risk failure mode (RPN = 180) through HFMEA^[8]. Following multidisciplinary discussions, standardized intervention measures were formulated: limiting the number of personnel in the operating room, optimizing the placement of items to reduce the need for movement, installing air purification equipment, and regularly monitoring bacterial colony counts. After implementation, the RPN value for this failure mode dropped to 60, and the surgical site infection (SSI) rate decreased from 1.2% to 0.5%. Additionally, HFMEA promoted the standardization of infection prevention and control processes in the operating room, such as the development of the “Operating Room Aseptic Technique Standards” and the “Surgical Instrument Cleaning and Disinfection Flow Chart”, providing clear guidance for frontline staff.

3.3. Dynamic risk monitoring and continuous improvement

The HFMEA model enables dynamic management of infection risks through regular process reviews and updates to RPN values. In a study by Jin Xiaoying and colleagues, after implementing HFMEA interventions in the infection prevention process for cardiac surgery, “incomplete disinfection of cardiopulmonary bypass circuits” was initially identified as a high-risk mode (RPN = 200)^[9]. By introducing single-use circuits and strengthening

disinfection process monitoring, the RPN value was reduced to 50. However, with the application of new antibacterial coating circuits, the team re-evaluated the risks in this area and found that “bacterial colonization due to coating detachment” had become a new potential failure mode (RPN = 150). Subsequently, the intervention strategy was adjusted to include a coating integrity check before circuit use. This dynamic feedback mechanism ensures that infection prevention and control measures remain aligned with clinical practice, avoiding the limitations of a one-size-fits-all management approach.

4. Progress in the application of EBM in hospital operating room infection prevention

4.1. Evidence grading and standardized recommendations for infection prevention measures

EBM integrates evidence from multicenter studies through systematic reviews and meta-analyses to provide graded recommendations for infection prevention measures in operating rooms^[10]. The “Global Guidelines for the Prevention of Surgical Site Infection” issued by the World Health Organization (WHO), based on the GRADE evidence grading system, explicitly recommend the following: preoperative skin disinfection with chlorhexidine-alcohol solution (strong recommendation, high-quality evidence), maintaining normal body temperature during surgery (strong recommendation, moderate-quality evidence), and discontinuing prophylactic antimicrobial agents within 24 hours postoperatively (strong recommendation, high-quality evidence)^[11]. These standardized recommendations provide clear guidance for clinical practice. After strictly adhering to the WHO guidelines in orthopedic surgeries, Liang Guangming and colleagues observed a reduction in the incidence of surgical site infections (SSI) from 2.1% to 0.8%^[12]. Additionally, EBM promotes the refinement of infection prevention and control measures in operating rooms, such as developing differentiated antimicrobial drug use protocols based on surgical type (clean surgery, clean-contaminated surgery, contaminated surgery) to avoid the development of drug-resistant bacteria caused by a “one-size-fits-all” approach to medication.

4.2. Evidence-based application of new technologies and materials

EBM provides a scientific basis for the introduction of new infection prevention and control technologies and materials in operating rooms. For instance, antimicrobial-coated sutures inhibit bacterial colonization at the incision site by locally releasing antimicrobial agents. Multiple randomized controlled trials (RCTs) have confirmed that they can reduce the risk of SSI (RR = 0.65, 95% CI 0.52–0.81), but their use should be strictly indicated (e.g., in high-risk surgical patients). EBM also guides the optimization of environmental disinfection techniques in operating rooms. For example, hydrogen peroxide vapor disinfection has been shown to more thoroughly eradicate drug-resistant bacteria (such as MRSA) compared to traditional ultraviolet irradiation and has lower corrosivity to equipment, making it the preferred disinfection method for high-risk operating rooms (such as those for organ transplantation)^[13]. Furthermore, EBM drives the upgrading of personal protective equipment (PPE) in operating rooms. The use of double gloves, for instance, can reduce the risk of blood exposure due to intraoperative glove rupture (from 4.2% to 1.1%), but it requires balancing operational dexterity with protective efficacy.

4.3. Evidence-based management of patient-specific factors and infection risks

EBM emphasizes the development of individualized infection prevention strategies based on patient characteristics. For example, patients with diabetes are prone to incisional infections due to blood glucose fluctuations. EBM recommends controlling preoperative blood glucose levels within the range of 7.8–10.0 mmol/

L to balance the risks of infection and hypoglycemia. For obese patients, due to their thick subcutaneous fat and high incisional tension, EBM suggests employing tension-reducing suture techniques and extending the duration of prophylactic antimicrobial use (from 24 hours to 48 hours)^[14]. Additionally, EBM also focuses on the impact of patients' psychological factors on infections. For instance, preoperative anxiety can lead to a decline in immune function. By alleviating anxiety through music therapy or psychological counseling, the incidence of surgical site infections (SSIs) can be reduced by 30% (OR = 0.7, 95% CI 0.5–0.9)^[15].

5. Application progress of HFMEA model combined with EBM in operating room infection prevention

5.1. Risk identification and evidence-based prioritization in operating room infection prevention

The FMEA model systematically examines infection prevention and control processes in the operating room, combining evidence-based medicine to accurately identify high-risk failure points and determine intervention priorities. Research has indicated that in the hand hygiene practices of surgical personnel, FMEA analysis revealed that traditional alcohol disinfection was insufficient in killing spore-forming microorganisms^[16]. Evidence-based medicine demonstrates that chlorhexidine-alcohol composite disinfectants can significantly reduce bacterial load on hands (RR = 0.42, 95% CI 0.31–0.57), leading to its prioritization for improvement. Another study showed that after hospitals applied FMEA in conjunction with EBM, differentiated prevention and control strategies were developed for high-risk areas (such as instrument cleaning and environmental disinfection), resulting in a reduction in the operating room infection rate from 1.8% to 0.9%^[17]. Furthermore, FMEA quantifies the risk priority number (RPN), identifying “contamination of sterile items during surgery” as the highest-risk item. Evidence-based medicine supports the use of disposable sterile packs instead of reusable sterilized instruments to further reduce the risk of cross-infection.

5.2. Optimization of infection prevention and control processes and integration of evidence-based measures

The FMEA model optimizes infection prevention and control processes in the operating room through a closed-loop management approach of “prevention-monitoring-improvement”, incorporating evidence-based medicine. The study by Zhu Guanmei and others pointed out that during the preparation of the surgical site, FMEA analysis revealed that traditional iodophor disinfection had issues such as significant skin irritation and low patient compliance^[18]. Evidence-based medicine recommends the use of chlorhexidine-alcohol solution (strong recommendation, high-quality evidence), which not only offers superior disinfection effects (reducing the risk of surgical site infections (SSI) by 40%) but also significantly enhances patient comfort. Another study combined FMEA with EBM to develop a stratified intervention plan for the high-risk process of “intraoperative temperature maintenance”: passive insulation (e.g., covering with an insulation blanket) was employed for low-risk surgeries, while active warming devices (e.g., forced-air warming devices) were used for high-risk surgeries (e.g., organ transplants), resulting in a reduction in the incidence of intraoperative hypothermia from 32% to 15%^[19]. Furthermore, through process reengineering, FMEA moved the “postoperative instrument pre-treatment” step to the operating room and, combined with the use of enzyme detergents recommended by evidence-based medicine, increased the instrument cleaning pass rate from 85% to 98%.

5.3. Multidisciplinary collaboration and evidence-based decision support

The FMEA model emphasizes cross-disciplinary teamwork and the development of comprehensive infection prevention and control plans based on evidence-based medicine. A study indicated that in the “management of high-risk surgical patients”, the FMEA team integrated opinions from multiple disciplines, including surgery, infectious diseases, and pharmacy, to develop individualized strategies based on evidence-based medicine: for diabetic patients, preoperative blood glucose was controlled within the range of 7.8–10.0 mmol/L (strong recommendation, moderate-quality evidence); for obese patients, tension-reducing suture techniques were employed, and the use of prophylactic antimicrobial agents was extended to 48 hours (weak recommendation, low-quality evidence) ^[20]. Additionally, Lin Danzhu et al., through multidisciplinary FMEA analysis, found that the “timing of intraoperative antimicrobial agent administration” was a key factor affecting SSI ^[21]. By adopting the EBM-recommended protocol of “administering the drug 0.5–1 hour before skin incision”, the incidence of SSI decreased from 2.5% to 1.2%. Furthermore, FMEA established an evidence-based decision support system to update infection prevention and control guidelines in real-time, ensuring that team decisions are based on the latest evidence.

5.4. Constructing a precise risk priority number evaluation system

To address the issue of strong subjectivity in RPN scoring, it is essential to establish unified and objective scoring criteria. This involves consulting extensive literature and conducting clinical research to clearly define the specific manifestations and quantitative data of each risk factor at different levels. Additionally, developing specialized software to incorporate these scoring criteria can reduce human error and ensure the accuracy and consistency of scoring. Meanwhile, establishing a data-sharing platform will facilitate data exchange among different research institutions, providing a basis for refining the scoring criteria.

5.5. Innovating a research model integrating multiple theories

Given the limitations of HFMEA, it is crucial to actively explore research models that combine HFMEA with evidence-based medicine, quality management theory, and other methodologies. For instance, applying evidence-based medicine evidence retrieval and evaluation methods to HFMEA can make risk factor analysis and improvement methods more scientific. By integrating quality management theory, a continuous quality improvement cycle model can be constructed to continually refine the process of preventing surgical infections. Through the integration of multiple theories, a comprehensive and dynamic infection prevention system can be established to adapt to the complex and ever-changing clinical environment.

6. Conclusion

In summary, the HFMEA model, with its systematic and forward-looking risk management characteristics, can accurately identify potential infection risk points in surgical procedures and provide a scientific basis for intervention measures through quantitative assessment. Evidence-based medicine, centered on the best available evidence and combined with individual patient needs and medical resources, offers standardized references for formulating and optimizing infection prevention and control measures. The integration of these two approaches helps strengthen the deepening of multidisciplinary collaboration models, promotes the establishment of risk priority assessment systems, and drives innovation in research models that integrate multiple theories. With

the continuous advancement of medical care and the growing demand for infection prevention and control, the HFMEA model and evidence-based medicine will play an increasingly important role in preventing and controlling infections in operating rooms, contributing to improved medical quality and enhanced patient safety.

Disclosure statement

The author declares no conflict of interest.

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Rehabilitation Nursing for a Patient with Acute Respiratory Failure Combined with Heart Failure and Obesity: A Case Report

Xuelian Jiang^{1*}, Jingjing Xie², Chengyang Wan³

¹ Nursing Department, TaiHe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei, China

² Intensive Care Unit, Wudangshan Branch, TaiHe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei, China

³ Neurological Rehabilitation Center, TaiHe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei, China

*Corresponding author: Xuelian Jiang, 527530264@qq.com

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Abstract: This paper summarizes the systematic rehabilitation nursing experience for a patient with acute respiratory failure combined with heart failure and obesity (BMI = 39.1). Key nursing interventions included implementing a sequential respiratory support strategy (high-flow oxygen therapy → non-invasive ventilation → transition to home ventilator), conducting phased exercise rehabilitation training, delivering precise nutritional management (total daily calorie intake controlled at 1500–1800 kcal), enhancing interdisciplinary risk prevention and control, and employing SMART goal setting for behavioral intervention. Following systematic intervention, after 4 days of hospitalization, the patient's SpO₂ increased from 80% to 92% while off mechanical ventilator support, and the self-care ability score rose to 85 points. One week after discharge, the patient's body weight had decreased by 2 kg, pulmonary function indices showed improvement, and the patient successfully returned to work.

Keywords: Acute respiratory failure; Heart failure; Obesity; Rehabilitation nursing

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1. Introduction

Acute respiratory failure combined with heart failure represents one of the critical conditions in clinical practice. Patients often experience complex conditions and poor prognosis due to impaired gas exchange and reduced cardiac pump function. Obesity, as a common comorbidity, further aggravates cardiopulmonary load, increases treatment difficulty, and significantly impacts patient rehabilitation process and quality of life. The rehabilitation process for such patients requires comprehensive multi-dimensional strategies including respiratory support, nutritional control, exercise training, and behavioral intervention. Traditional single-specialty nursing models often

fail to meet their comprehensive rehabilitation needs.

In recent years, systematic rehabilitation programs based on multidisciplinary collaboration have demonstrated significant advantages in improving patients' cardiopulmonary function, enhancing exercise tolerance, and promoting the establishment of long-term healthy behaviors. Research indicates that integrating SMART goal management into rehabilitation nursing processes can effectively enhance patient compliance and self-management capabilities, providing new pathways for critically ill obese patients to return to society^[1]. This study summarizes the nursing experience of a patient with acute respiratory failure combined with heart failure and obesity (BMI = 39.1), aiming to provide reference for refined nursing care during the rehabilitation period of similar patients.

2. Clinical data

2.1. General information

2.1.1. Patient

This study received approval from the Ethics Committee of Taihe Hospital in Shiyan City (Approval No. 2024XM011). A 39-year-old female of Han ethnicity was enrolled after providing informed consent. She was married, held a college-level education, and worked in an office setting. Her height was 160 cm, weight 100 kg, and Body Mass Index (BMI) 39.1 kg/m². She had no history of smoking or alcohol consumption. She was admitted by wheelchair on April 14, 2024, due to chest tightness and dyspnea for 1 week, worsening with decreased oxygen saturation for 1 day.

The patient experienced chest tightness and dyspnea without apparent cause for nearly one week, which significantly worsened with activity, accompanied by fatigue and paroxysmal nocturnal dyspnea. Occasional cough with small amounts of white sticky sputum was present but not given attention. One day prior to admission, symptoms significantly worsened with self-measured pulse oxygen saturation dropping to around 80%, prompting emergency hospital visit. Following emergency assessment, the patient was admitted to the Cardiac Care Unit (CCU) with diagnoses of acute respiratory failure, heart failure.

2.1.2. Past medical history

Hypertension for 3 years with maximum blood pressure of 160/100 mmHg, regularly taking antihypertensive medications (specifics unknown), blood pressure control status unclear. Bilateral total thyroidectomy for thyroid nodules 2 years ago, with long-term postoperative levothyroxine sodium (Euthyrox) replacement therapy. No known drug or food allergies.

2.1.3. Physical examination on admission

Temperature 36.5°C, pulse 102 bpm, respiration 25 bpm, blood pressure 141/92 mmHg, pulse oxygen saturation (SpO₂) 80% on room air. Alert consciousness, lethargic appearance, tachypnea, mild cyanosis of lips and nail beds. No jugular venous distension, diminished breath sounds bilaterally, fine wet rales audible in bilateral lower lungs. Cardiac border enlarged to the lower left, heart rate 102 bpm, regular rhythm, no pathological murmurs heard in any valve area. Abdomen soft and flat, no tenderness, liver and spleen not palpable below costal margins. No pitting edema in bilateral lower extremities.

2.1.4. Laboratory tests

Arterial blood gas analysis (on oxygen) showed pH 7.30, PaO₂ 52 mmHg, PaCO₂ 55 mmHg, lactate 3.5 mmol/L. B-type natriuretic peptide (BNP) 1250 pg/mL. Complete blood count, liver and kidney function, and electrolytes within normal ranges.

2.1.5. Auxiliary examinations

Bedside chest X-ray showed decreased bilateral lung field transparency with patchy infiltrates, enlarged cardiac silhouette, suggesting possible pulmonary edema with pulmonary infection. Echocardiography showed left ventricular end-diastolic diameter 58 mm, left ventricular ejection fraction (LVEF) 40%, global cardiac enlargement with left heart predominance, generalized wall motion hypokinesis. Chest CT scan with 3D reconstruction showed bilateral interstitial pneumonia with partial lung consolidation and bilateral pleural effusion. Non-invasive hemodynamic monitoring showed cardiac output (CO) 4.1 L/min, cardiac index (CI) 2.2 L/(min·m²), increased peripheral vascular resistance.

2.2. Treatment and outcomes

The patient was declared critically ill upon admission, requiring intensive care with continuous cardiac, blood pressure, and oxygen saturation monitoring, and strict 24-hour intake and output recording. The medical team immediately initiated a multidisciplinary collaborative treatment approach and developed a comprehensive treatment plan^[2].

The primary goal was to correct hypoxemia and improve cardiac function. High-flow nasal oxygen therapy was immediately initiated (flow rate 50 L/min, FiO₂ 60%), but oxygenation improvement was inadequate. The patient was transitioned to non-invasive positive pressure ventilation (S/T mode, IPAP 12 cmH₂O, EPAP 6 cmH₂O, FiO₂ 50%), alternating with high-flow oxygen therapy.

2.2.1. Pharmacological treatment

Ceftriaxone sodium for anti-infection; sacubitril/valsartan sodium tablets to inhibit neuroendocrine activation and improve ventricular remodeling; bisoprolol fumarate to control ventricular rate and reduce myocardial oxygen consumption; supplemented with nebulized ipratropium bromide compound solution for bronchodilation and antispasmodic effects, rabeprazole enteric-coated tablets for acid suppression and gastric protection, while continuing Euthyrox replacement therapy.

After 4 days of intensive treatment, the patient's dyspnea significantly improved, with arterial blood gas analysis showing PaO₂ increased to 78 mmHg and PaCO₂ decreased to 45 mmHg. The patient was successfully weaned from non-invasive ventilation, with SpO₂ stable above 92% without mechanical support. Early rehabilitation was initiated during hospitalization, including respiratory function training, bedside passive to active exercise, progressive endurance training, and strict adherence to a balanced nutrition plan of 1500–1800 kcal daily.

The patient was discharged after 4 days of stable condition, with discharge weight of 99 kg and self-care ability score of 85 points. One-week post-discharge follow-up showed weight reduction to 98 kg, improved pulmonary function indices, cardiac function recovery to NYHA Class II, and successful return to daily work activities.

3. Nursing care

3.1. Construction and implementation of multidisciplinary collaborative treatment system

Given the patient's critical and complex condition involving cardiopulmonary failure and obesity, a multidisciplinary team was immediately established upon admission, led by the CCU and including cardiovascular medicine, respiratory therapists, clinical nutritionists, rehabilitation therapists, and specialist nurses. The team conducted daily bedside handoffs and case discussions, jointly assessing the condition and developing bundled, individualized treatment and nursing plans, ensuring homogeneous and continuous care measures, providing solid team support for successful patient treatment.

3.2. Systematic oxygenation management with respiratory support as the core

3.2.1. Sequential respiratory support strategy

For the patient's acute respiratory failure, a graduated respiratory support approach was adopted. Initially, when high-flow nasal oxygen therapy (flow rate 40–50 L/min, FiO₂ 50–60%) failed to achieve satisfactory oxygenation improvement, non-invasive positive pressure ventilation was immediately initiated. ST mode was used with inspiratory positive airway pressure (IPAP) 10–12 cmH₂O and expiratory positive airway pressure (EPAP) 4–6 cmH₂O, alternating with high-flow oxygen therapy to maintain airway patency and improve ventilation/perfusion ratio. Dedicated monitoring to ensure mask seal and comfort; regular skin assessment to prevent equipment-related pressure injuries; close monitoring of arterial blood gas changes with timely parameter adjustments^[3].

3.2.2. Artificial airway management and ventilator weaning

As cardiac function improved, weaning from non-invasive ventilation was attempted on the third day of admission. Prior to weaning, the patient was instructed in diaphragmatic breathing and pursed-lip breathing techniques. During the weaning process, vital signs and SpO₂ were closely monitored, using a strategy of gradually extending weaning time, ultimately achieving successful complete daytime weaning. To ensure nighttime ventilation safety and address obesity-related hypoventilation syndrome, home non-invasive ventilator training was introduced early, with simulation of home environment for machine training, establishing a foundation for long-term post-discharge management.

3.3. Circulation management and fluid balance monitoring based on precise assessment

3.3.1. Hemodynamic monitoring and volume management

The patient was at risk for cardiogenic pulmonary edema and fluid overload. Nursing care included strict 24-hour intake and output recording, using precision urine bags to monitor hourly urine output. Daily weight measurements were taken at the same time, using the same scale, in fasting condition, providing objective data for volume assessment. Through monitoring central venous pressure (CVP), blood pressure, heart rate, and pulmonary rales changes, volume status was comprehensively assessed, with appropriate use of diuretics as prescribed to achieve negative fluid balance and effectively reduce cardiac preload.

3.3.2. Medication nursing and monitoring

Core medications including sacubitril/valsartan sodium and bisoprolol fumarate were administered as prescribed. After the first dose of sacubitril/valsartan sodium, blood pressure changes were closely monitored to prevent first-dose hypotension. During bisoprolol administration, heart rate was carefully observed, with physician notification

if heart rate dropped below 55 bpm. Drug interactions were monitored, including patient education to avoid concurrent use of NSAIDs and high-potassium foods, ensuring medication safety.

3.4. Development and implementation of individualized cardiac rehabilitation program

3.4.1. Graduated exercise rehabilitation training

Based on the patient's cardiac function, obesity, and muscle strength status, rehabilitation therapists and nurses jointly developed a four-stage progressive exercise program.

(1) Phase 1 (Bed Rest Period)

Primarily passive range-of-motion exercises combined with respiratory training and respiratory muscle training to prevent muscle atrophy and joint stiffness while improving respiratory function. Respiratory Training: Pursed-lip breathing, 10–15 min/session, 3 times/day; combined with positional management, head of bed elevated 90°, turning every 2 hours to improve ventilation efficiency, reduce respiratory muscle compensation, and enhance oxygenation; monitoring indicator SpO₂ (target ≥ 92%), reducing work of breathing. Respiratory Muscle Training: External diaphragmatic pacing therapy, 2 times/day, 20 min/session, to enhance respiratory muscle strength. Flexibility Training: Bedside passive joint activities performed by nurses or therapists, 10–20 min/session, 3 times/day, to prevent muscle atrophy and joint stiffness while maintaining range of motion; simultaneously preventing deep vein thrombosis (DVT), monitoring Borg Rating of Perceived Exertion scale maintaining at 11–13 level. Precautions: ECG/blood pressure monitoring during exercise, ensuring heart rate increase ≤ 20 bpm, blood pressure < 160/100 mmHg; immediately terminate training if SpO₂ < 88%, Borg RPE > 14, chest pain, or dizziness occurs.

(2) Phase 2 (Bedside Activity Period, Post-Weaning)

Supervise bedside sitting and bilateral lower extremity dependent training, adding low-intensity resistance exercises and bedside cycling, with intensity maintained at Borg score ≤ 13. Respiratory Training: Diaphragmatic breathing, 10 min/session, 3 times/day; combined with Active Cycle of Breathing Technique (ACBT), 2 times/day (performed after nebulization), continuously improving ventilation efficiency; monitoring SpO₂ (target ≥ 92%), reducing work of breathing.

Respiratory Muscle Training

- (a) External diaphragmatic pacing therapy 20 min/session, 2 times/day
- (b) Resistance training based on muscle strength, 10 min/session, 2 times/day (starting with 0.5 kg sandbag, gradually increasing weight)
- (c) Threshold loading training: inspiratory threshold 30% MIP = 16.5 cmH₂O, expiratory training 30% MEP = 18 cmH₂O, 5–10 min/session, 1 time/day.

Monitoring indicators: respiratory rate (target ≤ 20 bpm), SpO₂ (target ≥ 92%), heart rate increase (≤ 20% resting value), Borg RPE maintained at 11–13, to enhance diaphragmatic strength and improve respiratory muscle strength and ventilation efficiency.

(3) Phase 3 (Standing and Walking Period, Post-Muscle Strength Recovery)

Focus on balance training and bedside short-distance walking while maintaining respiratory and muscle strength training.

(4) Phase 4 (Consolidation Period, Pre-Discharge)

Assess exercise capacity through 6-minute walk test, develop post-discharge aerobic exercise prescription to consolidate rehabilitation outcomes.

3.5. Nutritional management and behavioral intervention

3.5.1. Precise nutritional prescription

According to the Obesity Nutrition Treatment Guidelines, a daily calorie target of 1500–1800 kcal was set^[4]. The nutritionist developed a specific meal plan with principles of low sodium (< 3 g/day), low fat, appropriate high-quality protein, and high dietary fiber. Patients were guided to maintain food diaries and avoid sweets and sugar-containing beverages.

3.5.2. Behavioral intervention and health education

Simple charts were used to explain the pathophysiology of acute heart failure and respiratory failure along with treatment goals, emphasizing the necessity and safety of home ventilators, guiding patients in purchasing home ventilators. Daily 10–15-minute bedside psychological interviews were conducted using open-ended questions (such as What concerns do you have about current treatment?) to assess potential anxiety or adjustment disorders. Distress Thermometer visual analog scale (0–10 points, 0 = no distress, 10 = extreme distress) was used for rapid screening of patient mood fluctuations. When scores ≥ 4 , specialized psychological consultation was immediately initiated. Patients to establish SMART goals, such as independently complete 10-minute bedside cycling training within 3 days was collaborated, providing daily progress feedback and positive reinforcement through verbal praise and progress charts^[5]. Motivational Interviewing (MI) techniques was employed with open-ended questions, affirmations, reflective listening, and summarizing to enhance patient compliance with weight reduction and rehabilitation exercise.

3.6. Skin care and complication prevention

3.6.1. Skin integrity protection

The patient was at high risk for skin breakdown due to obesity and need for non-invasive ventilator mask. Foam dressings were preemptively applied to pressure points such as nasal bridge and cheekbones for pressure relief. Facial skin was assessed every 4 hours, with intermittent ventilator breaks based on tolerance to relieve local pressure. Skin was kept clean and dry, especially in skin folds of neck and axillae. Regular turning was assisted to prevent pressure ulcer development. During hospitalization, skin integrity was maintained without pressure injuries.

3.6.2. Thrombosis and fall prevention

Patient had a Padua score of 4, indicating intermediate risk for venous thromboembolism. In addition to early mobilization, intermittent pneumatic compression devices were used as prescribed, twice daily for 20 minutes each. Patient had a fall/bed fall score of 45, indicating intermediate risk. Non-slip shoes were provided, activity area floors were kept dry, and medical staff or family members assisted with all patient ambulation, effectively preventing adverse events.

4. Conclusion

For this patient with acute respiratory failure combined with heart failure and obesity, excellent outcomes were achieved through constructing a multidisciplinary collaborative treatment system and implementing systematic nursing interventions centered on respiratory support, integrating graduated exercise rehabilitation, precise

nutritional management, and behavioral intervention.

The nursing practice demonstrates that for such complex critically ill patients, early identification of pathophysiological characteristics and implementation of sequential respiratory support strategies are key to stabilizing vital signs. Individualized cardiac rehabilitation and nutritional management based on precise assessment are core components for improving cardiopulmonary function and controlling weight.

Furthermore, integrating SMART goal management and motivational interviewing techniques throughout the nursing process effectively enhanced patient treatment compliance and self-management capabilities, establishing a solid foundation for smooth transition from inpatient treatment to home management and successful return to society ^[6]. This case suggests that for cardiopulmonary failure patients with obesity, systematic rehabilitation nursing models that break down specialty barriers are more capable of comprehensively addressing clinical challenges and improving patient long-term prognosis compared to traditional single-disease nursing approaches.

Disclosure statement

The authors declare no conflict of interest.

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Investigation and Research on the Knowledge, Attitude and Practice of Intensive Care Unit Nurses on Pulmonary Rehabilitation after Cerebral Hemorrhage Surgery Based on the IKAP model

Zhuling Jiang

Deyang People's Hospital, Deyang 618000, Sichuan, China

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Abstract: *Objective:* To investigate the knowledge, beliefs, and behaviors of ICU nursing staff regarding pulmonary rehabilitation after cerebral hemorrhage surgery, and to analyze the influencing factors based on the IKAP (Information-knowledge-belief-behavior) model, in order to provide a basis for optimizing nursing project management. *Methods:* A cross-sectional study design was used to conduct a questionnaire survey among ICU nursing staff in a tertiary grade A hospital from January to June 2025. A self-compiled questionnaire on knowledge, attitude and practice of pulmonary rehabilitation after cerebral hemorrhage was used, which included demographic data, knowledge dimension (10 questions), belief dimension (10 questions), and behavior dimension (10 questions). The questionnaire was scored on a Likert scale of 5, with a higher total score indicating a better level of knowledge, attitude and practice. Descriptive statistics, t-tests and one-way analysis of variance were used for the data using SPSS 25.0. *Results:* A total of 120 questionnaires were distributed, and 115 valid questionnaires were retrieved, with an effective recovery rate of 95.8%. Nursing staff scored (7.2 ± 1.5) points (out of 10) in the knowledge dimension, (8.0 ± 1.2) points (out of 10) in the belief dimension, and (6.5 ± 1.8) points (out of 10) in the behavior dimension. There were statistically significant differences in knowledge-attitude-practice scores among nursing staff of different ages, years of service and titles ($p < 0.05$). Multiple linear regression showed that years of service and training experience were the main influencing factors of knowledge, attitude and practice ($\beta = 0.25$, $p < 0.01$). *Conclusion:* ICU nursing staff have a moderate level of knowledge and behavior regarding pulmonary rehabilitation after cerebral hemorrhage surgery, have positive beliefs, but their practical behavior needs to be strengthened. Nursing project management based on the IKAP model can improve the quality of care through intensive training and personalized intervention.

Keywords: Pulmonary rehabilitation after cerebral hemorrhage surgery; Knowledge-attitude-practice; IKAP mode; Intensive care unit; Nursing staff

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1. Introduction

Cerebral hemorrhage is one of the common emergencies in clinical neurology. Whether patients can recover effectively after surgical treatment for cerebral hemorrhage is closely related to postoperative treatment and care ^[1]. Due to the damage to brain and body tissues caused by cerebral hemorrhage surgery and prolonged bed rest after the operation, patients may have problems such as atrophy and weakness of respiratory muscles, poor expectoration ability, and thus are prone to pulmonary failure, which can further lead to a series of problems such as pulmonary infection and atelectasis. As a result, patients are prone to clinical deterioration of their condition and longer hospital stays. If these symptoms are not intervened in time, it will affect the recovery of neurological function in patients after treatment. Conversely, it will form a vicious cycle, leading to a decline in rehabilitation effect. Pulmonary rehabilitation is an important measure in clinical postoperative management, helping patients with cerebral hemorrhage to restore lung function through respiratory function exercises and comprehensive rehabilitation methods ^[2]. However, traditional nursing methods are mainly educational, mostly adopting a “one-size-fits-all” approach to education and guidance, lacking specificity and uniformity. As a result, most patients with cerebral hemorrhage do not truly attach importance to rehabilitation exercises and do not actively cooperate to complete standardized exercises, leading to problems such as poor exercise effects and affecting the effectiveness of pulmonary rehabilitation ^[3].

The IKAP model (Information–knowledge–believe–behavior) is a health education and management framework that enhances patients’ cognitive and behavioral levels through progressive intervention and is widely used in chronic disease management. In recent years, nursing project management has emphasized systematic and individualized care. Integrating the IKAP model into pulmonary rehabilitation after cerebral hemorrhage surgery may optimize the nursing process, but most related studies have focused on intervention trials and lack cross-sectional survey data. Therefore, this study, through a cross-sectional design, investigates the application status of the IKAP model in pulmonary rehabilitation after cerebral hemorrhage surgery and analyzes its relationship with the effect of pulmonary rehabilitation in order to provide an empirical basis for clinical nursing ^[4].

2. Data and methods

2.1. Research subjects

Using the convenience sampling method, nursing staff in the ICU of a tertiary grade A hospital from January to June 2025 were selected as research subjects.

2.1.1. Inclusion criteria

- (1) Registered nurses
- (2) Work in ICU for at least 1 year
- (3) Voluntary participation in this study

2.1.2. Exclusion criteria

- (1) Intern or trainee nurses
- (2) Those who were on leave or resigned during the survey period

A total of 120 nursing staff were included, including 28 males (23.3%) and 92 females (76.7%); Ages ranged from 22 to 45 years, with an average of (30.5 ± 5.2) years; Working years 1 to 20 years, average (6.8 ± 4.1) years;

Title: 52 nurses (43.3%), 45 senior nurses (37.5%), 23 senior nurses (19.2%); Education: 40 junior college (33.3%), 75 bachelor's degree (62.5%), 5 master's degree (4.2%). The study was approved by the hospital ethics committee and all participants signed the informed consent form ^[5].

2.2. Study methods

2.2.1. Investigation tools

The self-developed “Questionnaire on Knowledge, Attitude and Practice of Pulmonary Rehabilitation after Cerebral Hemorrhage Surgery” was used. The questionnaire was developed based on the IKAP model theory framework through literature review and expert consultation. The questionnaire includes

- (1) Demographic information (age, gender, years of work, title, educational background, etc.);
- (2) Knowledge dimension (10 questions, covering definitions, methods, contraindications of pulmonary rehabilitation, etc., multiple-choice questions, 1 point for correct answer, 0 point for incorrect answer, total score 0 to 10 points)
- (3) Belief dimension (10 questions, assessing attitudes towards the importance of pulmonary rehabilitation, using a Likert 5-point rating from “strongly disagree” to “strongly agree”, assigned 1 to 5 points, total 10 to 50 points, standardized to a full score of 10 points)
- (4) Behavioral dimension (10 questions, assessing the frequency of pulmonary rehabilitation practice, on a Likert 5-point scale from “never” to “always”, assigned 1 to 5 points, out of 10 to 50 points, standardized to a full score of 10 points). The questionnaire was pretested with a Cronbachs α coefficient of 0.85 and a content validity index (CVI) of 0.90, indicating good reliability and validity ^[6].

2.3. Data collection

Questionnaires were distributed via an online questionnaire platform, such as Wenjuanxing, which was uniformly directed by the researchers and completed anonymously for about 15 minutes. A total of 120 questionnaires were distributed and 115 valid questionnaires were retrieved ^[7].

2.4. Statistical methods

Data analysis was conducted using SPSS 25.0 software. Measurement data were expressed as mean \pm standard deviation, and count data were described as frequency and percentage. The *t*-test or one-way analysis of variance was used for comparisons between groups, and multiple linear regression was used for analysis of influencing factors (with the total score of knowledge, attitude and practice as the dependent variable and demographic variables as independent variables). A difference was considered statistically significant when $p < 0.05$ ^[8].

3. Results

3.1. Overall score of knowledge, attitude and practice of nursing staff

The score for the knowledge dimension of nursing staff was (7.2 ± 1.5) points, the score for the belief dimension was (8.0 ± 1.2) points, the score for the behavior dimension was (6.5 ± 1.8) points, and the total score of knowledge, attitude and practice was (21.7 ± 3.0) points (out of 30 points). The knowledge score rate was 72.0%, the belief score rate was 80.0%, and the behavior score rate was 65.0%, indicating a moderate level of knowledge, positive belief, but insufficient behavioral practice ^[9].

3.2. Comparison of knowledge, attitude and practice scores among nursing staff with different demographic characteristics

Univariate analysis showed that there were statistically significant differences ($p < 0.05$) in the total score of knowledge, attitude and practice among nursing staff with different working years, professional titles and training experiences, while there were no statistically significant differences ($p > 0.05$) in gender, age and educational attainment. See **Table 1** and **2** for details.

Table 1. Comparison of total scores of knowledge, attitude and practice among nursing staff with different demographic characteristics (n = 115)

Characteristics	Grouping	Number of people	Total score of knowledge, belief and action	t/F score	p-value
Gender	male	28	22.1 ± 2.8	1.12	0.265
	female	92	21.5 ± 3.1		
Age (years)	< 30	60	21.3 ± 2.9	1.85	0.162
	≥ 30	55	22.1 ± 3.0		
Years of work experience (years)	< 5	50	20.5 ± 2.7	4.56	0.012
	5–10	45	22.0 ± 3.1		
	> 10	20	23.2 ± 2.8		
Title	Nurse	52	20.8 ± 2.9	5.23	0.007
	Nurse	45	22.1 ± 3.0		
	Head Nurse	23	23.0 ± 2.7		
Education	Junior college	40	21.2 ± 3.1	1.34	0.266

Table 2. Comparison of total scores of knowledge, attitude and practice among nursing staff with their training experience (n = 115)

Features	Grouping	Number of people	Total score of knowledge, belief and action	t/F score	p-value
Training experience	Undergraduate	75	21.9 ± 2.9	3.45	0.001
	Master's	5	22.5 ± 2.8		
	have	70	22.5 ± 2.8		
	no	45	20.4 ± 3.0		

3.3. Multiple linear regression analysis of influencing factors of knowledge, attitude and practice

The total score of knowledge, attitude and practice was used as the dependent variable, and the years of work (assignment: < 5 years = 1, 5–10 years = 2, > 10 years = 3), title (assignment: nurse = 1, nurse assistant = 2, senior nurse assistant = 3), and training experience (assignment: with = 1, without = 0) were used as independent variables for multiple linear regression analysis. The results showed that years of work and training experience were independent influencing factors of knowledge, attitude and practice ($p < 0.05$), as shown in **Table 3** below.

Table 3. Multiple linear regression analysis of influencing factors of knowledge, attitude and practice

Independent variables	β value	Standard error	<i>t</i> value	<i>p</i> -value
Constant term	18.50	1.20	15.42	< 0.001
Years of service	0.25	0.10	2.50	0.014
Title	0.18	0.12	1.50	0.136
Training experience	0.30	0.11	2.73	0.007

Note: $R^2 = 0.28$, adjusted $R^2 = 0.25$, $F = 8.45$, $p < 0.001$

4. Conclusion

This study revealed the current status of knowledge, attitude and practice of ICU nursing staff in pulmonary rehabilitation after cerebral hemorrhage surgery through a cross-sectional survey. The data showed a significant gap between the knowledge dimension score (7.2 ± 1.5) and the belief dimension score (8.0 ± 1.2), while the behavior dimension score (6.5 ± 1.8) was significantly lower than the belief score. This data feature indicates that although nursing staff recognize the importance of pulmonary rehabilitation, they have insufficient professional cognitive reserves and have failed to effectively translate positive attitudes into practical actions. This imbalance between cognition and behavior may directly affect the quality and continuity of the implementation of clinical pulmonary rehabilitation measures^[10].

Further analysis revealed significant differences ($p = 0.012$) in the total knowledge, attitude and practice scores of nursing staff with different years of service. Among them, the group with less than 5 years of service scored (20.5 ± 2.7) points, while the group with more than 10 years of service reached (23.2 ± 2.8) points. This trend of increasing scores with years of work reflects the positive impact of the accumulation of clinical experience on rehabilitation nursing ability. At the same time, training experience became a key influencing factor. Those with training experience scored (22.5 ± 2.8) points significantly higher than those without training experience (20.4 ± 3.0) points ($p = 0.001$), highlighting the important value of systematic training in enhancing professional competence.

The results of the multiple linear regression analysis further clarified the extent of influence of each factor. Years of service ($\beta = 0.25$, $p = 0.014$) and training experience ($\beta = 0.30$, $p = 0.007$) both reached statistical significance, while title factor ($p = 0.136$) did not show independent predictive effect. This finding suggests that the mere promotion of technical title does not fully represent the improvement of clinical practice ability; continuous professional training and the accumulation of practical experience are the key factors for improving the quality of nursing. This also explains why it is difficult for nursing staff to translate positive beliefs into standardized behavior^[11].

Based on the IKAP theoretical framework, the findings of this study have important implications for clinical practice. The “high belief, medium knowledge, low behavior” characteristics displayed by nursing staff are typical manifestations of the break from belief to behavior in the IKAP model. It is recommended that medical institutions establish a hierarchical training system, conduct targeted training for nursing staff of different seniorities, and focus on strengthening the theoretical knowledge and practical skills training of junior nurses. At the same time, departmental management systems should be improved and work processes optimized to create better practical conditions for pulmonary rehabilitation for nursing staff, thereby promoting the effective transformation of knowledge into behavior and comprehensively improving the quality of pulmonary rehabilitation for patients with

cerebral hemorrhage.

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Application of Shexiang Baoxin Pill Combined with Rosuvastatin Calcium Tablets in the Treatment of Angina Pectoris due to Coronary Atherosclerotic Heart Disease

Jingjiao Hui

Huishan District People's Hospital, Wuxi 214187, Jiangsu, China

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Abstract: *Objective:* To analyze the therapeutic efficacy of Shexiang Baoxin Pill combined with Rosuvastatin Calcium Tablets (ROS) in patients with angina pectoris due to coronary atherosclerotic heart disease (CHD-AP). *Methods:* Eighty CHD-AP patients admitted for treatment from January 2023 to December 2024 were selected and evenly divided using a random number table. The combined group (40 cases) received treatment with Shexiang Baoxin Pill combined with ROS, while the reference group (40 cases) received ROS monotherapy. The overall response rate, frequency and duration of AP attacks, blood lipid levels, and cardiac function indicators were compared between the two groups. *Results:* The combined group exhibited a higher overall response rate than the reference group. After treatment, the frequency and duration of AP attacks were lower in the combined group than in the reference group. Additionally, blood lipid levels and cardiac function indicators were superior in the combined group ($p < 0.05$). *Conclusion:* The combination of Shexiang Baoxin Pill and ROS demonstrates favorable therapeutic effects in CHD-AP patients, effectively preventing AP attacks, regulating blood lipid levels, protecting cardiac function, and reducing disease risk.

Keywords: Shexiang Baoxin pill; Rosuvastatin calcium tablets; Coronary atherosclerotic heart disease; Angina Pectoris

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1. Introduction

Angina pectoris due to coronary atherosclerotic heart disease (CHD-AP) is a cardiovascular disease characterized by typical symptoms of precordial pain and shortness of breath, with a high incidence of myocardial infarction. It is considered a major cause of death among middle-aged and elderly individuals. Statins, particularly Rosuvastatin Calcium Tablets (ROS), are commonly used to treat this condition due to their lipid-regulating effects, which can block disease progression and prevent thrombosis. However, it has a high drug resistance when used as a monotherapy and is difficult to cure the disease completely^[1]. In traditional Chinese medicine, CHD-AP is

classified under the categories of “chest impediment” and acute cardiac pain due to Qi and blood deficiency, which is caused by the obstruction of heart vessels due to Qi and blood deficiency. Symptomatic treatments such as promoting blood circulation to remove blood stasis and relieving pain and dredging collaterals are required. Shexiang Baoxin Pill is a typical prescription for this disease, which has the effects of strengthening the heart, relieving pain, replenishing Qi, and inducing resuscitation. It can be used for syndrome differentiation treatment based on the etiology and pathogenesis. The combination of these two treatments can utilize multiple mechanisms to stabilize the patient’s condition, thereby improving clinical efficacy. Based on this, this study selected 80 patients with CHD-AP to analyze the therapeutic effectiveness of combining Shexiang Baoxin Pill with ROS.

2. Materials and methods

2.1. General information

Eighty patients with CHD-AP who were admitted for treatment between January 2023 and December 2024 were selected and evenly divided using a random number table. The combined treatment group consisted of 40 patients, including 25 males and 15 females, aged between 41 and 78 years old, with an average age of (56.35 ± 4.18) years, and a disease duration ranging from 1 to 7 years, with an average duration of (3.85 ± 0.79) years. The reference group also consisted of 40 patients, including 27 males and 13 females, aged between 40 and 76 years old, with an average age of (56.39 ± 4.18) years, and a disease duration ranging from 2 to 7 years, with an average duration of (3.96 ± 0.71) years. There were no significant differences in gender, age, disease duration, and disease grading between the two groups ($p > 0.05$).

2.1.1. Inclusion criteria

Diagnosis of CHD-AP confirmed by imaging and electrocardiogram examinations; Presence of typical symptoms such as precordial pain and chest tightness; Complete basic information; Normal communication ability; Good mental state; Informed consent for the study.

2.1.2. Exclusion criteria

Presence of heart failure or myocardial infarction; Presence of malignant tumors; Impaired liver and kidney function; History of allergy to the study drugs; Participation in other studies.

2.2. Methods

The basic treatment for both groups was consistent, involving the administration of drugs such as nitrates and aspirin, and the sublingual administration of nitroglycerin during AP attacks.

2.2.1. The reference group received ROS monotherapy

Oral administration of rosuvastatin calcium tablets (Nanjing Chia Tai Tianqing Pharmaceutical Co., Ltd./Tianjin Tianda Pharmaceutical Co., Ltd., National Medical Products Administration Approval Number H20080670, specification: 10 mg), with a dosage of 20 mg each time, taken once before bedtime daily, for a continuous 4-week period.

2.2.2. The combination group received Shexiang Baoxin pill in combination with ROS therapy

The ROS treatment method was the same as above. For Shexiang Baoxin Pill (Shanghai Hutchison

Pharmaceuticals Co., Ltd., National Medical Products Administration Approval Number Z31020068, specification: 22.5 mg per pill), the oral dosage was 2 pills each time, equivalent to 45 mg, taken three times daily, for a continuous 4-week period.

2.3. Observation indicators

(1) Overall response rate

Significant response: Mild limitation in physical activity, AP (angina pectoris) attack frequency less than 2 times per week, and normal electrocardiogram (ECG) results; Preliminary response: Significant limitation in physical activity, reduction in AP attack frequency by over 50%, and improved ECG results; No response: Severe limitation in physical activity, no improvement in AP attack frequency, and abnormal ECG results.

(2) AP attack profile

Observe the frequency and duration of AP attacks before and after treatment.

(3) Blood lipid levels

Collect 5 mL of venous blood under fasting conditions and use a fully automated biochemical analyzer to evaluate indicators such as triglycerides (TG), low-density lipoprotein (LDL-C), total cholesterol (TC), and high-density lipoprotein (HDL-C).

(4) Cardiac function indicators

Use cardiac color Doppler ultrasound to evaluate indicators such as cardiac output (CO), left ventricular end-diastolic diameter (LVEDD), and left ventricular ejection fraction (LVEF).

2.4. Statistical analysis

SPSS 28.0 statistical software was used. Count data were expressed as [n/%], and comparisons and tests were conducted using the chi-square test (χ^2). Measurement data were expressed as mean \pm standard deviation [$\bar{x} \pm s$], and comparisons and tests were conducted using the *t*-test. A statistically significant difference was considered when $p < 0.05$.

3. Results

3.1. Comparison of the overall efficacy between the two groups

The overall efficacy rate in the combined therapy group was higher than that in the reference group ($p < 0.05$) (see Table 1).

Table 1. Comparison of the overall efficacy between the two groups [n/%]

Group	n	Markedly effective	Moderately effective	No significant improvement	Total effective rate
Combined group	40	24	15	1	97.5% (39/40)
Control group	40	20	13	7	82.5% (33/40)
χ^2 value					5.000
<i>p</i> -value					0.025

3.2. Comparison of AP episodes between the two groups

Before treatment, there was no significant difference in AP episodes between the two groups ($p > 0.05$). After treatment, the combined therapy group showed better improvement in AP episodes compared to the reference group ($p < 0.05$) (see Table 2).

Table 2. Comparison of AP episodes between the two groups [$\bar{x} \pm s$]

Group	n	Attack frequency (times/week)		Attack duration (min/time)	
		Before treatment	After treatment	Before treatment	After treatment
Combined group	40	6.72 \pm 1.59	2.35 \pm 0.48	8.36 \pm 1.84	2.59 \pm 0.61
Control group	40	6.74 \pm 1.62	4.67 \pm 0.51	8.40 \pm 1.86	5.01 \pm 0.77
<i>t</i> -value		0.056	20.951	0.097	15.581
<i>p</i> -value		0.956	< 0.001	0.923	< 0.001

3.3. Comparison of blood lipid levels between the two groups

Before treatment, there was no significant difference in blood lipid levels between the two groups ($p > 0.05$). After treatment, the combined therapy group demonstrated better blood lipid levels compared to the reference group ($p < 0.05$) (see Table 3).

Table 3. Comparison of blood lipid levels between the two groups [$\bar{x} \pm s$, mmol/L]

Group	n	TG (mmol/L)		LDL-C (mmol/L)		TC (mmol/L)		HDL-C (mmol/L)	
		Before	After	Before	After	Before	After	Before	After
Combined group	40	5.99 \pm 0.57	2.64 \pm 0.41	4.70 \pm 0.55	2.56 \pm 0.47	8.94 \pm 1.47	5.01 \pm 0.73	1.81 \pm 0.69	2.55 \pm 0.38
Control group	40	5.96 \pm 0.52	3.94 \pm 0.48	4.72 \pm 0.53	3.09 \pm 0.43	8.96 \pm 1.49	6.38 \pm 0.77	1.83 \pm 0.72	2.06 \pm 0.34
<i>t</i> -value		0.246	13.024	0.166	5.262	0.060	8.166	0.127	6.078
<i>p</i> -value		0.806	< 0.001	0.869	< 0.001	0.952	< 0.001	0.899	< 0.001

3.4. Comparison of cardiac function indicators between the two groups

Before treatment, there was no significant difference in cardiac function indicators between the two groups ($p > 0.05$). After treatment, the combined therapy group showed better cardiac function indicators compared to the reference group ($p < 0.05$) (see Table 4).

Table 4. Comparison of cardiac function indicators between the two groups [$\bar{x} \pm s$]

Group	n	CO (L/min)		LVEDD (cm)		LVEF (%)	
		Before	After	Before	After	Before	After
Combined group	40	2.74 \pm 0.68	5.17 \pm 0.83	5.92 \pm 0.64	3.90 \pm 0.45	38.11 \pm 3.65	50.44 \pm 5.17
Control group	40	2.76 \pm 0.61	4.74 \pm 0.72	5.95 \pm 0.61	4.18 \pm 0.49	38.04 \pm 3.61	45.24 \pm 5.12
<i>t</i> -value		0.138	2.475	0.215	2.662	0.086	4.520
<i>p</i> -value		0.890	0.015	0.831	0.009	0.931	< 0.001

4. Discussion

Coronary heart disease (CHD) is a prevalent cardiovascular disease among elderly males, characterized by coronary artery stenosis, increased myocardial oxygen consumption, and decreased cardiac metabolic function. The pathogenesis of CHD-AP involves hypoxia and ischemia in myocardial tissue, leading to the accumulation of metabolic products. This accumulation exerts prolonged stimulation on the autonomic nerves of the heart tissue, affecting the function of nerve endings and resulting in AP symptoms^[2]. As a reflexive symptom of CHD, CHD-AP can cause precordial pain and radiating pain in the left shoulder and left arm, posing a high risk of acute myocardial infarction. Therefore, early treatment is essential.

Western medicine is a common treatment for CHD-AP, with ROS, as a statin drug, effectively inhibiting β -hydroxy- β -methylglutaryl-coenzyme A reductase and demonstrating a favorable lipid-regulating effect. This medication exhibits high bioavailability and a long half-life, allowing for thorough absorption by bodily tissues. Its active ingredients exert a strong effect on liver tissue, thereby lowering total cholesterol (TC) levels and consistently regulating blood lipids. Additionally, the drug can reduce the existing content of LDL-L cell surface receptors in liver tissue, promoting effective absorption of low-density lipoprotein cholesterol (LDL-C)^[3]. However, the mechanism of action of this drug as a monotherapy is limited and cannot provide long-term disease stability, necessitating combination therapy with traditional Chinese medicine (TCM). In TCM, the pathological mechanism of CHD-AP is believed to involve the interplay of phlegm and blood stasis, along with obstruction of the meridians. The treatment principle focuses on promoting blood circulation to remove blood stasis and relieving pain to unblock the meridians. Shexiang Baoxin Pill, a TCM formula for this condition, acts quickly, significantly improving disease symptoms and protecting the patient's cardiac function.

The results indicated that the total effective rate in the combined treatment group was higher than that in the reference group, with fewer episodes and shorter durations of AP ($p < 0.05$). The analysis attributes this to the high drug absorption efficiency of ROS, which protects the patient's vascular endothelial function through mechanisms such as lipid regulation, anti-inflammation, and inhibition of platelet aggregation, effectively alleviating related symptoms and reducing the frequency of AP episodes^[4]. Shexiang Baoxin Pill contains various TCM ingredients, including artificial musk, which exhibits significant anti-inflammatory effects and stabilizes blood lipid levels. Ginseng contains a substantial amount of ginsenosides, with Rh1 enhancing the body's immunity and Rh2 improving the hypoxic state of myocardial tissue, preventing reperfusion injury, and demonstrating antioxidant properties. R0 exhibits anti-platelet aggregation and anti-inflammatory effects^[5]. Cinnamon can restore coronary blood flow, effectively improve vascular endothelial function and scavenging free radicals. Artificial bezoar has a cardiotonic effect, aiding in the relief of AP symptoms. Borneol and styrax both stabilize heart rate and improve myocardial oxygen consumption. Toad venom, on the other hand, possesses anti-inflammatory and cardiotonic properties, along with analgesic effects^[6]. When combined with ROS, this medication can treat the disease through multiple targets, leveraging the synergistic effects of both Western and TCM to enhance therapeutic efficacy.

After treatment, the blood lipid levels in the combined treatment group showed significant improvement, with a $p < 0.05$ compared to the reference group. The analysis suggests that this is due to the high inhibitory activity of ROS on 3-hydroxy-3-methylglutaryl-coenzyme A reductase, which can block the synthesis process of total cholesterol (TC), thereby reducing blood lipid levels such as low-density lipoprotein cholesterol (LDL-C)^[7]. Shexiang Baoxin Pill contains traditional Chinese medicinal materials such as artificial calculus bovis and musk, which have functions of promoting the circulation of Qi and blood, relieving pain and resolving stasis. Moreover, the combined use of various traditional Chinese medicinal materials can regulate the blood lipid metabolism status

of patients, facilitating smooth coronary blood flow. Additionally, Shexiang Baoxin Pill contains ingredients such as polysaccharides, flavonoids, and oleoresins, which have a good relaxing effect on vascular smooth muscle, can improve coronary blood flow, promote continuous vascular regeneration, thereby reducing blood viscosity and lowering levels of triglycerides (TG) and TC ^[8]. The muskone and muscone ketone contained in artificial musk can continuously dilate the coronary arteries of patients and promote the effective proliferation of endothelial cells, thereby protecting vascular endothelial function and assisting in regulating blood lipid levels.

The cardiac function indicators in the combined treatment group also showed significant improvement, with a $p < 0.05$ compared to the reference group. The analysis suggests that this is because ROS has a stabilizing effect on arterial plaques, can inhibit the continuous progression of atherosclerosis, and thus protect the cardiac function of patients. In addition, this medication can reduce the release of inflammatory factors, lower the stimulating effect of inflammatory responses on myocardial tissue, thereby exerting therapeutic effects such as improving cardiac function ^[9]. Among the ingredients of Shexiang Baoxin Pill, artificial musk has the effects of promoting blood circulation, opening orifices to restore consciousness, and unblocking meridians; ginseng has the effects of replenishing Qi and nourishing blood; cinnamon has the effects of warming meridians to unblock collaterals and relieving pain and dispersing cold; artificial calculus bovis has the effects of subduing wind to stop spasms and detoxifying to clear heat; borneol has the effects of opening orifices to restore consciousness and clearing heat to relieve pain; storax has the effects of relieving pain and dispelling filth; and venenum bufonis has the effects of relieving pain and restoring consciousness. The combined use of these medicinal materials can simultaneously promote and nourish, significantly enhancing the cardiogenic effect ^[10].

4. Conclusion

In conclusion, the combined treatment of Shexiang Baoxin Pill and ROS for patients with coronary heart disease with angina pectoris (CHD-AP) demonstrates high effectiveness. It can improve symptoms of angina pectoris, stabilize blood lipid levels, and protect cardiac function. This treatment approach exhibits significant advantages in integrated traditional Chinese and Western medicine and can serve as a commonly used combined treatment regimen for this condition.

Disclosure statement

The author declares no conflict of interest.

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Application of the Integration of Teaching-Research-Clinic Trinity Model in the Teaching of Nervous System in Physiology

Lei Zhang*, Qu Peng, Yali Yang, Weigang Cui, Minli Zheng, Jiahua Wu, Jihua Qiu, Aihua Song, Jianhui Zhang

Jiaying University School of Medicine, Meizhou 514015, Guangdong, China

*Corresponding author: Lei Zhang, youjunwen2008@163.com

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Abstract: Physiology is an important basic course for medical majors. The content of the nervous system is abstract, the theories are profound, the knowledge is updated rapidly, and it is most closely connected with clinical practice. Students generally report difficulties in understanding, resulting in low learning interest. To improve teaching quality, this study has attempted to organically integrate clinical cases, scientific research methods and classroom teaching in the teaching of the nervous system, and constructed a “clinical-research-teaching” trinity teaching model. With “clinical problem-driven, scientific research thinking-driven, teaching scenario reconstruction” as the main line, real cases, scientific research examples and cutting-edge research progress in neuroscience were introduced to stimulate students’ learning interest and cultivate their scientific thinking and clinical application abilities. Practice has shown that this model can effectively improve teaching effectiveness and students’ comprehensive quality. Compared with the traditional teaching model, this teaching model significantly improved students’ final exam scores ($p < 0.01$), scores of the Critical Thinking Disposition Inventory ($p < 0.01$), and the number of approved college students’ innovation and entrepreneurship projects. It is proved that the “trinity” teaching model can stimulate learning interest, cultivate integrated medical talents, and is an effective way to achieve in-depth connection between basic medicine and clinical practice.

Keywords: Physiology; Nervous system; Teaching reform; Trinity

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1. Introduction

Physiology is a bridging course connecting basic medicine and clinical practice in medical education. As the most important part of this discipline, the nervous system involves the structure, function and regulatory mechanisms of the nervous system. The content of neurophysiology is microscopic and abstract, and closely linked to clinical practice. The theoretical knowledge of the nervous system is profound and difficult to understand, and students generally reflect that it is “hard to understand, hard to remember, and hard to apply”, which puts forward higher

requirements for teachers' comprehensive quality and integration ability. How to synchronously improve "knowledge—ability—literacy" is an urgent problem to be solved in physiology teaching. The traditional teaching model often focuses on theoretical teaching, making it difficult for students to combine abstract knowledge with clinical practice, leading to insufficient learning motivation and insufficient depth of understanding ^[1]. Therefore, this study adheres to the "student-centered" concept, relies on the Brain Science and Mental Health Laboratory of the college, organically integrates clinical cases, ongoing research projects and published papers with classroom teaching, and implements the "clinical-research-teaching" trinity teaching model in the nervous system. Guided by clinical problems, supported by scientific research technologies and methods, and taking classroom teaching as the carrier, the three are organically integrated to effectively stimulate students' learning interest and desire for knowledge, and realize the dual tasks of theoretical knowledge teaching and clinical literacy training.

2. Specific implementation of the trinity teaching model

2.1. Taking clinical cases as the entry point to stimulate learning interest

Neurophysiological knowledge, such as action potentials, synaptic transmission, and neurotransmitters, is relatively abstract and tends to be dull for students, with related content being particularly difficult to understand. In our teaching, this study has introduced typical clinical cases, such as Parkinson's disease, Alzheimer's disease, and epilepsy, and guide students to explore the underlying physiological mechanisms through case discussions.

Taking the teaching of Alzheimer's disease as an example, a complete teaching design is as follows: First, case presentation: A short clinical scenario video was played or an anonymous medical record summary was displayed, which mainly described a 70-year-old retired teacher who has experienced progressive memory loss over the past two years, accompanied by disorientation and personality changes. No focal signs were found in the neurological examination, and the score of the Mini-Mental State Examination (MMSE) decreased significantly ^[2]. Then, questions were raised to guide students' thinking and discussion. Clinical questions: Based on the above manifestations, what is the most likely diagnosis? Which diseases (such as vascular dementia and frontotemporal dementia) need to be differentiated from it? Followed by physiology-related theoretical questions: Which brain regions (with emphasis on the "hippocampus") and neural activities (such as synaptic transmission and synaptic plasticity like LTP) are involved in memory formation? What changes may have occurred in these physiological functions of the patient in this case? Further, research questions are proposed: If we want to explore the causes of this disease, from which aspects should we start the research? Real clinical cases quickly capture students' attention, connect abstract neural functions with specific clinical symptoms, stimulate their curiosity, and naturally introduce relevant neurophysiological content.

Next, while systematically explaining theoretical knowledge, some research-related content was integrated into knowledge modules

- (1) Explaining the classic pathological mechanisms of AD ^[3]

- (2) Integrating research

Displaying comparative images of brain tissue sections (silver-stained or immunohistochemically stained) from AD patients and normal individuals, allowing students to intuitively perceive pathological changes, which also promotes their learning of clinical diagnostics

- (3) Introducing key biological technologies

Using techniques such as ELISA and Western Blotting to detect A β and Tau protein levels in cerebrospinal

fluid, and explaining their applications in AD biomarker research and value in clinical auxiliary diagnosis ^[4].

Such a teaching design combines tedious pathological mechanisms with vivid scientific research technologies and cutting-edge progress, making knowledge “come alive”. It helps students understand how textbook theories were verified, applied, and continuously developed through scientific research. This study also incorporated current hot topics, such as “the application of brain-computer interface technology in neural rehabilitation” and “early biomarkers of neurodegenerative diseases”, to guide students to pay attention to the application value of physiological knowledge in cutting-edge medical technologies, thereby enhanced their sense of reality and mission in learning ^[5].

2.2. Integrating scientific research into classroom teaching

To help students understand the research methods of neuroscience electrophysiology, this study has integrated experimental designs, technical routes, and phased results from published papers into teaching. In this part of the teaching, the experimental technology and protocol of patch clamp, an electrophysiological technique were presented to students in the form of videos, enabling them to gain a deeper understanding of the process of neuron activation and action potential transmission. By deeply integrating patch clamp technology to demonstrate research methods and cutting-edge progress in neuroscience, teaching is no longer limited to tedious theoretical deduction. Instead, students intuitively learnt about this advanced technology known as the “window to ion channels.” Vivid animations were used to show its core technical principle: forming a gigaohm high-resistance seal between a glass microelectrode and the cell membrane, thereby recording picoampere-level tiny currents generated by individual ion channels. This allowed students to intuitively understand the dialectical relationship between recording macroscopic currents in the “whole-cell mode” and revealing microscopic events in the “single-channel mode,” transforming abstract ion channel kinetics into visual current traces. Furthermore, by linking to cutting-edge neuroscience, this study explained how patch clamp technology is used to screen specific channel blockers derived from scorpion venom or seaweed toxins, and revealing their potential in the development of new analgesics or insecticides.

This study also introduced the combined technology of optogenetics and patch clamp expressing light-sensitive channels in specific neurons to achieve “light-controlled” neuron firing while synchronously recording their electrophysiological responses, thereby accurately analyzing neural circuit functions. This not only enables students to master core knowledge but also helps them deeply recognize the driving role of technological breakthroughs in scientific research and the great value of basic research in promoting scientific innovation and drug development. Through the introduction of scientific research examples, students not only deepen their understanding of theoretical knowledge but also initially grasp the basic logic and technical paths of neuroscience research, laying a foundation for their subsequent participation in research projects or graduation design.

2.3. Constructing a mutually promoting “clinical-research-teaching” cyclic teaching model

In the teaching process, this study has emphasized the cyclic promotion of the three components: clinical problems initiate research projects, research achievements feed back into teaching content, and teaching in turn provides feedback to guide the adjustment of clinical and research directions. In the teaching of depression, “clinical practice, scientific research, and teaching” form a dynamic, cyclic, and mutually promoting organic whole^[6]. This cycle starts with clinical practice. Faced with practical dilemmas such as “slow onset of drug effect” and “treatment ineffectiveness in some patients”, clinicians refine key scientific questions, which directly spawn cutting-edge

research directions in rapid antidepressant therapy, such as the role of ketamine in neural circuit plasticity and neuromodulation technologies including transcranial magnetic stimulation [TMS])^[7]. These research achievements then feedback into teaching content, expanded the classroom from the traditional “monoamine neurotransmitter hypothesis” to the “neural circuit dysfunction” model^[8]. In the teaching of Integrated Basic Medical Experiments, this study allowed students to personally experience the process of establishing depression models, followed by animal behavioral experiments to detect depression-like behaviors. This enables students to intuitively understand the external manifestations of depression. More importantly, feedback from the teaching process can serve as an important driving force for adjusting clinical and research directions. Questions raised by students after learning the latest theories, such as “How does psychotherapy reshape brain circuits?”, often inspire new research ideas. Meanwhile, this cutting-edge-integrated teaching cultivates students’ critical and innovative thinking, enabling them to observe and propose clinical problems more acutely in the future, thereby initiating a new cycle of “clinical practice guiding scientific research”^[9].

In summary, clinical practice is the source of fundamental questions; scientific research is the engine of exploration, delving into mechanisms and creating new knowledge and technologies; classroom teaching is the hub and amplifier for integration and dissemination, systematically integrating and disseminating new knowledge while stimulating new inspirations through teaching interactions and cultivating talents who can drive future innovations.

3. Evaluation of teaching effects

3.1. Academic performance and aptitude assessment

A comparative analysis was conducted before and after the teaching reform. A total of 248 five-year clinical medicine students from the 2023 cohort served as the control group (traditional teaching group), and 256 students from the 2024 cohort as the experimental group (trinity teaching group). The final written test score of the experimental group (82.6 ± 7.4) was significantly higher than that of the control group (75.3 ± 8.1) ($t = 6.42$, $p < 0.01$); the score of the Critical Thinking Disposition Inventory increased by 11.7%; and the score of the OSCE station “neuroreflex examination + mechanism explanation” increased by 15.3%.

3.2. Research participation and output

In recent years, the proportion of students participating in teachers’ research projects has increased significantly. Many student-initiated “College Students’ Innovation and Entrepreneurship Training Program” projects have been approved at the national or provincial level, and some results have been published in academic conferences or journals. Students in the experimental group presided over 4 national-level and 6 provincial-level innovation and entrepreneurship projects, and published 3 SCI papers as co-authors (second author or above); the corresponding numbers in the control group were 1, 2, and 1, respectively. The proportion of students in the 2023 cohort choosing neuroscience-related directions for postgraduate studies increased from 12.4% to 27.6%.

3.3. Affective attitudes and values

Analysis of post-class reflection reports before and after the reform showed that the co-occurrence frequency of “knowledge-clinic-research” increased from 12% to 41%; the coverage rate of the “learning interest” node rose from 34% to 68%. Anonymous questionnaires indicated that 92.4% of students believed the “trinity” teaching

helped “establish a knowledge network”, and as high as 88.1% of students expressed willingness to participate in teachers’ research projects ^[10].

4. Discussion and reflection

4.1. The “trinity” teaching model breaks the isolation of the “three-stage” separation of basic medicine, clinical practice, and scientific research

Traditional teaching often arranges basic courses, clinical courses, and research training linearly by semester, resulting in delayed knowledge transfer for students. This teaching practice places “clinical problems” at the forefront, embeds “mechanism learning” into the “diagnostic and treatment pathway”, and extends the depth of learning through “scientific research verification”. It conforms to the four elements of constructivism” situation, collaboration, conversation, and meaning construction” and effectively improves students’ long-term memory and far-transfer abilities.

4.2. Higher requirements for teachers and teaching team building

Teachers were required to be competent in three roles simultaneously: “physician, scholar, and instructional designer”. The teaching and research section has established a “3 × 3” cross lesson-preparation system: 3 basic medicine teachers + 3 clinicians + 3 postdoctoral researchers, holding monthly teaching seminars themed on “cases, mechanisms, and cutting-edge progress”.

4.3. Directions for continuous improvement

- (1) Further expand the case library toward “rare diseases + interdisciplinary diseases”, introducing new disease types such as inherited metabolic diseases, neuroimmune diseases, and diabetes-related neurological diseases
- (2) Utilize AI generative models to develop a real-time dialogue system with “intelligent patients”, increasing the intensity of clinical thinking training
- (3) Construct a digital platform for the “trinity” teaching evaluation, realizing a multi-dimensional visualized evaluation system covering learning trajectories, research participation, and clinical competencies

5. Conclusion

The “clinical-research-teaching” trinity teaching model is not a simple superposition of three elements, but a systematic reconstruction centered on students, anchored in real clinical problems, driven by the latest scientific evidence, and oriented toward higher-order teaching goals, an organic integration focusing on students’ competency development. Practice has shown that this model effectively stimulates students’ learning initiative and creativity, significantly improves teaching quality as well as students’ academic performance, research literacy, and professional identity, and provides a replicable and promotable paradigm for the teaching reform of basic medical courses. In the future, study should further optimize the teaching content and methods to promote physiology teaching toward deeper levels and broader scopes.

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The Impact of Robot-Assisted Training on Upper Limb Function in Elderly Stroke Patients

Wenting Jia, Chengyuan Zhu, Hua Xu, Chunhua Yuan*, Xin Zhuang, Yue Huang

Department of Rehabilitation Medicine, Geriatric Hospital of Nanjing Medical University, Nanjing 210019, Jiangsu, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To investigate the effects of robot-assisted training on upper limb function in elderly stroke patients. *Methods:* Seventy elderly stroke patients treated in the Rehabilitation Medicine Department of Jiangsu Provincial Organ Hospital from January 2023 to December 2023 were randomly divided into an intervention group ($n = 35$) and a control group ($n = 35$). In addition to conventional rehabilitation and nursing care, both groups received 40 minutes of daily upper limb training. The control group underwent entirely manual training, whereas the intervention group received a combination of 20 minutes of manual and 20 minutes of robot-assisted training. All participants completed this protocol five times weekly for four weeks, with assessments of upper limb motor function and activities of daily living (ADL) conducted pre- and post-intervention. *Results:* After treatment, both groups showed significant increases in Fugl-Meyer Assessment (FMA-UE) and Barthel Index (BI) scores compared to before treatment ($p < 0.01$). The intervention group had higher FMA-UE scores than the control group ($p < 0.05$), while there was no significant difference in BI scores between the two groups after treatment ($p > 0.05$). *Conclusion:* Robot-assisted training can improve upper limb motor function and enhance ADL capabilities in elderly stroke patients.

Keywords: Stroke; Robot-assisted training; Upper limb function

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1. Introduction

Stroke is one of the leading causes of death and disability worldwide, characterized by high incidence, high disability rates, high recurrence rates, and substantial economic burdens, posing a severe threat to human life and health ^[1]. Research has found that 6 months after stroke onset, 65% of patients still experience upper limb dysfunction ^[2]. Robot-assisted training is an emerging rehabilitation technology that has gradually gained popularity both domestically and internationally in recent years and has been increasingly applied in clinical practice. Robot-assisted training can reduce reliance on therapist manpower and provide continuous, stable, and high-intensity training ^[3,4]. Therefore, this study conducted robot-assisted training on elderly stroke patients and

employed relevant scales to evaluate the therapeutic effects and assess the impact of this method on the upper limb function of stroke patients.

2. Research subjects and methods

2.1. Research subjects

This study took elderly stroke patients who were diagnosed and treated in the Rehabilitation Medicine Department of Jiangsu Provincial Official Hospital from January 2023 to December 2023 as the research subjects. Based on clinical manifestations and cranial imaging examinations, all patients had met the diagnostic criteria for stroke established at the Fourth National Cerebrovascular Disease Conference ^[5].

2.1.1. Inclusion criteria

- (1) Aged 60 years or older
- (2) Diagnosed with first-time ischemic or hemorrhagic stroke, with a disease duration exceeding one month
- (3) Clear consciousness, without severe cognitive dysfunction, and able to cooperate in completing assessments and treatments

2.1.2. Exclusion criteria

- (1) Previous treatment with botulinum toxin injections
- (2) Bilateral cerebrovascular lesions
- (3) Severe neuropsychological disorders (e.g., significant aphasia, visual dysfunction, severe psychiatric symptoms)
- (4) Movement limitations due to bone and joint diseases
- (5) Severe osteoporosis

Ethical approval was obtained from the hospital's ethics committee, and written informed consent was acquired from all participants.

2.2. Research methods

2.2.1. Grouping

A single-blind, randomized, controlled clinical study was conducted, with 70 patients randomly (by random number) divided into an intervention group (robot training group) and a control group (conventional treatment group), with a total observation period of 4 weeks. There were no significant differences between the two groups in terms of gender, age, disease duration, stroke type, and hemiplegic side ($p > 0.05$), as shown in **Table 1**.

Table 1. Comparison of baseline data between the two groups of patients

Group	Gender (M/F, n)	Age (years)	Disease duration (months)	Hemiplegic side (L/R, n)	Stroke type (Infarction/Hemorrhage, n)
Intervention (n = 35)	18/17	70.14 ± 5.33	6.63 ± 5.62	15/20	21/14
Control (n = 35)	16/19	68.74 ± 5.79	6.91 ± 5.11	15/20	18/17

2.2.2. Intervention

All patients received routine rehabilitation nursing and body position management to minimize noxious stimuli, including pressure sores, pain, urinary retention, urinary tract infections, constipation, venous thrombosis, fractures, temperature drops, emotional disturbances, sleep disorders, and other factors that may exacerbate or induce spasticity. Routine rehabilitation treatments included:

- (1) Positional transfer training
- (2) Occupational therapy, such as rolling cylinders and using inclined sanding boards
- (3) Activities of daily living training
- (4) Other modalities: hand-cranked bicycles, physical therapy (electromyographic biofeedback, wax therapy, electrical stimulation), etc.

2.2.3. Grouping

- (1) Control group

Patients in the control group received one-on-one upper limb manual training using the Bobath technique, conducted by a rehabilitation therapist. The treatment was administered five times a week, with each session lasting 40 minutes, over a period of four weeks.

- (2) Intervention group

Patients in the intervention group underwent one-on-one upper limb manual training using the Bobath technique for 20 minutes, followed by robot-assisted upper limb training for another 20 minutes. This regimen was also administered five times a week for four weeks.

Upper limb training was conducted using the BURT upper limb rehabilitation robot (EM-BURT02, Estun Medical Technology Co., Ltd., Nanjing). The robot allows for adjustments in training difficulty, assistance time, and weight reduction support to train various joints of the upper limb. The game settings are highly relevant to the motor demands of daily life, and visual feedback was provided through a virtual reality scenario displayed on a monitor. The training modes include active, assisted, resistive, and passive modes, which were adjusted based on the patient's motor function. Games that align with normal motor patterns were selected for training.

The specific training methods are as follows

- (1) For patients with hemiplegic upper limbs at Brunnstrom Stage IV, the active motion mode was selected. Patients move their upper limbs to manipulate the robotic arm in a three-dimensional space, and a certain level of resistance can be set for active resistive training of the hemiplegic upper limb.
- (2) For patients with the affected upper limb at stage III of the Brunnstrom classification for hemiplegia, the assisted exercise mode was selected. A certain amount of auxiliary force was provided according to the condition of the patient's limb to help the patient achieve maximum full-space range of motion of the affected upper limb.
- (3) For patients with the affected upper limb at stage II of the Brunnstrom classification for hemiplegia, the passive exercise mode was selected, and the robot should provide guiding force to drive the affected upper limb for passive training.

2.3. Efficacy evaluation

An experienced therapist not involved in the treatment will evaluate all patients before treatment and after 4 weeks of treatment using the following indicators.

2.3.1. Fugl-Meyer assessment for upper extremity (FMA-UE)

Motor function of the affected upper limb was assessed using the Fugl-Meyer Assessment for the Upper Extremity (FMA-UE). This 33-item scale has a maximum score of 66, with higher scores denoting superior motor function.

2.3.2. Barthel index (BI)

Patient independence in performing activities of daily living (ADLs) was assessed using the Barthel Index (BI). This 100-point scale was comprised with 10 sub-items, where a higher total score reflects a greater level of functional independence.

2.4. Statistical analysis

All data was processed using SPSS 21.0 software. For continuous data, if each group satisfies normality and the variances between the two groups were equal, the statistical description was represented by the mean \pm standard deviation, and the *t*-test was used for inter-group comparison; otherwise, the median and interquartile range was considered for statistical description, and the rank sum test will be used for inter-group comparison.

All statistical tests were two-tailed, and a *p*-value < 0.05 has indicated a statistically significant difference.

3. Results

3.1. Comparison of FMA-UE scores

Prior to treatment, no significant difference in FMA-UE scores was observed between the two groups ($p > 0.05$). Following the 4-week intervention, both groups exhibited a significant increase in scores compared to their baselines ($p < 0.01$). Notably, the robot-assisted training group achieved a significantly higher FMA-UE score than the conventional treatment group at the end of the treatment ($p < 0.05$). See **Table 2**.

Table 2. Comparison of FMA-UE scores between two groups before and after treatment

Group	Before treatment	After treatment	Within-group	
			<i>t</i> -value	<i>p</i> -value
Intervention group (n = 35)	26.83 \pm 8.20	36.71 \pm 7.27	-5.335	< 0.01
Control group (n = 35)	25.66 \pm 7.62	32.94 \pm 7.23	-4.104	< 0.01
<i>t</i> -value (Between-group)	-0.619	-2.176		
<i>p</i> -value (Between-group)	0.538	0.033		

3.2. Comparison of BI scores

Before treatment, the two groups had comparable BI scores ($p > 0.05$). Following the 4-week intervention, both groups demonstrated significant improvements in their BI scores from baseline ($p < 0.01$). However, no significant difference was observed between the robot-assisted training group and the conventional treatment group at this stage ($p > 0.05$). See **Table 3**.

Table 3. Comparison of BI scores between two groups before and after treatment

Group	Before treatment	After treatment	<i>t</i> -value	<i>p</i> -value
Intervention (n = 35)	40.43 ± 9.80	56.00 ± 8.89	-6.959	< 0.001
Control (n = 35)	41.29 ± 11.59	56.57 ± 11.74	-5.481	< 0.001
Between-group <i>t</i> -value	0.334	0.229		
Between-group <i>p</i> -value	0.739	0.819		

4. Discussion

Motor dysfunction after stroke is the most common complication of stroke and a significant factor affecting patients' ability to live independently^[6,7]. Given that the upper limbs have a larger projection area in the cerebral cortex, perform more delicate functions, and have more complex motor functions than the lower limbs^[8], their recovery is much more challenging. Currently, clinical approaches to improve upper limb function in stroke patients include exercise therapy, occupational therapy, physical factor therapy, and traditional medical therapies. However, satisfactory outcomes have not been achieved, and there is a continuous need to explore more effective treatment methods for patients.

Robot-assisted training is an emerging rehabilitation treatment technology that has been gradually gaining popularity domestically and internationally in recent years. It can reduce reliance on therapist manpower and provide continuous, stable, high-intensity training with greater repeatability^[3,4]. Additionally, robot-assisted training incorporates game elements, enhancing treatment enjoyment and encouraging patient motivation and active participation. A meta-analysis included 19 randomized controlled trials, and the statistical results showed that robot-assisted training is effective for improving upper limb motor function in stroke patients^[9]. This study of 70 randomized patients revealed that after 4 weeks, both robot-assisted and conventional training groups showed significant improvements in FMA-UE scores. However, the robot-assisted group demonstrated superior upper limb recovery compared to the control group, aligning with previous findings.

Zhang Haiyan et al. conducted a 4-week upper limb rehabilitation robot-assisted training on 20 patients and found that the modified Barthel score in the robot group was superior to that in the conventional group^[10]. Patel et al. combined virtual reality technology with upper limb rehabilitation robots and found that it could better improve patients' ability to perform activities of daily living^[11]. Another study discovered that the efficacy of upper limb robot-assisted therapy in improving activities of daily living was similar to that of conventional therapy^[12]. This study found that Barthel scores significantly increased in both groups after treatment, but there was no significant difference in BI scores between the robot-assisted training group and the conventional therapy group. This inconsistency may be related to factors such as patient age, disease duration, condition severity, treatment duration, robot type, and the combination of robot training with other modalities.

5. Conclusion

In summary, upper limb robot-assisted training provides significant improvements in motor function and activities of daily living for elderly stroke patients. However, this study has some limitations: the short-term (4-week) study requires long-term follow-up, the small sample size necessitates multi-center large-sample studies, and the lack of exploration into mechanisms requires further investigation.

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Study on the Effects of Umbilical Acupuncture's "Wind-Thunder Interaction Method" on Neuro-Vascular Regulatory Peptide Groups in SCH Patients with Liver Stagnation and Spleen Deficiency

Yongfeng Li, Jialin Cheng, Hairong Wang, Bihai Zhou, Jianguo Mao

Shiyan Hospital of Integrated Traditional and Western Medicine, Shiyan 442000, Hubei, China

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Abstract: *Objective:* To evaluate the therapeutic efficacy of the umbilical acupuncture's "Wind-Thunder Interaction Method" in treating schizophrenia (SCH) patients with liver stagnation and spleen deficiency. *Methods:* A total of 120 SCH patients with liver stagnation and spleen deficiency were selected and evenly divided by ball drawing. The umbilical acupuncture group received the "Wind-Thunder Interaction Method", while the Western medicine group received pure Western medicine treatment. The outcomes were compared in terms of efficacy and other indicators. *Results:* The umbilical acupuncture group showed a higher total effective rate, a decrease in disease symptom scores, lower scores on the side effect rating scale, improved cognitive function scores, and excellent laboratory indicators, with $p < 0.05$ between the groups. *Conclusion:* The "Wind-Thunder Interaction Method" of umbilical acupuncture demonstrated a relatively high effectiveness in treating SCH patients with liver stagnation and spleen deficiency, alleviating symptoms, reducing side effects, improving cognitive function, and facilitating the recovery of neuro-vascular regulatory peptide groups.

Keywords: Umbilical acupuncture's "Wind-Thunder interaction method"; SCH; Liver stagnation and spleen deficiency; Neuro-vascular regulatory peptide groups

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1. Introduction

SCH is characterized by abnormal behavior and cognitive dysfunction, with patients often exhibiting symptoms such as weak willpower and emotional indifference. The disease has a high disability and recurrence rate, which can have a long-term impact on patients' daily lives and increase their family's burden. Western medicine treatment is the preferred therapy for this condition, as it can stabilize disease symptoms and prevent further progression. However, Western medicine has numerous side effects, and its long-term effectiveness is generally

limited, making traditional Chinese medicine treatment a viable alternative ^[1]. Umbilical acupuncture is a safe and effective traditional Chinese medicine therapy. By utilizing the “Wind-Thunder Interaction Method”, it can provide dialectical treatment for the liver stagnation and spleen deficiency pathology in SCH patients, with rapid symptom relief and strong operability, resulting in favorable therapeutic outcomes. Therefore, this study selected 120 SCH patients with liver stagnation and spleen deficiency to assess the effects of implementing the “Wind-Thunder Interaction Method” of umbilical acupuncture.

2. Materials and methods

2.1. General information

A total of 120 patients with SCH (schizophrenia) and liver stagnation and spleen deficiency syndrome, admitted between September 2024 and June 2026, were selected and randomly divided into two groups using a ball-drawing method. The detailed information between the groups is as follows (see **Table 1**).

Table 1. Detailed information for comparison between groups [n/%, mean \pm standard deviation ($\bar{x} \pm s$)]

Group	n	Gender [n(%)]		Age (years)	Disease duration (years)
		Male	Female		
Umbilical acupuncture	60	35 (58.33)	25 (41.67)	30.53 \pm 3.15	4.06 \pm 1.33
Western medication	60	36 (60.00)	24 (40.00)	30.15 \pm 3.20	4.09 \pm 1.35
Statistical test (χ^2/t)		0.035	0.656	0.123	
p-value		0.853	0.513	0.903	

2.2. Methods

The Western medicine group received pure Western medicine treatment: oral administration of risperidone, with an initial daily dose of 1 mg. The dose was increased based on the degree of symptom improvement in the patients, and it could be combined with benzodiazepines and benzotropine, among other drugs. After two weeks of administration, the daily dose of risperidone was increased to 3 to 6 mg, and the medication was continued for 4 weeks.

The umbilical acupuncture group received umbilical acupuncture using the “Wind-Thunder Interaction Method” in addition to Western medicine treatment: the Zhen (Thunder), Xun (Wind), and Kun (Earth) points were selected. After disinfecting the treatment area, disposable sterile acupuncture needles (0.25 \times 25 mm) were used. Taking the umbilical center as the focal point and based on the order of acupoint selection, the needles were inserted approximately one-third of the way up the umbilical wall, using a twisting method at a 30° angle to the abdominal wall skin. The needles were inserted to one-third of their depth, ensuring there was no sense of emptiness. After acupuncture, the needle bodies intersected, and they were retained for 30 minutes. The treatment frequency was three times per week, with one course of treatment lasting one week, and a total of four courses were administered.

2.3. Observation indicators

(1) Overall response rate

Based on the reduction in scores on the Positive and Negative Syndrome Scale (PANSS), a significant

response was defined as a reduction rate exceeding 75%, a preliminary response as a reduction rate between 25% and 75%, and no response as a reduction rate less than 25%.

(2) Disease symptom score

The PANSS scale was used, which includes three items, with scores calculated in a positive direction.

(3) Side effect score

The Treatment Emergent Symptom Scale (TESS) was used, which includes six items such as nervous system reactions, totaling 34 items. Each item is scored from 1 to 4, with the degree of reaction calculated in a positive direction.

(4) Cognitive function score

The Mini-Mental State Examination (MMSE) was selected, consisting of five items, with scores calculated in a positive direction.

(5) Laboratory indicators

Serum level of human neuropeptide Y (NPY), human calcitonin gene-related peptide (CGRP), and vasoactive intestinal peptide (VIP) were evaluated.

2.4. Statistical analysis

Data were processed using SPSS 28.0 software. Measurement values were compared and tested using *t*-values, while count values were compared and tested using chi-square (χ^2) values. Statistical significance was considered as $p < 0.05$.

3. Results

3.1. Comparison of overall effectiveness rates between groups

The overall effectiveness rate in the umbilical acupuncture group was higher, with a comparison between groups showing $p < 0.05$ (see **Table 2**).

Table 2. Comparison of overall effectiveness rates between groups [n/%]

Group	n	Markedly effective	Effective	Ineffective	Total effective rate
Umbilical acupuncture	60	41	17	2	96.67% (58/60)
Western medication	60	36	15	9	85.00% (51/60)
χ^2					4.904
<i>p</i> -value					0.027

3.2. Comparison of disease symptom scores between groups

After treatment, the disease symptom scores in the umbilical acupuncture group decreased, with a comparison between groups showing $p < 0.05$ (see **Table 3**).

Table 3. Comparison of disease symptom scores between groups [$\bar{x} \pm s$, points]

Group	n	Positive symptoms		Negative symptoms		General psychopathology	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Umbilical acupuncture	60	35.18 \pm 4.15	27.53 \pm 2.65	35.27 \pm 3.74	27.15 \pm 2.62	89.41 \pm 5.79	67.53 \pm 3.94
Western medication	60	35.14 \pm 4.10	30.02 \pm 2.69	35.26 \pm 3.79	29.97 \pm 2.66	89.49 \pm 5.81	71.05 \pm 3.97
<i>t</i> -value		0.053	5.108	0.015	5.851	0.076	4.875
<i>p</i> -value		0.958	0.000	0.988	0.000	0.940	0.000

3.3. Comparison of side effect scores between groups

The side effect score in the umbilical acupuncture group was (5.19 \pm 1.75) points, while that in the Western medicine group was (8.14 \pm 1.98) points, with $t = 8.647$ and $p = 0.000$.

3.4. Comparison of cognitive function scores between groups

After treatment, the cognitive function score in the umbilical acupuncture group was higher, with a comparison between groups showing $p < 0.05$ (see Table 4).

Table 4. Comparison of cognitive function scores between groups [$\bar{x} \pm s$, points]

Group	n	Orientation		Recall		Memory		Attention & calculation		Language ability	
		Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx
Umbilical acupuncture	60	4.63 \pm 0.98	8.15 \pm 1.20	1.85 \pm 0.43	2.39 \pm 0.35	1.68 \pm 0.34	2.41 \pm 0.33	2.35 \pm 0.71	4.11 \pm 0.52	4.25 \pm 1.32	7.29 \pm 1.41
Western medication	60	4.66 \pm 0.94	6.87 \pm 1.14	1.87 \pm 0.46	2.05 \pm 0.31	1.70 \pm 0.32	2.19 \pm 0.30	2.37 \pm 0.70	3.83 \pm 0.46	4.28 \pm 1.30	6.73 \pm 1.37
<i>t</i> -value		0.171	5.990	0.246	5.633	0.332	3.821	0.155	3.124	0.125	2.206
<i>p</i> -value		0.864	0.000	0.806	0.000	0.741	0.000	0.877	0.002	0.900	0.029

3.5. Comparison of laboratory indicators between groups

After treatment, the laboratory indicators in the umbilical acupuncture group were superior, with a comparison between groups showing $p < 0.05$ (see Table 5).

Table 5. Comparison of laboratory indicators between groups [$\bar{x} \pm s$]

Group	n	NPY (ng/L)		CGRP (ng/L)		VIP (pg/L)	
		Pre-Tx	Post-Tx	Pre-Tx	Pre-Tx	Post-Tx	Pre-Tx
Umbilical acupuncture	60	427.95 \pm 28.65	178.53 \pm 10.22	49.36 \pm 4.53	79.90 \pm 8.37	155.03 \pm 19.74	171.86 \pm 15.39
Western medication	60	426.88 \pm 29.13	250.36 \pm 10.94	49.41 \pm 4.57	65.12 \pm 8.20	154.93 \pm 19.66	165.02 \pm 15.23
<i>t</i> -value		0.203	37.165	0.060	9.771	0.028	2.447
<i>p</i> -value		0.840	0.000	0.952	0.000	0.978	0.016

4. Discussion

The incidence rate of SCH is approximately 1%. The disease has a long course, complex disease progression, and a high risk of deterioration. It can also reduce patients' social functioning and have a long-term impact on their quality of life ^[2]. In traditional Chinese medicine (TCM), this disease falls under the category of “mania-depression syndrome”, characterized by symptoms such as indifferent expression, psychological depression, murmuring to oneself, and a preference for inactivity and quietness. It is primarily a syndrome of liver stagnation and spleen deficiency. Additionally, patients exhibit reduced willpower, excessive worry, and irritability. TCM symptoms include chest and hypochondriac distension, epigastric fullness and belching, and being easily startled and having difficulty sleeping, accompanied by thin white tongue coating and pale red tongue.

Modern medical theories for treating this disease are relatively mature, such as the “Holographic Biology Theory” and the “Abdomen-Brain Theory”. The former posits that life is a holographic embryo, and acupuncture points can be stimulated based on acupoint theories such as the “Holographic Law”. The latter suggests that the abdomen is the body's second brain, and acupuncture in the abdominal region can act on the etiology and pathogenesis of the disease. Based on these theories, this study employed umbilical acupuncture (navel needle therapy) for patients with this condition. The umbilicus, also known as the “Shenque acupoint”, connects the umbilicus and the heart. The term “Shen” refers to the primordial spirit, dominated by the heart, reflecting the patient's mental state. “Que” means the central gate, serving as the portal through which the mind interacts with the external world ^[3]. In traditional Chinese medicine, SCH is classified as a “mental disorder”, and it is proposed that the umbilical region is interconnected with the Governor Vessel, Conception Vessel, and the internal organs of patients, capable of regulating the flow of Qi and blood as well as the state of meridian operation, acting on the limbs, bones, and internal organs, while also improving the function of meridians, muscles, and bones. Umbilical needle therapy is an umbilical acupuncture technique developed based on the aforementioned theories, which can regulate Qi, blood, Yin, and Yang, and improve the state of internal organs. The “Wind-Thunder Mutual Reinforcement Method” is the primary therapeutic concept of umbilical needle therapy, where thunder refers to the vibration and is associated with wood, representing the liver. Wind refers to the gentle breeze and is also associated with wood, representing the gallbladder. It can thus be seen that this concept enables wind and thunder to complement each other, thereby enhancing the wood element and effectively exerting effects such as regulating emotions and soothing the liver to relieve depression, ultimately improving treatment outcomes.

The results showed that the total effective rate of the umbilical needle group increased, and the disease symptom score decreased, with a significant difference between the two groups ($p < 0.05$). The analysis of the reasons is as follows: During the embryonic period, the blood vessels and nerves in the umbilical region are densely distributed, which can influence the function of the autonomic nervous center and have a certain reflexive connection with the hypothalamus-pituitary axis. Umbilical needling can act on the vagus nerve-gut-brain axis, thereby improving the release of central neurotransmitters and exerting antipsychotic effects. The Bagua orientations of Zhen, Xun, and Kun can produce a synergistic mechanism. The Zhen position is in the east, belongs to wood, and governs liver wind. Needling this area can soothe the liver and relieve depression, having a good regulatory effect on the prefrontal-limbic system and alleviating positive symptoms. The Xun position is in the southeast, belongs to wind, and governs the gallbladder meridian. It can improve the degree of neural excitement and reduce psychological symptoms such as agitation and anxiety in patients ^[4]. The Kun position is in the southwest, belongs to earth, and needling this area has effects such as invigorating the spleen and resolving phlegm. It can act on the gut microbiota-brain axis, increase the content of short-chain fatty acids, thereby down-

regulating the levels of inflammatory factors and reducing the degree of neuroinflammation. Umbilical needling has a good regulatory effect on the default mode network, preventing its overactivity and acting on abnormal neural oscillations, thus alleviating positive symptoms such as delusions or hallucinations. Umbilical needling can enhance the plasticity of the synaptic regions in the prefrontal lobe, stimulate patients' desire for emotional expression, and thereby improve negative symptoms such as emotional indifference or social withdrawal. Moreover, needling at the Xun position can increase the specific release of acetylcholine, significantly improve patients' attention and thereby enhance their social interactions ^[5]. The Kun position corresponds to the patients' spleen and stomach functions. Needling this area can down-regulate cortisol levels, thereby improving general psychotic symptoms and reducing manifestations such as hostility.

The side effect score of the umbilical needle group was low, with a significant difference between the two groups ($p < 0.05$). The analysis of the reasons is as follows: Umbilical needling can regulate the overall release of endogenous opioid peptides, enhancing the antipsychotic effect, thereby reducing the dosage of Western medications, preventing extrapyramidal reactions, and alleviating metabolic side effects. Compared with administration methods such as oral medications, umbilical needling does not involve liver metabolism and can prevent drug interactions, thereby improving treatment safety.

The cognitive function scores of the umbilical needle group increased after treatment, with a p -value less than 0.05 when compared between the two groups. The analysis suggests that umbilical needling has a strong activating effect on the ventral tegmental area, which can regulate the dopamine pathway in the prefrontal cortex, thereby enhancing patients' executive function and memory ^[6]. Umbilical needling can prevent the massive release of inflammatory factors, thereby reduce neurotoxicity and protect hippocampal neurons, thus improving patients' attention. Moreover, this therapy has a certain repairing effect on synaptic function, protecting nerves and facilitating the recovery of cognitive function.

The laboratory indicators of the umbilical acupuncture group were excellent after treatment, with a statistically significant difference between the two groups ($p < 0.05$). Following umbilical acupuncture treatment, the levels of the aforementioned laboratory indicators improved. The analysis suggests that umbilical acupuncture exerts a strong stimulating effect on the umbilical region, acting on the branches of the vagus nerve and activating NPY-ergic neurons in the nucleus of the solitary tract-hypothalamus area, thereby regulating NPY levels. The selection of the “Zhen” (vibration) position in umbilical acupuncture treatment can prevent excessive expression of stress-induced cortisol, thereby regulating NPY synthesis and establishing a negative feedback relationship between cortisol and NPY levels ^[7,8]. The “Kun” (earth) position in umbilical acupuncture treatment has a spleen-strengthening effect, acting on the vagus nerve- $\alpha 7$ nicotinic acetylcholine receptor anti-inflammatory pathway to prevent excessive activation of microglia, thereby reducing the expression levels of inflammatory factors such as interleukin-6 and regulating CGRP levels. The “Xun” (wind) position treatment can improve the function of the gallbladder meridian, increase cerebral blood flow, prevent excessive mediation of CGRP, and sustain vasodilation, thereby regulating neuronal excitability. VIP regulates cognitive function in patients and participates in biological rhythm processes. Umbilical acupuncture can act on the VIP-ergic pathway, regulating the suprachiasmatic nucleus and improving the function of the biological clock center, thereby regulating circadian rhythms and improving the physiological state of patients ^[9]. Combined treatment with the “Zhen” and “Xun” positions can regulate the activity of GABA-ergic interneurons in the prefrontal cortex, thereby enhancing synaptic plasticity.

5. Conclusion

In conclusion, the overall therapeutic effect of the umbilical needle “Wind and Thunder Interaction Method” for patients with SCH (schizophrenia) and liver stagnation and spleen deficiency syndrome is relatively good. It can improve positive and negative symptoms, alleviate general psychotic symptoms, reduce side effects during treatment, improve patients’ cognitive function, facilitate the recovery of neuro-vascular regulatory peptide groups, and demonstrate high therapeutic efficacy.

Disclosure statement

The authors declare no conflict of interest.

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Technical Guidelines for Autologous Skin-Grafting Surgery to Prevent Stenosis Following Super Minimally Invasive Resection of Large-Area Esophageal Lesions

Qianqian Chen[†], Runze Wang[†], Huikai Li, Enqiang Linghu*

Department of Gastroenterology, First Medical Center, Chinese People's Liberation Army General Hospital, Beijing 100853, China

[†] These authors contributed equally to this work and share the first authorship.

*Corresponding author: Enqiang Linghu, linghuenqiang@vip.sina.com

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Abstract: Autologous Skin-Grafting Surgery after Super Minimally Invasive Resection (ASGS-SMIR) is a novel endoscopic repair technique developed under the guidance of the Super Minimally Invasive Surgery (SMIS) concept. Based on previous clinical research results and combined with the ten core treatment principles of SMIS, this guideline systematically elaborates on the indications, contraindications, preoperative evaluation, surgical operation standards, postoperative management, and efficacy evaluation system of ASGS-SMIR. This surgery achieves effective repair of large-area mucosal defects and stenosis prevention in the esophagus through the technical process of “skin flap harvesting, mesh processing, sleeve suture, and stent fixation”. The purpose of this guideline is to promote the standardized and normalized application of this technique and provide guidance for clinical practice.

Keywords: Esophageal stenosis; Super minimally invasive surgery; Autologous skin flap transplantation; Technical standards; Therapeutic endoscopy

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1. Introduction

1.1. Background

Autologous Skin-Grafting Surgery after Super Minimally Invasive Resection (ASGS-SMIR) is a novel endoscopic repair technique developed under the guidance of the Super Minimally Invasive Surgery (SMIS) concept for preventing stricture after extensive endoscopic resection of large esophageal lesions. Based on preliminary clinical research and integrating the ten core principles of SMIS, this standard systematically elaborates the indications,

contraindications, preoperative evaluation, surgical procedural standards, postoperative management, and efficacy evaluation system for ASGS-SMIR. Utilizing a technical process characterized by “skin harvesting, meshing, oversleeve suturing, and stent fixation”, ASGS-SMIR achieves effective repair of large esophageal mucosal defects and prevention of stricture. The establishment of this standard aims to promote the standardized and normative application of the technique, providing guidance for clinical practice.

1.2. Establishment of technical standards for ASGS-SMIR under the SMIS framework

With the continuous development of digestive endoscopy technology, super minimally invasive surgery (SMIS) has become an important direction for the treatment of early esophageal cancer and precancerous lesions^[1–3]. For large superficial lesions with a lesion area exceeding 3/4 of the esophageal circumference or involving the entire circumference, the incidence of postoperative esophageal stenosis can be as high as 88–100%, seriously affecting patients’ quality of life^[4]. Therefore, it is necessary to provide preventive measures for postoperative stenosis after endoscopic resection (ER) of superficial lesions involving the entire esophageal circumference^[5,6]. Data from previous clinical studies indicate that one important factor in preventing postoperative esophageal stenosis after endoscopic submucosal dissection (ESD) surgery is re-epithelialization^[7–9]. ASGS-SMIR, as an innovative repair technique under the SMIS concept, effectively prevents postoperative stenosis by combining autologous skin grafting with endoscopic technology^[10–14]. Based on the ten core principles of SMIS and combined with previous clinical practical experience, this specification establishes the technical standards for ASGS-SMIR to promote the standardized development, promotion, and application of this technique^[15].

2. Indications and contraindications

2.1. Indications

- (1) After undergoing complete circumferential endoscopic submucosal tunneling dissection (ccESTD) or circumferential endoscopic submucosal dissection (cESD) for esophageal lesions, a full-circumference or near-full-circumference mucosal defect is formed, with a longitudinal length of ≥ 5 cm.
- (2) Preoperative assessment revealed no evidence of lymph node or distant metastasis (confirmed by EUS, CT, etc.).
- (3) The patient is generally in good condition and can tolerate the surgery and postoperative recovery process.
- (4) The patient has provided informed consent and demonstrates good treatment compliance.

2.2. Contraindications

- (1) Presence of active infection or immune dysfunction
- (2) Severe cardiopulmonary insufficiency, unable to tolerate prolonged endoscopic procedures or anesthesia
- (3) Coagulation dysfunction, which still fails to meet the surgical requirements after correction
- (4) Active dermatosis in the skin harvesting area of the thigh or insufficient skin supply due to previous surgery
- (5) The patient refuses or is unable to cooperate with postoperative nutritional support and long-term follow up

3. Preoperative preparation

3.1. Multidisciplinary evaluation

Establish an MDT team consisting of gastroenterology, plastic surgery, and anesthesiology to jointly assess the

feasibility and plan of surgery.

3.2. Equipment and apparatus

- (1) Endoscope system
Therapeutic endoscope with accompanying water supply system, transparent cap
- (2) Electrosurgical equipment
High Frequency generator (such as VIO300D), Dual knife, TT knife, IT knife
- (3) Transplantation materials
Humby dermatome, absorbable suture (VICRYL Plus 4-0)
- (4) Support system
Fully covered esophageal stent (FCES, such as Cook EVO-FC series), endoscopic clip (such as Micro-Tech clip)
- (5) Nutritional support
Nasal jejunal feeding tube

3.3. Patient preparation

- (1) Improving preoperative examinations
Blood routine, coagulation function, electrocardiogram, chest CT, gastroscopy + EUS
- (2) Skin preparation
Select the outer side of the right thigh as the skin harvesting area and prepare the skin
- (3) Fast for 8 hours and refrain from drinking water for 4 hours before the operation
- (4) Sign the informed consent form for surgery

4. Surgical operation specifications

4.1. Operation principles

The ASGS-SMIR procedure must adhere to the core principles of SMIS: the principle of preserving organs and functions, the principle of maintaining cavity integrity, the principle of prioritizing sterility, the principle of avoiding chemical stimulation, the principle of preferring natural cavities, the principle of following the nearest approach, the principle of having hemostatic measures in place, the principle of having measures to seal perforations, and the principle of tumor-free and metastasis prevention.

4.2. Surgical steps

The surgical steps were illustrated in the schematic diagram below (see **Figure 1**).

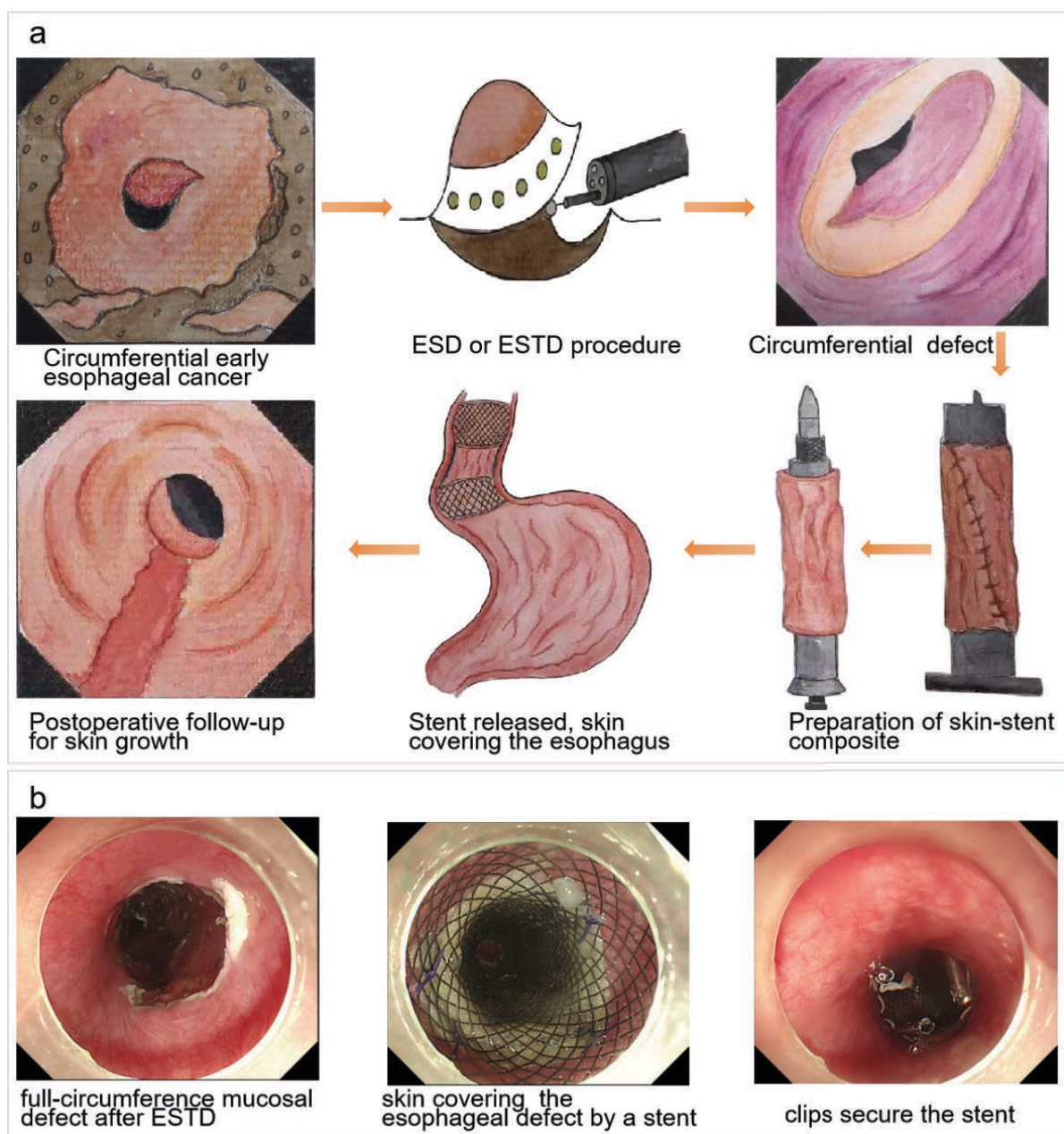


Figure 1. (a) Diagram of the ASGS-SMIR procedure; (b) Endoscopic images of ASGS-SMIR.

(1) Lesion resection

Perform ccESTD/cESD according to standard procedures to completely remove the lesion and form a circumferential surgical wound.

(2) Skin flap harvesting and processing

A medium-thick skin graft (thickness 0.3–0.5 mm) is harvested from the lateral side of the right thigh by a plastic surgeon. The size of the skin graft should be 10–15% larger than the area of the esophageal ulcer. The skin graft is made into a mesh shape with a surgical knife (with a hole spacing of about 5 mm). The skin graft is sutured into a “sleeve-like” structure using absorbable sutures.

(3) Preparation of flap-stent composite system

Fully release FCES *in vitro*; carefully cover the “sleeve-like” skin graft on the outer surface of FCES; ensure that the skin graft adheres closely to the stent without wrinkles or twists.

(4) Stent placement and fixation

Place the stent with a skin graft through the mouth; confirm the position of the stent under endoscopy (both ends should extend 2 cm beyond the edge of the ulcer); use endoscopic clips to fix the proximal end of the stent to the esophageal wall (usually 3–4 clips are required); place a nasojeunal feeding tube.

(5) Treatment of skin donor site

The skin donor site on the thigh is covered with vaseline gauze and bandaged with compression.

4.3. Intraoperative precautions

- (1) Always keep the surgical field clear, and perform timely irrigation and suction
- (2) Ensure that the skin graft is tightly fitted to the stent to prevent wrinkles
- (3) Secure the stent accurately to prevent displacement
- (4) Monitor the patient’s vital signs closely
- (5) Communicate with anesthesiologists about the patient’s condition in a timely manner

5. Postoperative management

5.1. Recent management

(1) Nutritional management

Postoperative fasting for 7 days, with enteral nutrition administered through a nasogastric tube; starting from the 8th day, gradually transitioning to liquid diet → semi-liquid diet → soft diet

(2) Pharmacotherapy

Intravenous PPI (such as esomeprazole 40 mg q12h) for 5 days, followed by oral PPI for 8 weeks; Intravenous antibiotics for 3 days

(3) Complication monitoring

Closely observe for complications such as bleeding, perforation, infection, and stent migration.

5.2. Prevention and treatment of complications

(1) Bleeding

For active bleeding during surgery, electrocoagulation or clamping is the preferred method for hemostasis; for delayed bleeding, emergency endoscopic treatment should be the first choice

(2) Perforation

During the operation, timely detection and correction of the operation are necessary to avoid major perforation; for postoperative perforation, a chest CT scan is required to clarify the situation, and conservative treatment or surgical repair should be selected according to the situation

(3) Stent migration

Adjustment or replacement under endoscopy

(4) Transplantation failure

Enhance nutritional support, and perform secondary intervention if necessary

(5) Infection in the skin grafting area

Regular dressing changes and antibiotic treatment

5.3. Efficacy evaluation and follow up

5.3.1. Healing evaluation

(1) Technical success

The stent-flap complex was accurately placed and fixed, with no severe complications after surgery

(2) Therapeutic success

No stenosis requiring intervention (inaccessible by standard endoscopy) at 3 months postoperatively

5.3.2. Follow-up protocol

(1) 4–6 weeks after surgery: Endoscopy to assess the survival of the skin flap and remove the stent

(2) 8 weeks, 6 months, and 12 months after surgery: regular endoscopic follow-up

(3) After that, have a gastroscopy review once a year

5.3.3. Follow-up content

(1) Evaluation of flap survival rate

Evaluate the survival rate segment by segment per centimeter and calculate the overall survival rate

(2) Stenosis assessment

The Mellow-Pinkas swallowing function score is used to assess the improvement of quality of life

(3) Pathological confirmation

Biopsy was taken from the transplantation area, and it was confirmed to be squamous epithelium with hyperkeratosis

6. Conclusion

ASGS-SMIR, as an innovative repair technology under the SMIS concept, achieves effective repair of large-area mucosal defects and prevention of stenosis in the esophagus through standardized operating procedures and strict quality control. Its technical core, “skin flap harvesting, mesh processing, sleeve suture, and stent fixation”, ensures the safety and effectiveness of the surgery. The formulation of this specification provides a standardized basis for the promotion and application of ASGS-SMIR technology, which is conducive to promoting the development of esophageal disease treatment towards super minimally invasive and precise directions.

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Disclosure statement

The authors declare no conflict of interest.

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Observation on the Efficacy of Roxadustat in Treating Low-risk Myelodysplastic Syndrome

Tao Guo, He Li, Hongfang Wang*, Feng Zhang

Department of Hematology, Kunming First People's Hospital, Kunming 650018, China

*Corresponding author: Hongfang Wang, 549458828@qq.com

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Abstract: *Objective:* To observe the effect of different doses and frequencies of roxadustat on low-risk patients with myelodysplastic syndromes (MDS). *Methods:* This study was conducted using a comparative treatment observation approach. Low-risk MDS patients admitted to our hospital from February 2022 to February 2023 were selected, excluding patients with a history of severe drug allergies or known allergies to roxadustat. A total of 60 patients were included and randomly divided into observation group A (20 cases, 100 mg, twice weekly), observation group B (20 cases, 50 mg, once daily), and observation group C (20 cases, 150 mg, twice weekly). Patient recovery, adverse reaction rate, and hemoglobin recovery time were compared and statistically analyzed. *Results:* The recovery rate of group B in the observation group was significantly higher than that in the other two groups, and the incidence of adverse reactions and the time to Hb recovery were also better in group B than in the other two groups ($p < 0.05$). *Conclusion:* Low-dose, high-frequency (50 mg, once daily) administration can effectively improve the hemoglobin level of low-risk MDS patients and help improve their general survival.

Keywords: Low-risk MDS; Roxadustat; Anemia

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1. Introduction

Myelodysplastic syndromes (MDS) are a group of heterogeneous myeloid clonal diseases originating from hematopoietic stem cells, characterized by ineffective hematopoiesis, varying degrees of cytopenia, hematopoietic failure, and high risk of progression to acute myeloid leukemia (AML). MDS is a chronic hematologic malignancy with high clinical heterogeneity^[1]. Because MDS has high heterogeneity and complexity, the prognosis varies greatly, with median survival ranging from 6 months to 5 years^[2]. Approximately 30% of MDS patients develop secondary acute leukemia within a few months to a few years^[3]. MDS is the most common clinical disease type, which is common in the elderly. Patients with MDS may have a decrease in peripheral blood mono- or multi-lineage cells. Patients may have anemia, such as dizziness, fatigue, ecchymosis, hematochezia, hematuria,

infection and fever. Chemotherapy may also cause severe bone marrow suppression, gastrointestinal symptoms, accompanied by nausea, vomiting, loss of appetite, etc. Therefore, MDS has a great negative impact on the health of patients, is difficult to treat, and has the characteristics of progressive development. If the diagnosis is not timely or targeted treatment is not received in time, it is easy to endanger the patient's life ^[4].

According to the revised International Prognostic Score System (IPSS-R), MDS is divided into lower-risk and higher-risk groups. The lower-risk group includes IPSS-low-risk group, intermediate-1 group, IPSS-very-low-risk group, low-risk group and intermediate-risk group (≤ 3.5 points), WPSS-very-low-risk group, low-risk group and intermediate-risk group. The higher-risk group includes IPSS-intermediate-2 group and high-risk group, IPSS-R-intermediate group (> 3.5 points), high-risk group and very-high-risk group, WPSS-high-risk group and very-high-risk group ^[5]. Patients with higher-risk MDS have shorter survival time and are more likely to progress to acute myeloid leukemia (AML). The main feature of low-risk MDS is hematopoietic progenitor cell apoptosis, which is related to epigenetic changes and immune dysregulation ^[6]. Since the etiology and pathogenesis of MDS are not fully understood, there is no consensus on the treatment plan for MDS, but there are the same treatment principles.

- (1) For patients in the lower risk group, blood transfusion dependence should be reduced as much as possible, the bone marrow hematopoietic microenvironment should be improved, and symptomatic or etiological treatment should be generally given
- (2) For patients in the higher risk group, there are abnormal changes in cytogenetics and the prognosis is poor. Disease progression should be stopped as much as possible, survival time should be prolonged, and even clinical cure should be achieved ^[7]. At present, the main treatment methods for MDS include supportive treatment, immunosuppressants, immunomodulators, demethylation, hematopoietic stem cell transplantation, etc.

Roxadustat is a small molecule hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor. It is the world's first HIF-PHI drug. As a new generation of renal anemia treatment drug with a brand-new mechanism, my country took the lead in completing the Phase III clinical trial in 2018 and was officially approved for marketing ^[8]. Chen N proved in a Phase III trial of chronic renal failure patients that roxadustat can improve renal anemia ^[9]. In the clinical study, 24 patients were treated with roxadustat at doses of 1.5, 2.0 and 2.5 mg/kg, respectively. Nine patients (37.5%) were weaned off transfusion at 28 and 52 weeks, of which 7 were treated with 2.5 mg/kg. None of the patients died or progressed to AML, indicating that roxadustat can effectively improve nephropathy-related anemia ^[10].

Roxadustat is a new drug for the treatment of renal anemia, so there is a lack of clinical experience in its use, and the clinical effect of some patients is not good. There is still a lack of large-sample analysis of the clinical factors affecting its efficacy. Chen Yanlin referred to the dosage adjustment principles of the 2018 Chinese Expert Consensus on the Diagnosis and Treatment of Renal Anemia and treated roxadustat orally for 4 weeks ^[11,12]. Finally, it was found that baseline serum ferritin was the influencing factor of the short-term efficacy of roxadustat in the treatment of renal anemia. Ideal mean serum albumin helps to improve the long-term efficacy of roxadustat. Improving iron metabolism and improving nutritional status can improve the clinical efficacy of roxadustat in the treatment of renal anemia. However, no reliable evidence was provided regarding the specific use of roxadustat. Patients with low-risk MDS have limited clonal hematopoiesis and minimal blast cell infiltration. Therefore, we found that adding roxadustat to the treatment of these patients may alleviate anemia and transfusion dependence to some extent, thereby improving their quality of life. Therefore, this study used roxadustat to treat low-risk

MDS. By observing different administration methods of roxadustat, we statistically analyzed the recovery status, incidence of adverse reactions, and hemoglobin recovery time of low-risk MDS patients to explore the specific value of roxadustat in treating low-risk MDS.

2. Materials and methods

2.1. General information

This study was conducted in the form of a comparative treatment observation, selecting 60 low-risk MDS patients admitted to our hospital from February 2022 to February 2023, who were randomly divided into 3 groups. This study was conducted in accordance with the principles of the Declaration of Helsinki, and informed consent was obtained from the patients and their families.

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Age ≥ 18 years, gender not limited.
- (2) MDS patients who meet the WHO revised classification and the International Prognostic Score IPSS-R < 3 .
- (3) Relevant laboratory values
Serum albumin > 30 g/L; ALT and AST ≤ 80 U/L; creatinine ≤ 198 $\mu\text{mol/L}$; total bilirubin ≤ 33 $\mu\text{mol/L}$.

2.2.2. Exclusion criteria

- (1) Patients with a clear history of bleeding, such as gastrointestinal bleeding, chronic active bleeding, etc ^[11].
- (2) Patients with a history of severe drug allergy or known allergy to Roxadustat ^[11].
- (3) Serum ferritin (SF) ≥ 500 ng/mL or parathyroid hormone (PTH) ≥ 800 pg/mL ^[11].
- (4) Mental illness and poor compliance, refusal to cooperate ^[11].

2.3. Methods

All three groups of patients received routine treatment, including gastric protection, liver protection and anti-infection treatment, and blood transfusion treatment was assessed based on the specific condition of the patients. On the basis of routine treatment, all three groups of patients were treated with roxadustat (manufacturer: FibroGen (China) Pharmaceutical Technology Development Co., Ltd., National Drug Approval Number: H20180023).

Dosage and administration

(1) Observation group A

11 males and 9 females, aged 54–79 years, mean (62.12 ± 1.23) , administration method: 100 mg, twice a week

(2) Observation group B

10 males and 10 females, aged 53–78 years, mean (61.02 ± 1.56) , administration method: 50 mg, once a day

(3) Observation group C

12 males and 8 females, aged 54–79 years, mean (61.88 ± 1.92) , administration method: 150 mg, twice a week.

Continue to take for 13 weeks, and follow up by telephone or visit the hospital for examination every week.

During the treatment, patients should be instructed to strictly follow the doctor's orders for medication.

2.4. Observation indicators

2.4.1. Recovery status

Based on the revised criteria for the efficacy of osteodystrophy syndrome by the International Working Group, the recovery status of patients was divided into three levels: complete remission (CR), partial remission (PR), and no remission (NR) ^[13].

Efficacy assessment

(1) CR

Anemia and bleeding symptoms improved, blood transfusion dependence was eliminated, hemoglobin increased by 30 g/L compared with one month before treatment, and blast cells < 5%

(2) PR

Anemia and bleeding symptoms disappeared, hemoglobin ≥ 90 g/L, platelets $\geq 80 \times 10^9$ L, bone marrow dysplasia was significantly reduced, and blast cells < 5%

(3) NR

Anemia and bleeding symptoms did not completely disappear, bone marrow dysplasia was not reduced, and hemoglobin < 60g/L.

Overall response rate (ORR) = (CR + PR + NR) / (number of cases / total number of cases) $\times 100\%$.

2.4.2. Incidence of adverse reactions

This study observed and recorded whether the three groups of patients experienced adverse reactions such as anemia, neutropenia, thrombocytopenia, nausea and vomiting, fever, and infection during the treatment period ^[14].

2.4.3. Hemoglobin (Hb) recovery time

Time for Hb to recover to ≥ 30 g/L, 60 g/L and 90 g/L.

2.5. Statistical methods

Data were processed using SPSS 20.0 statistical software. Normally distributed continuous data were expressed as mean \pm standard deviation ($\bar{x} \pm s$), and *t*-tests were used for comparisons between groups. Count data were expressed as [n(%)], and chi-square tests were used for comparisons between groups. *p* < 0.05 was considered statistically significant.

3. Results

3.1. Patient enrollment

According to the MDS prognostic system score (≤ 3 points) and the inclusion criteria, a total of 60 low-risk MDS patients were included, as shown in **Table 1**.

Table 1. Patient enrollment

Prognostic parameters	Male	Female	Total
Primitive cells > 10%	10	5	15
Platelets ≤ 80 g/L	13	7	20
Hemoglobin < 30×10^9 L	8	8	16
Neutrophils $\leq 0.8 \times 10^9$ L	2	7	9
Total	33	27	60

3.2. Comparison of recovery in the three groups

In terms of overall recovery, observation group B (ORR = 95%) was higher than observation group A (ORR = 75%) and observation group C (ORR = 85%). The comparison shows that observation group B had the best recovery ($\chi^2 = 10.883, p = 0.001 < 0.05$), see **Table 2**.

Table 2. Comparison of recovery status among the three groups [n(%)]

Group	n	Complete remission	Partial remission	No remission	Overall response rate
Observation group A	20	10 (0.50)	5 (0.25)	5 (0.25)	15 (0.75)
Observation group B	20	14 (0.70)	5 (0.25)	1 (0.05)	19 (0.95)
Observation group C	20	12 (0.60)	5 (0.25)	3 (0.15)	17 (0.85)
χ^2					10.883
<i>p</i>					0.001

3.3. Comparison of adverse reactions in the three groups

During treatment, the incidence of adverse reactions in observation group B (10%) was lower than that in observation group A (20%) and observation group C (25%), indicating that the treatment effect of observation group B was superior to the other two groups ($\chi^2 = 6.883, p = 0.001 < 0.05$), see **Table 3**.

Table 3. Comparison of adverse reactions among the three groups [n(%)]

Group	n	Anemia	Neutropenia	Thrombocytopenia	Nausea and vomiting	Fever	Infection	Total
Observation group A	20	0 (0.00)	2 (0.10)	0 (0.00)	0 (0.00)	0 (0.00)	2 (0.10)	4 (0.20)
Observation group B	20	1 (0.05)	0 (0.00)	0 (0.00)	1 (0.05)	0 (0.00)	0 (0.00)	2 (0.10)
Observation group C	20	2 (0.10)	0 (0.00)	12 (0.60)	1 (0.05)	1 (0.05)	1 (0.05)	5 (0.25)
χ^2								6.883
<i>p</i>								0.001

3.4. Comparison of Hb recovery time among the three groups

Regarding Hb recovery time, the recovery time required in observation group B (67.45 ± 2.91) was shorter than that in observation group A (83.23 ± 2.12) and observation group C (72.03 ± 1.99), indicating that Hb recovery time is shorter under low-dose, high-frequency treatment ($\chi^2 = 11.772, p = 0.001 < 0.05$), see **Table 4**.

Table 4. Comparison of time for Hb recovery ≥ 90 g/L

Group	Recovery ≥ 30 g/L, days	Recovery ≥ 60 g/L, days	Recovery ≥ 90 g/L, days
Observation group A	51.85 ± 3.29	62.95 ± 2.91	83.23 ± 2.12
Observation group B	39.05 ± 5.16	48.60 ± 4.70	67.45 ± 2.91
Observation group C	45.50 ± 5.92	54.95 ± 5.41	72.03 ± 1.99
χ^2	9.231	0.400	11.772
<i>p</i>	0.010	0.819	0.001

4. Discussion

MDS is a heterogeneous myeloid clonal disease, often manifested as chronic progressive anemia. As the disease

progresses, once thrombocytopenia or severe neutropenia occurs, it may lead to symptoms such as recurrent fever, infection, and bleeding, and progress to AML^[15]. Among them, low-risk MDS has always maintained a high incidence rate in clinical practice. The inducing factors of the disease are more complex, and the negative impact on the health of patients is more serious. There are many treatment methods for this disease in clinical practice, and blood transfusion and platelet therapy have a high implementation rate. However, in order to promote the rapid improvement of the patient's symptoms, it is necessary to adopt the best treatment plan.

Roxadustat is a novel hypoxia-inducible factor and a prolyl inhibitor. When applied to patients, it can stabilize hypoxia-inducible factors, reduce their degradation rate, accelerate the production of erythrocytes in patients, and improve iron regulation by regulating hepcidin levels^[16]. This can lead to a rapid improvement in various symptoms of patients. At the same time, it can regulate the non-specific cellular immune level of patients, which helps to improve the symptoms of myeloproliferative disorders^[17,18]. A phase III study of roxadustat (NCT03263091) showed initial efficacy in the treatment of low-risk MDS patients^[10]. Ikenoue reported a case of LR-MDS patient who failed to respond to EPO receptor activator treatment but recovered from anemia again after treatment with roxadustat and had a prolonged transfusion-free period^[19]. This confirms the effectiveness of roxadustat in the treatment of MDS, but there is no clear report on the administration method and dosage of roxadustat.

In this study, the low-dose, high-frequency drug treatment method was more effective in treating low-risk MDS patients. The recovery effect in observation group B (ORR = 95%) was higher than that in observation group A (ORR = 75%) and observation group C (ORR = 85%) ($\chi^2 = 10.883, p = 0.001 < 0.05$), indicating that roxadustat treatment can improve the overall response rate and facilitate patient recovery; the adverse reaction rate in observation group B (10%) was lower than that in observation group A (20%) and observation group C (25%) ($\chi^2 = 6.883, p = 0.001 < 0.05$), indicating that during medication, Low-dose, high-frequency dosing can effectively alleviate adverse reactions in patients, indicating that roxadustat has a high safety profile in treating low-risk MDS. Simultaneously, the time required for Hb recovery in observation group B (67.45 ± 2.91) was shorter than that in observation groups A (83.23 ± 2.12) and C (72.03 ± 1.99) ($\chi^2 = 11.772, p = 0.001 < 0.05$), suggesting that roxadustat has a positive effect on Hb survival time and can improve patients' immune function. These results indicate that low-dose, high-frequency dosing can effectively improve the treatment effect in low-risk MDS patients, with fewer adverse reactions, relatively high safety, and a positive effect on patient survival time. However, this study has limitations due to its small sample size and incomplete observation indicators. Further research should expand the sample size and add more observation indicators to obtain more complete and accurate results.

5. Conclusion

In summary, when using roxadustat to treat low-risk MDS, it is possible to use a low-dose, high-frequency administration method to improve the treatment effect on low-risk MDS patients.

Disclosure statement

The authors declare no conflict of interest.

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Evaluation of the Efficacy Rate of Rebamipide Combined with Triple Therapy in the Treatment of Senile Peptic Gastric Ulcers

Rong Li

Qilu Hospital of Shandong University, Jinan 250000, Shandong, China

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Abstract: *Objective:* To evaluate the efficacy rate of rebamipide combined with triple therapy in the treatment of senile peptic gastric ulcers. *Methods:* A cohort of 68 elderly patients diagnosed with peptic gastric ulcers was enrolled in this study between January 2022 and December 2024. Using the envelope method for randomization, the patients were divided into two equal groups: a control group administered standard triple therapy and an observation group that received the same triple therapy supplemented with rebamipide. The clinical efficacy, gastric mucosal morphology (mucosal thickness, gland density, active inflammatory cell infiltration, chronic inflammatory cell infiltration), and pepsinogen I/II were compared between the two groups. *Results:* The total effective rate in the observation group was significantly higher than that in the control group, with a statistically significant difference ($p < 0.05$). After treatment, the scores of all items in both groups were significantly lower than those before treatment, and the scores in the observation group were significantly lower than those in the control group, with statistically significant differences ($p < 0.05$). After treatment, the ratios in both groups were significantly higher than those before treatment, and the ratio in the observation group was significantly higher than that in the control group, with statistically significant differences ($p < 0.05$). *Conclusion:* Rebamipide combined with triple therapy can significantly improve the treatment efficacy of senile peptic gastric ulcers, effectively improve the histological status of the gastric mucosa, and promote the recovery of gastric mucosal function, with superior efficacy compared to triple therapy alone.

Keywords: Rebamipide; Triple therapy; Elderly; Peptic gastric ulcer; Gastric mucosal morphology; Pepsinogen

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1. Introduction

With the acceleration of the aging process of the global population structure, the prevention and treatment of digestive system diseases in the elderly have increasingly become a clinical focus. Peptic gastric ulcers have a high incidence rate among the elderly population. Due to characteristics such as physiological functional decline, the coexistence of multiple diseases, and reduced drug tolerance in patients of this age group, the difficulty of

treatment and the risk of recurrence significantly increase ^[1]. The traditional triple therapy, as a common regimen for *Helicobacter pylori* eradication, although having certain therapeutic effects, still presents issues such as slow ulcer healing and incomplete mucosal repair in some elderly patients, affecting overall treatment efficiency and prognostic quality ^[2]. Rebamipide is a gastric mucosal protective agent that can exert protective and repairing effects in multiple aspects by promoting epithelial cell proliferation, inhibiting the release of inflammatory mediators, and enhancing mucosal barrier function ^[3]. Therefore, this study aims to explore the clinical efficacy of rebamipide combined with triple therapy in elderly patients with peptic gastric ulcers through a retrospective analysis:

2. Materials and methods

2.1. General information

A total of 68 elderly patients with peptic gastric ulcers admitted to our hospital from January 2022 to December 2024 were selected and randomly divided into an observation group and a control group using the envelope method, with 34 cases in each group. There were no statistically significant differences in the basic information between the two groups of patients ($p > 0.05$), as shown in **Table 1**. This study was approved by the hospital's ethics committee. This study complies with the relevant ethical principles outlined in the Declaration of Helsinki.

Table 1. Comparison of general information between the two groups of patients ($\bar{x} \pm s/n$)

Characteristic	Observation group (n = 34)	Control group (n = 34)	t/χ^2	p -value
Gender (Male/Female)	18 / 16	19 / 15	0.059	0.808
Age (years)	60–87	61–89	0.043	0.966
	76.15 ± 6.84	76.08 ± 6.73		
Disease duration (years)	1–8	1–9	0.787	0.434
	3.69 ± 1.22	3.91 ± 1.08		

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Age ≥ 60 years old
- (2) Diagnosed with active gastric ulcers through gastroscopy
- (3) Positive *Helicobacter pylori* test results
- (4) Patients are conscious, possess basic communication skills, and can cooperate to complete treatment and follow-up
- (5) Complete clinical data
- (6) Signed informed consent forms

2.2.2. Exclusion criteria

- (1) Patients with concurrent gastric malignancy or suspicious malignant lesions
- (2) Patients who have received systemic treatment with proton pump inhibitors, antibiotics, or gastric mucosal protective agents within the past four weeks

- (3) Patients with a history of allergy to any medication used in this study
- (4) Patients with severe cardiac, hepatic, or renal insufficiency
- (5) Patients with coagulation dysfunction or those currently receiving anticoagulant therapy
- (6) Patients with mental illnesses that prevent cooperation with treatment

2.3. Methods

Patients in the control group received triple therapy: clarithromycin tablets (manufacturer: Livzon Pharmaceutical Group Inc., Livzon Pharmaceutical Factory; National Medical Products Administration Approval Number: H10960227; specification: 0.25 g) at a dose of 250 mg twice daily; amoxicillin capsules (manufacturer: Guizhou Bailing Enterprise Group Pharmaceutical Co., Ltd.; National Medical Products Administration Approval Number: H52020236; specification: 0.25 g) at a dose of 1 g twice daily; lansoprazole enteric-coated tablets (manufacturer: Shantou Special Economic Zone Tuobin Pharmaceutical Factory; National Medical Products Administration Approval Number: H10980136; specification: 15 mg) at a dose of 30 mg once daily. Medications were taken with warm water.

Patients in the observation group received rebamipide treatment in addition to the regimen given to the control group: rebamipide tablets (manufacturer: Beijing Tianheng Pharmaceutical Research Institute Nanyang Tianheng Pharmaceutical Factory; National Medical Products Administration Approval Number: H20255306; specification: 0.1 g) at a dose of 100 mg three times daily, taken with warm water.

The treatment duration for both groups was eight consecutive weeks, and efficacy indicators were evaluated uniformly after the completion of the treatment course.

2.4. Observation indicators

2.4.1. Clinical efficacy

The clinical efficacy of patients in both groups was observed and compared, categorized as follows: cured: complete disappearance of clinical symptoms such as abdominal pain and acid reflux, with complete healing of the ulcer observed under gastroscopy; effective: significant improvement in clinical symptoms, with a reduction in ulcer area of 50% or more observed via gastroscopy; ineffective: no significant relief of clinical symptoms, with a reduction in ulcer area of less than 50% observed under gastroscopy, or even an increase in ulcer area.

The overall effective rate was calculated as the percentage of the sum of cured and effective cases out of the total number of cases.

2.4.2. Gastric mucosal morphology

Observe and compare the gastric mucosal morphology of patients in both groups before and after treatment, including four aspects: mucosal thickness, gland density, active inflammatory cell infiltration, and chronic inflammatory cell infiltration. A four-grade scoring system is employed for evaluation, with each aspect categorized into normal, mild, moderate, and severe based on the severity of the lesion, corresponding to scores of 0 to 3, respectively. A lower total score indicates a better state of gastric mucosal morphology.

2.4.3. Pepsinogen I/II

Fasting venous blood samples are collected from patients in the morning before and after treatment. After serum separation by centrifugation, the concentrations of pepsinogen I and II are determined using chemiluminescence

immunoassay, and their ratio is calculated.

2.5. Statistical methods

Our hospital analyzed the study using the SPSS 21.0 statistical software package. Measurement data are presented as mean \pm standard deviation ($\bar{x} \pm s$) and conform to a normal distribution. Inter-group comparisons are conducted using the *t*-test. Count data are expressed as relative numbers, and inter-group comparisons are performed using the χ^2 test. Clinical efficacy comparisons are made using the rank-sum test, with $p < 0.05$ indicating a statistically significant difference.

3. Results

3.1. Comparison of clinical efficacy between the two groups

The total effective rate in the observation group is significantly higher than that in the control group, with a statistically significant difference ($p < 0.05$). See **Table 2**.

Table 2. Comparison of clinical efficacy between the two groups [n(%)]

Group	n	Cured	Effective	Ineffective	Total effective
Observation group	34	18 (52.94)	14 (41.18)	2 (5.88)	32 (94.12)
Control group	34	12 (35.29)	13 (38.24)	9 (26.47)	25 (73.53)
χ^2					5.314
<i>p</i> -value					0.021

3.2. Comparison of gastric mucosal morphology between the two groups

Before treatment, there are no significant differences in the scores of various aspects of gastric mucosal morphology between the two groups ($p > 0.05$). After treatment, the scores of all aspects in both groups are significantly lower than those before treatment, and the scores in the observation group are significantly lower than those in the control group, with statistically significant differences ($p < 0.05$). See **Table 3**.

Table 3. Comparison of gastric mucosal morphology between the two groups [n(%)]

Group	n	Mucosal thickness		Gland density		Active inflammatory cell infiltration		Chronic inflammatory cell infiltration	
		Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx	Pre-Tx	Post-Tx
Observation	34	2.35 \pm 0.48	0.82 \pm 0.39*	2.29 \pm 0.45	0.76 \pm 0.43*	2.41 \pm 0.51	0.68 \pm 0.18*	2.18 \pm 0.40	0.59 \pm 0.13*
Control	34	2.32 \pm 0.44	1.35 \pm 0.46*	2.26 \pm 0.42	1.41 \pm 0.44*	2.38 \pm 0.49	1.52 \pm 0.43*	2.21 \pm 0.43	1.47 \pm 0.42*
<i>t</i> -value		0.269	5.124	0.284	6.350	0.247	10.507	0.298	11.671
<i>p</i> -value		0.789	< 0.001	0.777	< 0.001	0.805	< 0.001	0.767	< 0.001

Note: Compared with the same group before treatment, * $p < 0.05$.

3.3. Comparison of pepsinogen I/II ratios between the two groups

Before treatment, the pepsinogen I/II ratio was comparable between the two groups ($p > 0.05$). Following treatment, both groups exhibited a significant increase in the ratio from their baseline levels. The observation

group demonstrated a more pronounced elevation, resulting in a significantly higher ratio than that of the control group ($p < 0.05$). See **Table 4**.

Table 4. Comparison of pepsinogen I/II ratios before and after treatment between the two groups ($\bar{x} \pm s$)

Group	n	Before treatment	After treatment
Observation group	34	5.82 ± 1.36	$9.45 \pm 1.87^*$
Control group	34	5.91 ± 1.41	$7.23 \pm 1.52^*$
<i>t</i> -value		0.268	5.372
<i>p</i> -value		0.790	< 0.001

Note: Compared with the same group before treatment, $*p < 0.05$.

4. Discussion

Peptic gastric ulcers have a high prevalence rate among the elderly population, and their occurrence and development are closely related to various pathophysiological mechanisms, such as the deterioration of the gastric mucosal barrier function, *Helicobacter pylori* infection, and enhanced attack factors like gastric acid and pepsin. Elderly patients often experience delayed ulcer healing and an increased risk of recurrence due to reduced mucosal blood flow, decreased cell renewal capacity, and the presence of multiple chronic diseases^[4].

As the standard treatment regimen for *Helicobacter pylori*-associated gastric ulcers, triple therapy involves the use of lansoprazole to inhibit gastric acid secretion, combined with clarithromycin and amoxicillin for synergistic bactericidal effects. However, this regimen primarily focuses on suppressing attack factors and has limited effects on the structural repair and functional reconstruction of the gastric mucosa. Some patients still experience issues such as poor ulcer healing quality and slow resolution of inflammation^[5]. In the control group of this study, 26.47% of patients still had poor therapeutic effects, suggesting that relying solely on bactericidal and acid-suppressing therapies has limitations in the elderly population.

Rebamipide, as a gastric mucosal protective agent, has a multi-target mechanism to promote mucosal repair^[6]. In the observation group of this study, the overall effective rate increased to 94.12% after the combined use of rebamipide. This result may be related to rebamipide's ability to activate the epidermal growth factor receptor signaling pathway, promote the proliferation and migration of gastric mucosal cells, and accelerate the epithelialization process at the ulcer margin. Meanwhile, this drug can also enhance the expression of heat shock protein 70, inhibit the activation of the nuclear factor- κ B pathway, and reduce the release of pro-inflammatory factors such as interleukin-8 and tumor necrosis factor- α , thereby effectively controlling mucosal inflammatory responses. In addition, rebamipide can increase gastric mucus secretion and improve mucosal microcirculation, further consolidating the gastric mucosal barrier function^[7,8].

In terms of pepsinogen levels, the pepsinogen I/II ratio in the observation group was significantly higher than that in the control group after treatment. The increase in this ratio primarily reflects the recovery in the number and function of chief cells in the gastric corpus glands, suggesting that rebamipide not only promotes mucosal repair structurally but also aids in restoring the physiological state of gastric glands functionally, thereby improving the gastric internal environment and reducing the risk of further mucosal damage^[9].

From the perspective of therapeutic mechanisms, the addition of rebamipide compensates for the deficiencies of triple therapy in the active repair of mucosa, forming a treatment strategy that emphasizes both bactericidal

action and mucosal repair. Its remarkable efficacy in elderly patients may be closely related to characteristics such as decreased mucosal self-healing capacity and persistent inflammatory states in this population^[10]. By providing exogenous repair signals and inhibiting inflammatory cascades, rebamipide helps break the vicious cycle commonly seen in elderly patients with gastric ulcers.

5. Conclusion

In conclusion, rebamipide combined with triple therapy can significantly improve the treatment outcomes for elderly patients with peptic gastric ulcers, effectively improving the histological state of the gastric mucosa and promoting functional recovery of the gastric mucosa, with superior efficacy compared to triple therapy alone.

Disclosure statement

The author declares no conflict of interest.

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Root Resorption Caused by Thin Roots Combined with Reciprocal Movement: A Case Report and Nursing Care Points

Aoshuang Wang*, Jiajia Wei

Dental Department, TaiHe Hospital, Hubei University of Medicine, Shiyan, Hubei, China

**Author to whom correspondence should be addressed.*

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Abstract: Root resorption is a significant complication in orthodontic treatment, with thin roots and reciprocal movement being recognized as high-risk factors. This paper reports a case of a 19-year-old female patient who underwent orthodontic treatment for dental irregularity. The patient had thin roots in the maxillary lateral incisors 12 and 22. During treatment, tooth 22 experienced reciprocal movement of labial expansion followed by retraction, while tooth 12 adopted passive ligation to reduce reciprocal movement. After 23 months of straight-wire extraction treatment, good occlusal relationships were achieved, but significant root resorption occurred in teeth 12 and 22, with tooth 22 showing more severe resorption. This case confirms the synergistic effect between thin roots and reciprocal movement, demonstrating that thin roots are more sensitive to reciprocal movement stimulation, producing a synergistic amplification effect. Additionally, standardized nursing guidance and patient compliance management play important roles in reducing resorption risk. This case emphasizes the importance of pretreatment risk assessment, individualized treatment strategy formulation, and comprehensive nursing intervention throughout treatment, providing reference for clinical prevention of root resorption.

Keywords: Root resorption; Orthodontic treatment; Thin roots; Reciprocal movement; Nursing intervention; Case report

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1. Introduction

Root resorption is an inevitable biological response in orthodontic treatment, with an incidence rate of over 90%^[1]. While mild resorption is usually of no clinical significance, moderate to severe resorption can seriously affect the long-term stability of teeth and may even lead to tooth mobility and loss. Among numerous risk factors, thin roots and reciprocal movement are considered two key factors leading to significant root resorption^[2]. Thin roots increase resorption susceptibility due to stress concentration effects, while reciprocal movement exacerbates the resorption process by disrupting normal repair window periods^[3]. When these two factors coexist, they often produce a synergistic amplification effect, resulting in more severe root damage. However, clinical evidence

regarding this synergistic effect is relatively limited, particularly lacking specific guidance principles in treatment strategy comparison and nursing management. This paper reports a typical case to analyze the occurrence process of severe root resorption caused by thin roots combined with reciprocal movement, explores its pathophysiological mechanisms, and combines nursing intervention points to provide prevention strategies and management experience for clinicians.

2. Case report

2.1. General information and clinical examination

Patient Wang, female, 19 years old, presented in March 2021 with the chief complaint of “dental irregularity affecting aesthetics”. The patient had no history of trauma, no harmful habits such as bruxism or clenching, regular menstrual cycle, and no history of systemic diseases or drug allergies.

Facial examination showed a convex profile, basically symmetrical face, aligned upper midline, and underdeveloped mandible and chin. Intraoral examination revealed bilateral molars in neutral to mesial relationship, bilateral canines in distal relationship, normal anterior overbite and overjet (overbite 2 mm, overjet thin roots and reciprocal movement are considered two key factors leading to significant root resorption mm), severe crowding in upper and lower dental arches (maxillary crowding 8 mm, mandibular crowding 4 mm), teeth 13 and 23 positioned labially outside the arch, teeth 12 and 22 positioned palatally, teeth 35 and 45 lingually ectopic eruption, and good overall oral hygiene. Functional examination showed normal mouth opening and closing patterns, mouth opening of 38 mm, with no temporomandibular joint clicking or pain.

Radiographic examination showed complete dentition on panoramic radiograph, with the key finding being significantly thin roots of teeth 12 and 22 (root-crown ratio approximately 1:1, much smaller than the normal 1:5–2:1), presenting as short conical shapes^[4]. Cephalometric analysis indicated SNA angle 82°, SNB angle 76° (2° smaller than normal), ANB angle 6° (2° larger than normal), suggesting normal maxillary development and mild mandibular deficiency. The diagnosis was skeletal Class II malocclusion with Angle Class I malocclusion and severe upper and lower dental crowding, with the high-risk factor of thin roots in teeth 12 and 22.

2.2. Treatment plan and nursing management

Straight-wire extraction treatment was employed, extracting teeth 14, 24, 34, and 44, with mini-implants for anchorage control. Given the high-risk characteristics of thin roots in teeth 12 and 22, differentiated treatment strategies were developed: tooth 12 adopted passive ligation with light force (25 g) to avoid reciprocal movement; tooth 22, due to anatomical position limitations, was directly incorporated into the treatment system and experienced reciprocal movement of labial expansion (50 g force for 3 months) followed by retraction (100 g force for 6 months), with a total movement distance of approximately 9 mm.

For nursing management, high-risk patient treatment files were established, standardized oral hygiene instruction was provided at each visit, emphasizing plaque control (PLI < 0.5), and patient compliance assessment scales were established. Strict 4–6 weeks follow-up intervals were maintained, radiographic monitoring was conducted every 6 months, and health education plans were developed, including dietary guidance and psychological support.

2.3. Treatment results and follow-up

After 23 months of treatment, the patient achieved good orthodontic results: upper and lower dental arches were well aligned, bilateral canine-molar neutral relationships were established, normal anterior overbite and overjet (overbite 2 mm, overjet 2.5 mm), aligned midlines, and good masticatory function.

Post-treatment radiographic evaluation showed significant root resorption in both teeth 12 and 22, with tooth 22 being more severely affected, presenting typical apical serrated resorption with resorption length approximately 1/3 of root length (about 4 mm), while tooth 12 had relatively milder resorption at approximately 1/4 of root length (about 3 mm). Although both teeth had the same thin root risk factor, significant differences existed in results after experiencing different treatment strategies. The roots of other teeth showed basically no abnormal changes.

During follow-up, the root resorption situation was explained in detail to the patient, and an individualized retention plan was developed: maxillary lingual fixed wire (13–23) combined with nighttime vacuum-formed retainer, and mandibular canine-to-canine fixed retainer. A regular follow-up system was established with clinical examinations every 3 months and radiographic monitoring every 6 months.

3. Discussion

3.1. Analysis of synergistic effect mechanisms

This case provides valuable evidence for understanding the synergistic effect of thin roots and reciprocal movement in causing root resorption. By comparing the outcome differences between teeth 12 and 22 under the same conditions but with different treatment strategies, it clearly reveals the crucial role of reciprocal movement in root resorption. Tooth 22 experienced typical “expansion followed by retraction” reciprocal movement, while tooth 12 effectively avoided this risk through passive ligation strategy. The final difference in resorption severity (tooth 22: 1/3 root length vs tooth 12: 1/4 root length) confirmed the adverse effects of reciprocal movement.

From a pathophysiological perspective, thin roots create stress concentration that provides the anatomical basis for resorption. According to the stress formula ($\sigma = F/A$), thin roots experience exponentially increased unit stress, making the periodontal ligament and root surface more susceptible to ischemia, necrosis, and inflammation^[5]. Reciprocal movement applies reverse stimulation during the repair window period, interrupting the normal repair process, with each new movement creating additional damage in vulnerable areas, forming cumulative pathological changes.

This case demonstrates the synergistic amplification effect of two risk factors, namely the “1 + 1 > 2” phenomenon. This synergistic effect involves multiple levels: at the molecular biology level, thin roots show higher sensitivity to inflammatory factors and resorption-related enzymes; at the cellular level, odontoblasts and periodontal ligament fibroblasts exhibit altered stress response patterns; at the tissue level, thin roots have low microvascular network density with insufficient local buffering capacity^[6]. The destructive effects of reciprocal movement are significantly amplified under this susceptible background.

3.2. Nursing management and clinical translation value

In innovative nursing management practices, this case demonstrates that implementing individualized and systematic nursing intervention strategies for high-risk patients has irreplaceable value. Through establishing specialized high-risk patient management files and standardized operational procedures, implementing more frequent and comprehensive oral hygiene instruction, compliance monitoring, and psychological support, the

adverse effects of various promoting factors on root resorption can be reduced across multiple dimensions. Particularly noteworthy is the nursing team's use of multimedia teaching methods and individualized communication techniques in patient education, which not only improved patients' cognitive level regarding the disease and treatment process but more importantly cultivated patients' self-management abilities and treatment compliance. This comprehensive, all-around nursing model played a positive role in reducing inflammation levels, maintaining oral health homeostasis, and early identification of abnormal signs, providing important guarantees for treatment success.

From a clinical translational medicine perspective, the findings of this case have important implications for establishing individualized treatment decision-making models. By integrating patients' basic disease information, anatomical morphological characteristics, biomechanical parameters, and psychosocial factors, more precise risk prediction models can be constructed to achieve truly personalized medicine. Additionally, this case provides clear clinical demand orientation for developing new biomaterials and treatment technologies, such as developing bioactive materials with root repair-promoting functions and designing more precise force control systems.

3.3. Clinical guidance significance and development directions

The clinical insights from this case have important and far-reaching practical guidance value, which can be summarized into several key points: First, comprehensive pretreatment risk assessment is the key to preventing severe root resorption, which should include not only routine clinical and radiographic evaluations but also establish systematic risk scoring systems for comprehensive assessment and graded management of multiple factors such as root morphology, movement distance, and movement patterns. Second, differentiated and individualized treatment strategies should be developed for patients with different risk levels, minimizing unnecessary reciprocal movement and excessive force through precise biomechanical design, optimized movement path planning, and dynamic force adjustment. Third, dynamic monitoring and timely adjustment mechanisms during treatment are equally important; establishing standardized monitoring procedures and early warning systems with regular radiographic examinations and biological indicator detection can enable early detection of resorption signs and timely strategy adjustments. Fourth, multidisciplinary collaborative modern nursing management models play an irreplaceable core role in comprehensive management of high-risk patients, significantly improving treatment safety, effectiveness, and predictability through standardized nursing procedures, individualized intervention measures, and continuous health education.

Meanwhile, this case profoundly suggests that we need to continue efforts and improvements in the following aspects: establishing more scientific and comprehensive risk assessment systems and prediction models, developing more detailed and standardized nursing procedures and operational guidelines, developing more advanced and precise monitoring technologies and early warning systems, and cultivating more professional and comprehensive medical and nursing teams and management personnel. Only through these systematic improvements and enhancements can we truly improve the overall safety and predictability of orthodontic treatment, providing patients with higher quality, safer, and more individualized medical services, and promoting the continuous development and progress of orthodontics.

4. Conclusion

This case report systematically confirms the synergistic mechanism of thin roots and reciprocal movement in

root resorption after orthodontic treatment, providing important evidence-based medical evidence for this clinical phenomenon. The case deepened understanding of the pathophysiological mechanisms of root resorption at the theoretical level and provided prevention strategies and management experience for clinicians at the practical level. The study emphasizes that when facing patients with high-risk factors such as thin roots, cautious individualized treatment strategies must be adopted, maximally protecting root health while achieving ideal treatment outcomes through precise biomechanical control, standardized nursing management, and systematic monitoring mechanisms, providing patients with high-quality and safe medical services.

Disclosure statement

The authors declare no conflict of interest.

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Application of Quality Control Circle Activities in Reducing Loss Rate During Storage of Traditional Chinese Medicine Decoction Pieces: An Effectiveness Study

Bin Liu, Meiling Shao, Li Chen*

Pharmacy Department, TaiHe Hospital, Hubei University of Medicine, Shiyan, Hubei, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To investigate the effectiveness of Quality Control Circle (QCC) activities in reducing the loss rate during storage of Traditional Chinese Medicine (TCM) decoction pieces in our hospital pharmacy department. *Methods:* A QCC team was established to systematically analyze the causes of TCM decoction piece losses. Using quality improvement tools including Pareto charts, the 80/20 rule, and fishbone diagrams, we identified key areas for improvement and developed targeted intervention strategies. The study period spanned from January to December 2023, with pre-intervention data collected from January to December 2022. Loss rates were calculated and compared before and after QCC implementation. *Results:* According to the “80/20 rule” analysis, the primary improvement targets were identified as inadequate maintenance of decoction pieces and dispensing losses. Following QCC implementation, the loss rate of TCM decoction pieces decreased significantly from 1.27% (pre-intervention) to 0.65% (post-intervention), achieving an improvement rate of 47.40%. The total monetary loss decreased from 9,592.62 RMB to 4,546.97 RMB. *Conclusion:* QCC activities can effectively reduce the loss rate of TCM decoction pieces in hospital pharmacy departments, improve the quality of herbal medicines, ensure patient medication safety, and enhance pharmaceutical service quality. This systematic approach provides a valuable framework for continuous quality improvement in TCM pharmacy management.

Keywords: Quality control circle; Traditional Chinese Medicine decoction pieces; Storage; Loss rate; Pharmacy management

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1. Introduction

Traditional Chinese Medicine (TCM) decoction pieces serve as essential therapeutic tools in clinical practice, enabling syndrome differentiation and targeted treatment. Their quality and dosage accuracy are critical

prerequisites for ensuring medication safety and therapeutic efficacy, representing a cornerstone of hospital pharmacy management. However, during the entire pharmaceutical process from procurement to dispensing, TCM decoction pieces inevitably experience quality deterioration and quantitative losses due to their inherent characteristics and various factors including packaging, transportation, storage conditions, and dispensing procedures^[1].

TCM decoction pieces are particularly susceptible to storage-related deterioration due to their complex chemical compositions and diverse physicochemical properties. Common forms of quality degradation include insect infestation, mold growth, oil rancidity, moisture loss, discoloration, volatile component evaporation, and fermentation, with insect damage and mold contamination being the most prevalent. These losses not only compromise dosing accuracy and complicate pharmacy management but also represent significant waste of valuable natural resources^[2].

Quality Control Circle (QCC), first introduced by Dr. Kaoru Ishikawa in Japan in 1962, is a systematic quality improvement methodology that empowers frontline staff to organize into quality improvement circles. Using scientific management tools, QCC teams develop effective solutions for real-world operational challenges. This approach has gained widespread adoption in healthcare systems and has demonstrated significant efficacy in enhancing medication safety and operational efficiency in hospital pharmaceutical services^[3].

The established QCC team has demonstrated substantial proficiency in quality improvement methodologies and possesses the necessary expertise to address complex operational challenges. Given the significant economic impact and therapeutic implications of TCM decoction piece losses, this study investigated the effectiveness of QCC activities in systematically reducing storage-related loss rates while identifying primary contributing factors and developing sustainable improvement strategies.

2. Materials and methods

This study employed a PDCA (Plan-Do-Check-Act) cycle management approach to implement QCC activities in the TCM pharmacy department from January to December 2023. The effectiveness was assessed by comparing TCM decoction piece loss rates before implementation (January-December 2023) with post-implementation results (January-December 2024).

A multidisciplinary QCC team was established using brainstorming methodology, with theme selection conducted through evaluation of five criteria: administrative policy alignment, importance, urgency, team capability, and feasibility. Based on previous successful QCC implementations, the team selected “Reducing Loss Rate During TCM Decoction Piece Storage” as the improvement focus.

2.1. Baseline analysis

Loss data were collected from January-December 2023. The pharmacy managed 489 different TCM species, with 363 species (74.23%) susceptible to storage losses. Total monetary loss was 9,592.62 RMB with approximately 11 kg of material lost, resulting in a loss rate of 1.27%. Using brainstorming methodology and checklists, four primary loss causes were identified: inadequate decoction piece maintenance, dispensing losses, poor inventory turnover, and weighing errors. According to the 80/20 rule, inadequate maintenance and dispensing losses were determined as primary improvement targets.

2.2. Target setting

Based on the baseline loss rate of 1.27‰ and using the 80/20 rule with team capability calculated at 60%, the target value was set at $\leq 0.667\%$ using the formula: $\text{Target} \leq \text{Current value} - (\text{Current value} \times \text{Improvement focus} \times \text{Team capability})$.

2.3. Root cause analysis

Comprehensive cause analysis was conducted using fishbone diagrams examining personnel, materials, methods, machinery, and environment. Key factors included inadequate maintenance practices, insufficient responsibility, processing losses, excessive inventory, inadequate equipment capacity, and poor environmental conditions.

2.4. Interventions

Five primary interventions were implemented

- (1) Flexible staffing adjustments during peak periods
- (2) Focused work protocols with reward/penalty systems
- (3) Regular calibration of weighing instruments
- (4) Dedicated personnel for systematic shelf maintenance
- (5) Daily monitoring of temperature and humidity in storage areas and refrigeration units

2.5. Data analysis

Loss rates were calculated as: $\text{Loss rate (\%)} = \text{Total loss amount} / \text{Total inventory value} \times 1000$. Improvement rate was calculated as: $\text{Improvement rate (\%)} = [(\text{Pre-intervention} - \text{Post-intervention}) / \text{Pre-intervention}] \times 100\%$. Statistical analysis compared monetary losses and loss rates between the two study periods. Tangible outcomes were evaluated through comparison of pre- and post-intervention data, while intangible outcomes were assessed through staff self-evaluation scores displayed using radar charts.

3. Results

3.1. Tangible outcomes

Following QCC implementation, the loss rate of TCM decoction pieces decreased significantly from 1.27% (pre-intervention) to 0.65% (post-intervention), representing a 48.82% improvement rate. The total monetary loss decreased from 9,592.62 RMB to 4,546.97 RMB, achieving a reduction of 5,045.65 RMB. The target achievement rate was 102.57% (target: $\leq 0.667\%$, achieved: 0.65%).

3.2. Loss distribution analysis

Among the 489 TCM species managed, 363 species (74.23%) were susceptible to storage losses in the pre-intervention period. Post-intervention analysis showed that losses were primarily concentrated in specific categories, with targeted interventions effectively addressing the main contributing factors identified through the 80/20 rule analysis.

3.3. Cost-benefit analysis

The annual cost reduction of 5,045.65 RMB demonstrates the economic effectiveness of QCC implementation.

When extrapolated across similar hospital pharmacy departments, this intervention model shows significant potential for system-wide cost savings and resource conservation.

3.4. Intangible outcomes

Staff evaluation scores improved across all assessed domains using radar chart analysis. Team members demonstrated enhanced problem-solving capabilities, increased job satisfaction, improved communication skills, and stronger commitment to quality improvement initiatives. The QCC process fostered a culture of continuous improvement and collective responsibility for quality outcomes.

3.5. Implementation success factors

The systematic application of quality improvement tools including Pareto analysis, fishbone diagrams, and PDCA cycles proved effective in identifying root causes and developing targeted solutions. The multidisciplinary team approach and structured methodology ensured comprehensive problem-solving and sustainable improvement.

4. Discussion and conclusion

The results demonstrate that QCC activities can effectively reduce storage losses of TCM decoction pieces through systematic problem identification and targeted interventions. The 48.82% reduction in loss rate from 1.27% to 0.65% exceeded the predetermined target, indicating the effectiveness of this quality improvement approach in TCM pharmacy management.

The application of structured quality improvement tools proved critical to project success^[4]. Pareto analysis enabled identification of primary loss contributors, focusing improvement efforts on inadequate maintenance and dispensing losses which accounted for over 80% of total losses. The fishbone diagram methodology provided comprehensive root cause analysis across personnel, materials, methods, machinery, and environmental factors, ensuring no critical contributors were overlooked.

The five implemented interventions addressed both immediate operational issues and underlying systemic problems. Flexible staffing during peak periods and focused work protocols with accountability measures directly targeted personnel-related causes, while equipment calibration and environmental monitoring addressed technical factors. The assignment of dedicated maintenance personnel created sustainable long-term improvement by establishing clear responsibility and systematic oversight.

The annual cost reduction of 5,045.65 RMB demonstrates significant economic benefits beyond the immediate quality improvements. This cost savings represents approximately 52.6% of the original losses, indicating substantial return on investment for QCC implementation. The financial benefits extend beyond direct cost savings to include improved inventory accuracy, reduced waste, and enhanced therapeutic reliability.

The success of this QCC implementation suggests broader applications for quality improvement in TCM pharmacy management. The methodology can be adapted to address other operational challenges such as prescription accuracy, dispensing efficiency, or inventory management^[5]. The systematic approach provides a replicable framework for continuous quality improvement in traditional medicine settings.

This study was conducted in a single institution with specific operational characteristics, which may limit generalizability to other settings. The one-year implementation period may not capture long-term sustainability of improvements, and continued monitoring is necessary to ensure maintained effectiveness. Long-term follow-up

studies should evaluate sustainability of improvements and identify additional applications of QCC methodology in TCM pharmacy operations. Expansion to multi-center studies would strengthen evidence for broader implementation across healthcare systems.

Disclosure statement

The authors declare no conflict of interest.

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The Value of Vestibular Rehabilitation Training Instruction in the Treatment of Sudden Deafness Accompanied by Vertigo

Tingting Jiang, Xiaorong Yang*, Juxiang Shang, Juan Yao, Ruiqi Li, Zhiquan Peng

Shaanxi Provincial People's Hospital, Xi'an 710068, Shaanxi, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To analyze the necessity and effectiveness of vestibular rehabilitation training instruction in the treatment of sudden deafness accompanied by vertigo. *Methods:* Sixty medical staff who learned the treatment methods for sudden deafness accompanied by vertigo (vestibular rehabilitation training) from January 2024 to February 2025 were selected as the research subjects. They were divided into two groups according to the time of study: the control group, who participated in the training teaching first, and the observation group, who participated later. Each group had 30 people. The control group received conventional training, while the observation group underwent continuous quality improvement. The effects and assessment results of different teaching methods were compared. *Results:* The theoretical and practical assessment scores of medical staff in the observation group were higher than those in the control group ($p < 0.05$); the satisfaction of medical staff in the observation group with the teaching mode was higher than that in the control group ($p < 0.05$). *Conclusion:* Vestibular rehabilitation training has significant effects on sudden deafness accompanied by vertigo. Training medical staff not only enhances their understanding of training methods but also enables them to provide specialized guidance to patients, improving their vertigo condition.

Keywords: Vestibular rehabilitation training instruction; Sudden deafness; Vertigo

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1. Introduction

Sudden deafness is a relatively common otolaryngological disease, with some patients experiencing vertigo, which has a significant impact on their quality of life. Sudden deafness is a sudden onset hearing impairment disease, often accompanied by ear fullness and tinnitus, further exacerbating patients' discomfort. More than 30% of patients develop vertigo, which affects their ability to live to some extent and may also lead to anxiety and depression ^[1]. Vestibular rehabilitation training is a non-pharmacological and non-surgical treatment method, which is widely recognized by medical staff. However, some medical staff have not mastered the training methods,

and departments need to provide training for medical staff to enable them to master balance training and eye movement training methods in vestibular rehabilitation training, and provide rehabilitation guidance for patients^[2]. Therefore, this study takes otolaryngological medical staff as the research object to analyze the methods and effects of vestibular rehabilitation training guidance.

2. Materials and methods

2.1. General information

Sixty medical staff who studied the treatment method for sudden deafness accompanied by vertigo (vestibular rehabilitation training) from January 2024 to February 2025 were selected as the research subjects. They were grouped according to the time of study, with those who participated in the training and teaching first serving as the control group and those who participated later serving as the observation group, with 30 individuals in each group.

2.1.1. Control group

19 males and 11 females, aged 25–49 (36.32 ± 4.18) years, with working experience ranging from 3 to 25 years, averaging (16.43 ± 2.10) years, including 16 doctors and 14 nurses.

2.1.2. Observation group

18 males and 12 females, aged 25–49 (36.43 ± 4.12) years, with working experience ranging from 3 to 25 years, averaging (16.32 ± 2.15) years, including 17 doctors and 13 nurses; there was no statistically significant difference in the basic information between the two groups of medical staff ($p > 0.05$).

2.2. Method

2.2.1. Control group

The control group received conventional vestibular rehabilitation training instruction. The department provided 2 practical sessions and 5 theoretical sessions. The theoretical sessions covered vestibular anatomical structures and physiological knowledge related to sudden deafness combined with vertigo, enabling medical staff to understand the causes of the disease and the necessity of training. The practical sessions involved specialist doctors providing training guidance to medical staff, demonstrating through their own examples, and after the 2 practical sessions, practical videos were distributed to medical staff for self-study.

2.2.2. Observation group

Continuous quality improvement teaching was adopted.

(1) Theoretical teaching

During this stage of teaching, the supervising teacher prepared courseware in advance, including pathological knowledge and vestibular function training methods, such as specific training methods and stimulating the vestibular system to help patients regain their sense of balance, improve vertigo symptoms, and enhance blood flow in the inner ear. Theoretical teaching was conducted twice, and during the other times, medical staff were instructed to actively learn and memorize, with weekly assessments.

(2) Practical teaching

This course was conducted five times. For example, during static balance training, teaching was

conducted through illustrations and text. The purpose of this training was to enhance patients' balance ability in a static state, with clear instructions on the training points. The supervising teacher demonstrated the training method for standing on both feet, with feet separated shoulder-width apart, keeping the body straight, eyes looking straight ahead, and hands naturally vertical. Medical staff were reminded to place their weight on both feet, feel the contact between the soles of their feet and the ground, and maintain body stability. This trained balance ability. During dynamic balance training, patients were first trained on balance control during movement. During the learning period, medical staff were instructed to keep their legs shoulder-width apart, keep their upper body straight, and move their body slowly without swaying, such as stepping with the right foot first and then following with the left foot. The supervising teacher emphasized precise learning and following the movements. Subsequently, adaptive training and visual and auditory training were conducted, with each course learning one training method. The courses were integrated into videos for medical staff to learn independently after class.

(3) Case discussion

To enhance the pertinence of vestibular rehabilitation training, the supervising teacher led medical staff to discuss teaching methods. Through successful case presentations, correct exercise methods were clarified, and vestibular rehabilitation training methods were matched according to each patient's individual needs, with appropriate adjustments to training intensity to achieve the best training effect. Failure cases were also presented, such as unreasonable training intensity and poor compliance. Through case analysis and discussion, medical staff integrated theory and practice, deepened their understanding, and improved teaching quality.

2.3. Observation indicators

(1) Assessment results

The theoretical score and practical score are investigated. The theoretical score is assessed through a questionnaire survey, while the practical score is evaluated through simulated drills. Both scores are on a 100-point scale, with a higher score indicating a better assessment result.

(2) Satisfaction

Survey the satisfaction of medical staff towards teaching methods, including very satisfied, satisfied, and dissatisfied.

2.4. Statistical analysis

The study employed SPSS 27.0 software for statistical analysis of the data. Measurement data were represented by mean \pm standard deviation ($\bar{x} \pm s$), with a test value of t . Enumeration data were represented by frequency and percentage, and were subjected to chi-square test. A p -value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of assessment scores between two groups of medical staff

The theoretical and practical assessment scores of medical staff in the observation group were higher than those in the control group ($p < 0.05$), as shown in **Table 1**.

Table 1. Comparison of assessment scores between two groups of medical students ($\bar{x} \pm s$, points)

Group	Number of cases	Theoretical score	Practical score
Observation group	30	91.34 \pm 2.13	91.28 \pm 1.83
Control group	30	83.32 \pm 2.73	85.39 \pm 2.01
<i>t</i>		6.832	5.812
<i>p</i>		0.001	0.001

3.2. Comparison of satisfaction with teaching mode between two groups of medical staff

The satisfaction of medical staff in the observation group towards the teaching mode was higher than that in the control group ($p < 0.05$), as shown in **Table 2**.

Table 2. Comparison of satisfaction with teaching mode between two groups of medical staff (n, %)

Group	Number of cases	Very satisfied	Satisfied	Dissatisfied	Satisfaction rate
Observation group	30	14 (43.33)	16 (53.33)	0 (0.00)	30 (100.00)
Control group	30	10 (33.33)	14 (46.67)	6 (20.00)	24 (80.00)
χ^2					5.712
<i>p</i>					0.024

4. Discussion

Sudden deafness accompanied by vertigo symptoms is relatively typical, encompassing vertigo, hearing loss, and tinnitus. Vertigo is a prominent condition, typically manifesting as dizziness and shaking, where patients feel the surrounding environment rapidly spinning, which may even affect their walking ability. After a vertigo attack, nausea and vomiting, pale complexion, and sweating are common. Some patients experience nystagmus. Hearing loss typically occurs suddenly, decreasing rapidly within minutes or hours, with varying degrees of severity. Tinnitus is a common symptom, where patients experience persistent buzzing, ringing, or other sounds in the ear before hearing loss, and some patients feel a sense of ear blockage. From the perspective of the underlying pathogenesis, it may be due to blood circulation disorders in the inner ear. The blood vessels in the inner ear are delicate, making them prone to thrombosis, vasospasm, increased blood viscosity, or insufficient blood supply. Hypoxia can damage the inner ear capillaries and auditory nerves. Some patients have a history of upper respiratory tract infections, such as mumps virus and influenza virus, which directly damage the nerves and inner ear structures. If patients suffer from autoimmune diseases, it may cause the immune system to mistakenly attack the inner ear tissues or lead to inflammatory cell damage. An imbalance in the inner ear lymph circulation may result in rupture of the membranous labyrinth and damage to hair cell function, triggering sudden deafness accompanied by vertigo. Other factors include ototoxic drugs, trauma and pressure, tumors, and neurological disorders.

For this disease, pure tone audiometry is often used to detect patients' hearing thresholds at different frequencies, facilitating accurate assessment of the extent of hearing loss. Conventional clinical therapies include pharmacotherapy and hyperbaric oxygen therapy. Among them, pharmacotherapy is a commonly used method, involving medications such as corticosteroids, neurotrophic drugs, and microcirculation-improving

drugs. Corticosteroids can exert anti-inflammatory and anti-edematous effects, reducing inflammation in the ear, promoting hearing recovery, and improving vertigo symptoms. In practice, drugs such as dexamethasone and prednisone are commonly used. Microcirculation-improving drugs commonly include ginkgo biloba extract and alprostadil. Neurotrophic drugs such as mecobalamin and vitamin B12 are commonly used to promote nerve cell metabolism and protect inner ear hearing function. However, these methods also have limitations, such as a high risk of adverse reactions, which can harm patients' health. Therefore, medical staff need to learn vestibular rehabilitation training to improve the condition of patients with sudden deafness, understand its principles, and implement it smoothly.

Vestibular rehabilitation training is a non-pharmacological and non-surgical therapy that has demonstrated significant efficacy in the treatment of patients with sudden deafness accompanied by vertigo. The vestibular system perceives head movements and positional changes, transmitting the information through the central nervous system. After receiving the information, the central nervous system regulates muscle relaxation and contraction through efferent muscle commands, maintaining body balance. The vestibular system is closely related to eye movements, and this association is achieved through vestibular reflexes. Vestibulo-ocular reflex is an important physiological reflex that acts on head movements, maintaining clear vision through the reciprocal movement of the eyeballs.

Under scientific teaching guidance, medical staff can master the theory and practical skills of vestibular rehabilitation training, providing patients with scientific and personalized rehabilitation training. During the theoretical knowledge teaching period, a comprehensive and in-depth explanation of vestibular anatomical structures and physiological knowledge lays the foundation for medical staff to understand the knowledge ^[3]. Practical training focuses on the practical operation ability and skills of medical staff. Through various training methods such as static balance training and dynamic balance training, combined with case analysis and practical training, medical staff can grasp the key points of various training methods and ensure patient safety during training ^[4]. For example, during static balance training, medical staff learn how to adjust the training intensity and exercise time according to the patient's condition to achieve the desired training effect ^[5]. The observation group implemented standardized training, reasonably planning the time for theoretical and practical courses, which significantly improved the assessment scores and training satisfaction of medical staff. In practical teaching, standardized vestibular rehabilitation training teaching guidance is a complex process, covering assessment and diagnosis, plan formulation, training implementation, and effect evaluation. For example, during the assessment stage, rehabilitation therapists should understand the patient's medical history, including the onset period and symptoms of sudden deafness and vertigo, and comprehensively complete vestibular function examinations, such as electronystagmography and vestibular evoked myogenic potentials, to assess the impairment of vestibular function. During the teaching process, medical staff develop a rehabilitation plan for patients, such as setting clear teaching goals and learning vestibular function training, including vertigo, balance training, and improving eye control ability. During the training process, medical staff should grasp the training intensity, understand the necessity of gradual and progressive training, and avoid excessive initial training intensity that may burden patients. For example, during the teaching period, start with simple static balance training, then allow patients to adapt to the training frequency and transition to dynamic balance training, with the training duration extended accordingly ^[6]. This avoids the rapid increase in training intensity, which may cause fatigue and fear in patients and affect their enthusiasm for training. Encouraging patients to actively cooperate is very important. Rehabilitation therapists introduce the necessity of vestibular rehabilitation training to patients, so that they understand the

training goals and expectations. Teachers need to explain the significance of encouragement, making medical staff realize that it is not only about training, but also about combining methods such as psychological support to enable patients to cooperate with the training ^[7].

In addition, during the training process, through balance training and eye movement training, medical staff are made aware of the impact of standardized training on head perception ability, thereby continuously improving vertigo symptoms and enabling patients to complete various activities in daily life ^[8]. During the teaching process, teachers need to conduct one-way teaching for each training item, so that medical staff understand the reasons for learning such knowledge, to avoid randomly combining vestibular rehabilitation training content for unknown reasons. The teaching teacher displays vestibular rehabilitation training methods and movements in detail through a large screen, taking eye movement training as an example ^[9]. The patient is instructed to sit in a chair and follow the movement of an object with their eyes, while keeping their body still. During the demonstration, the key points of the movement are emphasized: the eye movement needs to be slow and not too fast, to avoid causing discomfort and worsening vertigo in patients. For non-moving objects, the eyes should focus and not move randomly ^[10]. Such targeted and specialized teaching facilitates medical staff to understand the actual operation process and internalize the absorbed knowledge. Another point to note during practical training is to maintain a safe training environment, clear obstacles from the area, and keep the ground dry and flat to prevent patients from falling during training ^[11]. For example, during balance training, medical staff are informed to set up guardrails and soft cushions nearby to prevent accidental falls. The training intensity and time should be adjusted based on the patient's physical condition to avoid excessive training fatigue or causing other complications. If the sudden deafness patient faced in practical application is elderly, physically weak, and has a severe condition, the training frequency and number of times need to be appropriately reduced, and the rest interval should be increased. If the patient suddenly experiences worsening vertigo and nausea/vomiting during training, the training should be stopped, and the patient should be asked to sit down and then stop training, maintaining a comfortable position and avoiding violent head movements ^[12]. Provide warm water for the patient to gargle to alleviate nausea. If severe symptoms occur during training, oral anti-vertigo medication should be administered, and the patient's heart rate and blood pressure should be monitored. In teaching precautions, teachers need to emphasize this point, marking it in red on the large screen, and remember that medical staff can complete emergency treatment in practical application ^[13]. Through standardized teaching, breaking through the limitations of traditional teaching modes, medical staff acquire rich knowledge, clarify specific training processes and key points, and accurately apply the learned vestibular rehabilitation training methods in practice.

5. Conclusion

In summary, implementing standardized vestibular rehabilitation training instruction for patients with sudden deafness accompanied by vertigo during treatment will enhance the mastery of medical staff regarding this treatment method and provide support for patient treatment.

Disclosure statement

The authors declare no conflict of interest.

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Development and Reliability and Validity Analysis of an Assessment Tool for Postoperative Wound Healing in Adult Patients with Benign Anal Canal and Rectal Diseases

Xiaomei Chang¹, Shenglin Hu^{2*}, Min Zhu¹, Min Zou¹, Min Li³, Guorong Li², Zhi Feng¹, Hongbo Li¹

¹Department of Anorectal Surgery, Ya'an People's Hospital, Ya'an 625000, Sichuan, China

²Nursing Department, Ya'an People's Hospital, Ya'an 625000, Sichuan, China

³Wound Ostomy Clinic, Ya'an People's Hospital, Ya'an 625000, Sichuan, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* This study aims to develop an assessment tool for postoperative wound healing in adult patients with benign anal canal and rectal diseases and to validate its reliability and validity. *Methods:* Based on Levine's Conservation Model as the theoretical framework, an item pool was formed through literature review, and the initial draft of the scale was refined through two rounds of Delphi expert consultation. A total of 200 postoperative patients were selected for item analysis, internal consistency testing, content validity, and structural validity analysis. *Results:* The final tool comprises four dimensions: energy conservation, structural integrity, personal integrity, and social integrity, with a total of 24 items. It demonstrates good content validity (I-CVI 0.82–1.00, S-CVI/Ave 0.95, S-CVI/UA 0.87) and excellent internal consistency (Cronbach's α for the overall scale was 0.934). Exploratory factor analysis revealed a KMO value of 0.931, Bartlett's test of sphericity $\chi^2 = 4147.853$ ($p < 0.001$), and four common factors were extracted, accounting for a cumulative variance contribution rate of 64.345%, indicating ideal structural validity. *Conclusion:* The results indicate that the assessment tool has good reliability and validity and can systematically evaluate postoperative wound healing, providing a scientific basis for clinical individualized nursing interventions.

Keywords: Anal canal; Rectum; Benign diseases; Wound healing; Assessment tool; Reliability; Validity

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1. Introduction

Benign diseases of the anal canal and rectum (such as hemorrhoids, anal fissures, anal fistulas, perianal abscesses, and anal prolapse) are common and frequently occurring conditions, with an incidence rate of approximately

51.14% among adult urban residents in China ^[1]. Surgery is the primary treatment for cases where conservative treatment is ineffective ^[2]. However, postoperative wounds are often open and prone to contamination. Affected by multiple factors such as dressing packing, strain from defecation, and fecal residue, they frequently lead to delayed healing or recurrence, increasing the physical and mental burden on patients ^[3]. Wound assessment is a core component of scientific management, requiring a comprehensive consideration of both local characteristics and overall conditions ^[4]. Based on this, this study aims to develop and validate an assessment tool for postoperative wound healing in patients with benign anal canal and rectal diseases, providing a basis for the systematic evaluation of postoperative wound healing in this patient population.

2. Methods

This study is grounded in Levine's Conservation Model as its theoretical foundation ^[5]. An item pool was developed through a literature review, and the tool was refined through two rounds of Delphi expert consultations. Subsequently, 200 consecutive postoperative patients were recruited from the proctology department to test the reliability and validity of the tool. This study has been approved by the Ethics Committee of Ya'an People's Hospital (Approval Number: 2025053).

2.1. Theoretical framework

This study employs Levine's Conservation Model as its theoretical framework, interpreting the holistic nature of postoperative wound healing in benign anal and rectal diseases from four dimensions: energy, structure, individual, and social ^[5]. This model emphasizes the conservation of energy balance, tissue repair, self-integrity, and social function, which collectively promote patient recovery and provide theoretical support for the development and validation of the wound healing assessment tool.

2.2. Development of the item pool

Based on a literature review from Chinese and English databases, this study constructed an assessment tool for postoperative wound healing in adult patients with benign anal and rectal diseases under the guidance of Levine's Conservation Model. The tool comprises four primary indicators and 26 secondary indicators, utilizing a five-point scoring system to ensure scientific rigor and rationality.

2.3. Expert consultation

In this study, anorectal specialists, nurses, wound care experts, and nursing researchers were selected nationwide to establish a Delphi expert panel. The inclusion criteria were as follows.

- (1) Doctors or nurses with over 10 years of experience in anorectal specialty and holding an associate senior or higher professional title
- (2) Individuals with over 5 years of wound care experience and possessing wound/ostomy therapist qualifications
- (3) Those with at least 5 years of research experience and holding a postgraduate degree or higher.

Expert consultations were conducted via email and the "Questionnaire Star" platform, with both rounds of questionnaires collected within one month. In the first round, 25 experts were involved, and items were screened and the questionnaire revised based on a mean score > 4.0 and a coefficient of variation < 2.0. In the second round,

statistical analysis was completed on this basis, ultimately resulting in the first draft of an assessment tool for postoperative wound healing in adult patients with benign anorectal and rectal diseases.

2.4. Expert authority level

The expert authority coefficient (Cr) was calculated using the formula $Cr = (Cs + Ca) / 2$, where Cs represents the expert's familiarity with the content and Ca represents the reliability of the judgment basis^[6]. Familiarity was graded on a 5-point scale (0–1 point), and the judgment basis was categorized into three levels: “large”, “medium”, and “small”, with assigned values of 0.30, 0.20, and 0.10, respectively.

2.5. Evaluation of the scale's reliability and validity

In this study, 200 patients were consecutively recruited in the order of their visits to the anorectal ward, and a numbered table was established for sequential registration. The inclusion criteria were as follows: confirmed diagnosis of benign anorectal disease with surgical treatment; age ≥ 18 years; postoperative period ranging from 1 day to 4 weeks; clear consciousness; and voluntary signing of the informed consent form. The exclusion criteria were patients with malignant tumors, pregnancy or lactation, and mental disorders. This study examined three aspects: content validity, internal consistency, and structural validity. First, content validity was assessed through expert consultation, calculating item-level (I-CVI) and scale-level (S-CVI/Ave, S-CVI/UA) indices. An $I-CVI \geq 0.78$ and $S-CVI/Ave \geq 0.90$ indicated good content validity^[7]. Second, internal consistency was tested using Cronbach's α coefficient, with $\alpha \geq 0.70$ considered as high reliability^[8]. Finally, exploratory factor analysis was employed to evaluate the construct validity. After passing the Kaiser-Meyer-Olkin (KMO) and Bartlett's tests, principal component analysis and maximum variance rotation were utilized. The number of factors was determined based on eigenvalues > 1 and the scree plot, with factor loadings ≥ 0.40 considered indicative of a reasonable structure^[9].

3. Results

3.1. Average importance ratings and coefficients of variation for each indicator

Based on expert recommendations, three new secondary indicators were added (adding “Personal Autonomy and Participation” and “Perception of Privacy Protection” under the “Personal Integrity” dimension, and adding “Primary Healthcare Support” under the “Social Integrity” dimension); “Self-awareness of Wounds” was merged into “Adherence to Nursing Behaviors”; and “Anxiety/Depression” was split into “Anxiety Level” and “Depression Level”. Some suggestions were not adopted after discussion, such as the overlap between “Home Care Capacity” and the connotation of “Social Integrity”, and the redundancy between “Recent Bowel Movement Patterns” and “Defecation-related Injuries”. After two rounds of consultations, expert opinions converged. The response rate and authority coefficient of experts are shown in **Table 1**, and the coordination degree is shown in **Table 2**. Ultimately, four primary indicators and 29 secondary indicators were established (see **Table 3**).

Table 1. Response rate and authority degree of expert consultation

Consultation round	Questionnaire recovery rate (Recovered/Responded)	Ca	Cs	Cr
Round 1	88.00% (22/25)	0.92	0.85	0.91
Round 2	100% (22/22)	0.96	0.87	0.92

Table 2. Coordination degree of expert consultation

Consultation round	Kendall's W	χ^2 value	<i>p</i> -value
Round 1	0.60	365.40	< 0.001
Round 2	0.81	493.29	< 0.001

Table 3. Average importance ratings and coefficients of variation for each indicator [points, mean \pm standard deviation (SD)]

Dimension	Indicator	Mean \pm SD	Coefficient of variation
Energy conservation	Age (≥ 60 years)	4.73 \pm 0.42	0.089
	Comorbidities	4.86 \pm 0.35	0.072
	Smoking history	4.58 \pm 0.47	0.103
	Obesity (BMI ≥ 28)	4.69 \pm 0.44	0.094
	Nutritional status	4.82 \pm 0.36	0.075
	Pain condition	4.64 \pm 0.48	0.104
	Sleep quality	4.56 \pm 0.50	0.110
	Mobility	4.71 \pm 0.43	0.091
Structural integrity	Multiple surgeries/Recurrence	4.72 \pm 0.41	0.087
	Wound type	4.78 \pm 0.40	0.084
	Wound location	4.80 \pm 0.38	0.079
	Area & Depth	4.79 \pm 0.39	0.081
	Exudate volume & character	4.73 \pm 0.42	0.089
	Wound Edge Status	4.74 \pm 0.41	0.087
	Granulation tissue	4.76 \pm 0.40	0.084
	Epithelialization	4.68 \pm 0.46	0.098
	Local signs of infection	4.77 \pm 0.39	0.082
	Defecation-related injury	4.70 \pm 0.44	0.094
	Complication occurrence	4.83 \pm 0.36	0.075
Personal Integrity	Anxiety	4.62 \pm 0.49	0.106
	Depression	4.62 \pm 0.49	0.106
	Shame	4.59 \pm 0.50	0.109
	Personal autonomy & participation	4.71 \pm 0.43	0.091
	Perception of privacy protection	4.74 \pm 0.41	0.087
Social Integrity	Family care support	4.69 \pm 0.45	0.096
	Self-care ability	4.73 \pm 0.42	0.089
	Return to social roles	4.61 \pm 0.49	0.106
	Nursing compliance behavior	4.72 \pm 0.43	0.091
	Primary healthcare support	4.66 \pm 0.47	0.101

3.2. Screening results of initial tool items

3.2.1. General information of subjects

This study included 200 patients with an average age of 45.7 ± 12.6 years. Among them, there were 118 males (59.0%) and 82 females (41.0%). The ethnic composition was predominantly Han Chinese, with 186 cases (93.0%), and 14 cases (7.0%) from ethnic minorities. In terms of marital status, there were 148 married cases (74.0%), 36 unmarried cases (18.0%), 10 divorced cases (5.0%), and 6 widowed cases (3.0%). In terms of residence, there were 124 cases (62.0%) in urban areas and 76 cases (38.0%) in rural areas. Regarding educational attainment, there were 61 cases (30.5%) with high school/technical secondary school education, 52 cases (26.0%) with junior high school education, 36 cases (18.0%) with junior college education, and 39 cases (19.5%) with undergraduate education or above. In terms of medical insurance or payment methods, there were 78 cases (39.0%) with urban employee medical insurance, 64 cases (32.0%) with urban and rural resident medical insurance, 38 cases (19.0%) with the New Rural Cooperative Medical Scheme, 12 cases (6.0%) paying out-of-pocket, and 8 cases (4.0%) with other payment methods. Regarding religious beliefs, there were 182 cases (91.0%) without any religious beliefs. The primary caregivers were mainly spouses, accounting for 126 cases (63.0%), followed by children, accounting for 48 cases (24.0%). The main diagnoses included hemorrhoids in 86 cases (43.0%), anal fistula in 54 cases (27.0%), anal fissure in 28 cases (14.0%), perianal abscess in 22 cases (11.0%), and others in 10 cases (5.0%).

3.2.2. Item analysis

This study employed the discrete trend method, discrimination method, correlation coefficient method, and Cronbach's α coefficient method to screen items. The standard deviations for all items were greater than 0.8, indicating good discrimination. The differences between high and low groups were statistically significant, and no items needed to be deleted. Correlation coefficient analysis revealed that five items ("history of multiple surgeries/recurrence", "local manifestations of infection", "defecation-related injuries", "occurrence of complications", and "feelings about privacy protection") had a correlation coefficient (r) with the total score of less than 0.4. Cronbach's α analysis also showed a slight increase in the overall scale α after deletion. Based on the results of the four methods, the aforementioned five items were ultimately deleted to optimize the scale structure. In this study, methods such as correlation coefficient analysis were used as preliminary screening tools to eliminate items with low correlation with the overall scale. Subsequently, exploratory factor analysis was conducted on the remaining items to ensure the robustness of the factor analysis results and the clarity of the scale structure.

3.2.3. Exploratory factor analysis for construct validity

After eliminating inappropriate items, exploratory factor analysis was conducted on 200 samples. The KMO value was 0.931, and the Bartlett's test of sphericity yielded $\chi^2 = 4147.853$, $df = 276$, $p < 0.001$, indicating that the data were suitable for factor analysis. Four factors with eigenvalues greater than 1 were extracted using the principal axis factoring method, with a cumulative variance contribution rate of 60.46%. The factor structure became clear after maximum variance orthogonal rotation (**Table 4**). Although some items did not meet the factor loading criteria, they were retained in the final scale to ensure clinical comprehensiveness.

Table 4. Exploratory factor analysis of construct validity

Indicator	Factor 1	Factor 2	Factor 3	Factor 4
Age (≥ 60 years)	0.352	0.086	0.900	0.145
Comorbidities	0.408	0.214	0.161	0.835
Smoking history	0.432	0.081	0.184	0.199
Obesity (BMI ≥ 28)	0.348	0.200	-0.027	0.152
Nutritional status	0.269	0.920	0.186	0.135
Pain condition	0.560	0.242	0.147	0.240
Sleep quality	0.623	0.227	0.163	0.205
Mobility	0.613	0.329	0.153	0.229
Wound type	0.740	0.271	0.284	0.259
Wound location	0.732	0.254	0.276	0.201
Wound area & depth	0.770	0.154	0.248	0.199
Exudate volume & character	0.252	0.928	0.180	0.144
Wound edge status	0.698	0.213	0.289	0.255
Granulation tissue	0.296	0.095	0.910	0.195
Epithelialization	0.378	0.226	0.140	0.877
Anxiety	0.183	0.287	0.002	0.244
Depression	0.277	0.073	0.152	0.181
Shame	0.319	0.411	0.139	0.165
Personal autonomy & participation	0.115	0.103	0.256	-0.006
Family care support	0.740	0.249	0.313	0.199
Self-care ability	0.777	0.169	0.283	0.180
Return to social roles	0.715	0.297	0.267	0.249
Nursing compliance behavior	0.655	0.162	0.238	0.260
Primary healthcare support	0.496	0.203	0.230	0.027
Eigenvalue	11.438	1.602	1.298	1.105
Variance explained	47.659%	6.674%	5.408%	4.603%
Cumulative variance	47.659%	54.333%	59.741%	64.345%

3.2.4. Reliability and validity

Experts consulted in the second round were invited to evaluate the content validity of the assessment tool, with an I-CVI ranging from 0.82 to 1.00, an S-CVI/Ave of 0.95, and an S-CVI/UA of 0.87, indicating good content validity. The Cronbach's α for the overall scale was 0.934, with all four dimensions exceeding 0.87, suggesting good internal consistency.

4. Discussion

This study constructed an assessment tool for postoperative wound healing in adults with benign anorectal diseases

based on Levine's Conservation Model and systematically evaluated its reliability and validity through two rounds of Delphi expert consultations, item analysis, and exploratory factor analysis.

During the expert consultation phase, the response rate for the two rounds of the Delphi method was high, with authority coefficients (Cr) all exceeding 0.9. Kendall's W increased from 0.60 to 0.81 ($p < 0.001$), indicating that expert opinions tended to converge, the item system was reasonable, and the theoretical framework provided strong guidance. Feedback from multidisciplinary experts ensured the scientific rigor and representativeness of the items while validating the applicability of Lewin's Conservation Model in postoperative wound assessment. Item screening utilized methods such as the discrete trend method, discrimination method, correlation coefficient method, and Cronbach's α coefficient method. Multidimensional analysis revealed that five items had low correlations with the total score ($r < 0.4$). After their removal, the overall reliability of the scale improved, the structure was optimized, discrimination was enhanced, and both practicality and statistical performance were better.

The construct validity analysis showed that the KMO value was 0.931, and the Bartlett's test of sphericity yielded $p < 0.001$, indicating suitability for factor analysis. Four common factors were extracted, with a cumulative variance contribution rate of 64.345%. The factor loadings were clear, corresponding to the energy conservation, structural integrity, personal integrity, and social integrity dimensions of Lewin's model, thus verifying theoretical consistency. In terms of content validity, the Item-Content Validity Index (I-CVI) ranged from 0.82 to 1.00, the Scale-Content Validity Index/Average (S-CVI/Ave) was 0.95, and the Scale-Content Validity Index/Universal Agreement (S-CVI/UA) was 0.87, all exceeding recognized standards. This indicates a high degree of alignment between the items and the research objectives, as well as comprehensive coverage of core wound healing domains. Reliability analysis revealed a Cronbach's α of 0.934 for the overall scale, with all four dimensions exceeding 0.87, demonstrating good internal consistency.

From a clinical perspective, this tool provides a systematic and standardized framework across multiple dimensions, including wound characteristics, function, psychology, and social support. Previous studies have suggested that wound assessment tools can enhance assessment consistency and decision-making confidence among non-specialist nurses, optimize clinical interventions, and improve healing outcomes^[10]. Compared to general-purpose tools, this tool combines specialization with systematization, offering strong clinical applicability and guidance value.

5. Conclusions and limitations

The assessment tool developed in this study demonstrates good reliability and validity, with a well-structured design that encompasses energy conservation, structural integrity, personal integrity, and social integrity. It provides a scientific basis for postoperative nursing assessment and individualized interventions. However, the study is limited by its single-center design and relatively small sample size. The construct validity requires further refinement through confirmatory factor analysis with a larger sample. Additionally, the tool's applicability across different regions, healthcare institutions, and in long-term follow-up settings requires further validation.

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Disclosure statement

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The Application of Scenario Simulation Teaching Method Based on Debriefing-GAS Mode in the Teaching of Clinical Nursing students

Shasha Liu

Deyang People's Hospital, Deyang 618000, Sichuan, China

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Abstract: *Objective:* To explore the application effect of scenario simulation teaching method based on Debriefing-GAS mode in the teaching of clinical nursing students in neurosurgery and its influence on critical thinking, clinical practice ability and teaching satisfaction. *Methods:* A total of 100 nursing students who were doing their internship in the Department of Neurosurgery at a tertiary hospital in Sichuan Province from July 2024 to June 2025 were selected and divided into a control group and an experimental group, with 50 students in each group, using the historical control grouping method. The control group used the traditional teaching method for scenario simulation, while the experimental group used the Debriefing-GAS model for scenario simulation teaching. The teaching effect was evaluated using the DASH scale, the CIDI-CV scale, the clinical practice ability scale and the self-made teaching satisfaction questionnaire, and statistical analysis was conducted using SPSS 25.0. *Results:* The total DASH score of the experimental group (6.45 ± 0.41) was significantly higher than that of the control group (5.12 ± 0.47 , $t = 14.01$, $p < 0.001$); The total score of critical thinking ability (338.6 ± 22.5) was higher than that of the control group (307.8 ± 24.1 , $t = 6.55$, $p < 0.001$); The score of clinical practice ability (189.4 ± 15.2) was significantly higher than that of the control group (168.7 ± 14.9 , $t = 6.49$, $p < 0$). Teaching satisfaction was 96% in the experimental group and 82% in the control group, statistically significant ($\chi^2 = 4.32$, $p = 0.038$). *Conclusion:* The scenario simulation teaching method based on the Debriefing-GAS model can significantly improve the learning initiative, reflective ability, critical thinking level and clinical practice ability of clinical nursing students, and enhance teaching satisfaction.

Keywords: Debriefing-GAS mode; Situational simulation teaching; Clinical nursing students; Critical thinking; Clinical practice ability

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1. Introduction

The scenario simulation teaching method has been widely applied in nursing education in recent years. It uses highly simulated clinical scenarios to allow students to “learn by doing” and experience the entire process of nursing work in a simulated clinical environment, which can consolidate theoretical knowledge and improve

practical operation and communication skills. This teaching method overcomes the shortcomings of traditional lecture-based teaching, such as students' passive acceptance of knowledge and lack of practical opportunities. It is student-centered and focuses on the cultivation of learners' active participation and clinical thinking ability. However, traditional simulation teaching focuses too much on the cultivation of operational skills during the operation process. Teachers' feedback after teaching is mostly simple summaries, without systematic and structured reflection and guidance of the teaching process. Students' internalization and transfer of the learned knowledge are insufficient, and the maximum benefits of simulation teaching cannot be fully exerted^[1].

Debriefing is a key part of situational simulation teaching, the process by which learners review, reflect, and discuss the simulation experience into knowledge and skills. In recent years, the Debriefing GAS model (Gather-Analyze-Summarize) has been widely applied in medical education, focusing on the three stages of "reaction-analysis-summary" to prompt students to reflect on their performance and analyze the gaps in knowledge and skills in a safe and open learning environment. Summarize experiences and areas for improvement. This model emphasizes the combination of emotional guidance and cognitive construction, enabling students to enhance their clinical judgment and communication skills through reflection.

The introduction of the Debriefing-GAS model in nursing teaching is conducive to teachers conducting feedback activities in an organized manner, stimulating students' enthusiasm for learning, and encouraging students to reorganize the knowledge system and achieve deep learning. Especially in high-risk and emergency-intensive clinical departments like neurosurgery, it is particularly important to cultivate critical thinking and clinical adaptability of nursing students. Therefore, this study chose neurosurgical practice nursing students as the research subjects to investigate the effect of the Debriefing-GAS model scenario simulation teaching method in clinical teaching, and to verify its advantages in improving the critical thinking ability, clinical practice ability and teaching satisfaction of nursing students by using the traditional scenario simulation teaching control method To provide practical evidence for the improvement of the nursing teaching model^[2].

2. Materials and methods

2.1. General information

This study used convenience sampling to select 100 full-time nursing students who were doing neurosurgery practice at a tertiary general hospital in Sichuan Province from July 2024 to June 2025 as the research subjects. All the subjects had the same pre-internship nursing basic knowledge and skills from the same institution, received the same basic theoretical knowledge and operational skills training, and had roughly the same knowledge base and academic level. Based on the duration of the internship, the historical control group method was used. Fifty nursing students who interned in the department from July 2024 to December 2024 were set as the control group, and the traditional scenario simulation teaching method was adopted; The 50 nursing students who did their internship from January 2025 to June 2025 were assigned to the experimental group, using the Debriefing-GAS model for scenario simulation teaching^[3].

There were no statistically significant differences ($p > 0.05$) between the two groups of students in terms of gender, age, educational structure, and pre-internship theoretical performance, and they were comparable. There were 4 male students and 46 female students in the control group, with an average age of (21.6 ± 0.7) years; There were 5 boys and 45 girls in the experimental group, with an average age of (21.7 ± 0.6) years. All subjects were informed of the purpose and process of the study and voluntarily signed written informed consent.

2.1.1. Inclusion criteria

- (1) Full-time nursing interns
- (2) Good communication and comprehension skills
- (3) Be informed and voluntarily participate in this study
- (4) Be able to participate in teaching activities and assessments

2.1.2. Exclusion criteria

- (1) Those who have previously received situational simulation teaching or Debriefing training
- (2) Those who are participating in other teaching research projects
- (3) Those who quit or are absent from mock teaching courses for personal reasons ^[4].

2.2. Methods

2.2.1. Teaching methods for the control group

Use the traditional teaching method, namely the scenario simulation teaching method. The teaching content is designed in accordance with the nursing practice syllabus and the nursing objectives for common neurosurgical diseases. The teaching process consists of five sections: theoretical instruction, scenario design, role assignment, simulation implementation, and teacher summary. In the third week of the internship, the instructor gives lectures on the basic knowledge related to the internship, common disease care, and communication skills; Scenario simulation training in the fourth week. The simulated scenarios are pre-set by the teacher, such as observation after craniocerebral injury or cerebral hemorrhage surgery, care for neurological dysfunction, etc. Students were randomly divided into several groups, and each group took turns playing the roles of nurse, patient, and family member to simulate the operation. After the teacher finished teaching, the students were evaluated collectively. The students evaluated themselves and each other based on the teacher's comments, summarizing their experiences and shortcomings ^[5].

2.2.2. Teaching methods of the experimental group

Use scenario simulation teaching based on Debriefing-GAS mode. In the teaching preparation stage, in accordance with the internship outline and learning objectives, the instructor formulates detailed lesson plans, identifies key points, difficulties and competency development objectives. Prepare the standardized patient (SP), with trained volunteers playing the role of the patient to ensure the scenario is realistic and communication is natural. The items used for teaching include medical records, models, medical devices and medicines, etc. During the teaching implementation stage, before the teaching begins, the instructor introduces the purpose, content and rules of this scenario simulation, distributes task cards, and clarifies the tasks and roles each student is to undertake. Interns work in groups to determine the sequence of scenarios by drawing lots and perform the simulation operations and role-playing in sequence. Teachers observe students' technical movements, communication styles, teamwork during the simulation and record them. Debriefing-GAS Reflection Session After the scenario simulation is completed, teachers and students enter a quiet learning space together and have a Debriefing discussion chaired by the tutor.

(1) Reaction phase (G)

The teacher guides students to recall the just-ended scenario process, allowing students to express their emotions and intuitive feelings, helping students get out of tension and establish psychological safety.

(2) Analysis stage (A)

Teachers guide students to analyze the nursing process based on teaching objectives and observation records, reflect on their strengths and weaknesses in aspects such as assessment, communication, and emergency handling, analyze the basis of clinical decision-making, and think about ways to improve

(3) Summary stage (S)

Students, under the guidance of teachers, summarize their experiences, reflect on their insights, and form structured knowledge transfer. Teachers provide targeted feedback based on students' performance, reinforce correct behavior, point out deficiencies and offer suggestions for improvement, enabling students to apply the knowledge they have learned to clinical practice^[6].

2.3. Observation indicators

(1) Debriefing quality was evaluated using the Debriefing Assessment for Simulation in Healthcare (DASH) scale developed by Harvard University, which included six dimensions such as structural integrity, learning atmosphere, leading discussion, and stimulating reflection. Each dimension was scored on a 7-point scale, with higher scores indicating better quality of Debriefing.

(2) Critical thinking ability

Based on the revised Chinese version of the Critical Thinking Ability Scale (CIDI-CV) by Peng et al., which includes seven dimensions: pursuit of truth, open thinking, analytical ability, systematization ability, critical self-confidence, thirst for knowledge, and cognitive maturity, there are 70 items in total, ranging from 70 to 420 points. The higher the score, the stronger the critical thinking ability.

(3) Clinical practice ability

Using the clinical Practice ability scale for undergraduate nursing students developed by Yao Pingping, which includes seven dimensions of clinical nursing, communication and coordination, health education, scientific research and innovation, emergency cooperation, humanistic care and teaching ability, with a total of 44 items, with a Likert 5-level score ranging from 44 to 220 points, the higher the score, the stronger the practice ability.

(4) Teaching satisfaction was evaluated using a self-made teaching satisfaction questionnaire from five aspects: teaching objectives, teaching content, teaching methods, teaching process, and teaching effect, with a total score of 100, and a score of 80 or above was considered satisfactory.

2.4. Statistical processing

Analysis was performed using SPSS 25.0. Measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$), and independent sample *t*-tests were used for comparisons between groups; Count data were analyzed using the χ^2 test, and a *p*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of debriefing quality between the two groups of nursing students

The quality of Debriefing for the two groups of nursing students was evaluated using the DASH scoring scale. The results showed that the experimental group scored higher than the control group in six dimensions including teaching structure orderliness, learning atmosphere, promotion of reflection and communication feedback, and the differences were statistically significant ($p < 0.01$). See **Table 1**.

Table 1. Comparison of debriefing quality between the two groups of nursing students ($\bar{x} \pm s$, points)

Items	Teaching structure orderliness	Learning atmosphere	Stimulate discussion and reflection	Point out gaps and feedback	Maintain good performance	Total score
Control group (n = 50)	5.18 \pm 0.64	5.06 \pm 0.59	4.95 \pm 0.71	5.10 \pm 0.67	5.08 \pm 0.65	5.12 \pm 0.47
Experimental group (n = 50)	6.42 \pm 0.52	6.38 \pm 0.47	6.40 \pm 0.44	6.36 \pm 0.48	6.33 \pm 0.50	6.45 \pm 0.41
<i>t</i> -value	10.31	11.39	12.02	10.44	10.08	14.01
<i>p</i> -value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.2. Comparison of critical thinking ability between two groups of nursing students

The critical thinking ability of the two groups of nursing students was evaluated using the CIDI-CV scale. The results showed that the experimental group scored significantly higher than the control group in the dimensions of truth pursuit, analytical ability, systematization ability and cognitive maturity, and the differences were statistically significant ($p < 0.01$). See **Table 2**.

Table 2. Comparison of critical thinking ability between the two groups of nursing students ($\bar{x} \pm s$, points)

Items	Pursuit of truth	Open mind	Analytical skills	Systematic ability	Critical confidence	Thirst for knowledge	Cognitive maturity
Control group (n = 50)	42.8 \pm 4.6	44.5 \pm 4.9	43.2 \pm 4.4	46.0 \pm 4.7	44.1 \pm 4.8	45.3 \pm 5.1	42.0 \pm 5.0
Experimental group (n = 50)	48.2 \pm 4.1	49.7 \pm 4.3	49.5 \pm 4.5	51.6 \pm 4.2	48.6 \pm 4.6	49.8 \pm 4.7	48.7 \pm 4.8
<i>t</i> -value	6.12	5.29	6.73	5.87	4.43	4.35	6.76
<i>p</i> -value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.3. Comparison of clinical practice ability between the two groups of nursing students

The two groups of students were evaluated using the Clinical Practice Ability Scale for Undergraduate nursing students. The results showed that the experimental group scored higher than the control group in clinical nursing, communication and coordination, health education, humanistic care and scientific research innovation, and the differences were statistically significant ($p < 0.01$). See **Table 3**.

Table 3. Comparison of clinical practice ability between the two groups of nursing students ($\bar{x} \pm s$, points)

Item	Clinical care	Communication and coordination	Health education	Research and innovation	Emergency coordination	Humanistic care	Clinical teaching	Total score
Control group (n = 50)	36.8 \pm 3.9	22.5 \pm 2.8	18.3 \pm 2.4	24.9 \pm 3.1	19.4 \pm 2.3	27.5 \pm 3.0	19.3 \pm 2.1	168.7 \pm 14.9
Experimental group (n = 50)	41.3 \pm 3.6	26.4 \pm 2.3	21.6 \pm 2.0	28.0 \pm 2.5	22.0 \pm 2.2	31.2 \pm 2.8	22.0 \pm 1.9	189.4 \pm 15.2
<i>t</i> -value	6.08	7.12	6.88	5.19	5.57	6.28	6.78	6.49
<i>p</i> -value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

4. Conclusion

Through research, it is found that the scenario simulation teaching adopting the Debriefing-GAS mode can

significantly improve the critical thinking ability, clinical practice ability and teaching satisfaction of nursing students. It can also stimulate students to learn and reflect actively more than the traditional teaching methods. The Debriefing-GAS model uses three stages of reaction, analysis, and summary to allow learners to express their true feelings in a safe learning atmosphere, analyze the strengths and weaknesses of nursing in the nursing process, thereby achieving the purpose of internalizing experience and transferring knowledge. The DASH score of the experimental group in this study was higher than that of the control group, indicating that the teaching feedback of this model is highly structured and inspiring, and can guide students to conduct in-depth reflection.

At the same time, the experimental group had higher scores for critical thinking and clinical practice ability, indicating that systematic reflection is conducive to the cultivation of students' logical analysis and clinical decision-making abilities, and to the transformation of theoretical knowledge into practical skills. The improvement in students' satisfaction with teaching indicates that they have gained positive learning experiences and a sense of achievement in the activities. In summary, the Debriefing-GAS model has effectively improved the quality of nursing teaching by improving the teaching structure and strengthening feedback and reflection, and has a positive effect on improving the comprehensive quality and practical ability of clinical nursing students, which is worthy of promotion in nursing education.

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Analysis of the Efficacy of High-Flow Nasal Cannula Oxygen Therapy and Non-Invasive Ventilation in COPD Patients

Xue Yin, Yan Li, Yan Ma, Yue Sun, Li Li, Wenmei Yan, Jianhua Zhang, He Zhang, Haisheng Yang*

Department of Respiratory and Critical Care Medicine, Wuhai People's Hospital, Wuhai 016000, Inner Mongolia Autonomous Region, China

*Corresponding author: Haisheng Yang, yinxuelove52@163.com

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Abstract: Patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) often suffer from respiratory failure and require respiratory support therapy. High-flow nasal cannula oxygen therapy (HFNC) and non-invasive positive pressure ventilation (NIPPV) are commonly used non-invasive respiratory support methods. HFNC can provide precisely heated and humidified high-flow oxygen, reducing dead space and increasing alveolar ventilation. NIPPV can supply stable high-concentration oxygen and improve gas exchange. This article reviews the application of HFNC and NIPPV in the acute exacerbation stage of COPD, aiming to provide references for reasonable clinical selection.

Keywords: Chronic obstructive pulmonary disease; High-flow nasal cannula oxygen therapy; Non-invasive ventilation; Acute exacerbation stage

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and airflow limitation, usually caused by airway and/or alveolar abnormalities resulting from exposure to toxic particles or gases^[1]. The acute exacerbation stage of COPD refers to a sustained deterioration in the patient's condition beyond their daily state, necessitating a change in the routine medication for underlying COPD. The condition often progresses rapidly and can be complicated by respiratory failure, posing a serious threat to the patient's life and health^[2]. Timely and effective respiratory support therapy is crucial for improving the prognosis of patients with acute exacerbation of COPD. High-flow nasal cannula oxygen therapy (HFNC) and non-invasive positive pressure ventilation (NIPPV) are two important non-invasive respiratory support modalities that play a pivotal role in the treatment of acute exacerbations of chronic obstructive pulmonary disease (COPD). However, there are certain differences between the two in terms of efficacy, applicable

populations, and other aspects. A thorough understanding of the application of HFNC and NIPPV during acute exacerbations of COPD can assist clinicians in formulating more precise and effective treatment plans for patients.

2. Pathophysiological changes during acute exacerbations of COPD

During acute exacerbations of COPD, multiple factors lead to a significant increase in airway inflammatory responses in patients. Viral or bacterial infections are common triggers, which can promote the aggregation of inflammatory cells such as neutrophils and macrophages in the airways, releasing a large number of inflammatory mediators, such as tumor necrosis factor- α (TNF- α) and interleukin-8 (IL-8) ^[3]. These inflammatory mediators cause congestion and edema of the airway mucosa, as well as hypersecretion of mucus, leading to airway narrowing and further exacerbation of airflow limitation ^[4]. Simultaneously, inflammation damages the normal function of airway cilia, obstructing the expulsion of sputum and exacerbating ventilation disorders.

COPD patients inherently experience a decrease in lung elastic recoil and premature closure of small airways, resulting in gas retention during exhalation and pulmonary hyperinflation. During acute exacerbations, the aforementioned pathological changes intensify, leading to a further increase in residual volume and more pronounced dynamic pulmonary hyperinflation ^[5]. This not only increases the work of the respiratory muscles, leading to respiratory muscle fatigue, but also elevates intrathoracic pressure, affecting cardiac diastolic function and further exacerbating the respiratory and circulatory burden. Due to airway obstruction and mismatched ventilation/perfusion ratios in the lungs, patients experience ventilation dysfunction, with impaired carbon dioxide excretion and insufficient oxygen intake, resulting in hypoxemia with or without hypercapnia, namely respiratory failure. Severe respiratory failure can trigger a series of complications, such as pulmonary encephalopathy and arrhythmias, endangering the patient's life.

3. HFNC

3.1. Working principle of HFNC

HFNC precisely adjusts the inhaled oxygen concentration through an air-oxygen blender. Its high-flow gas delivery device can provide a gas flow rate of up to 80 L/min, which far exceeds the peak inspiratory flow rate of patients' spontaneous breathing. This ensures that patients receive a stable, high-flow gas supply throughout the inspiratory process, maintaining a constant inhaled oxygen concentration ^[6]. Before delivery, the gas passes through a warming and humidifying device, where it is heated to 31–37°C and humidified to a level of 33–44 mg/L, closely approximating the temperature and humidity of the gas in the respiratory tract under physiological conditions in the human body. When this gas with appropriate temperature and humidity enters the respiratory tract, it reduces irritation to the airway mucosa, maintains the normal function of the airway mucociliary clearance system, and facilitates the expectoration of sputum. The high-flow gas creates turbulence in the nasal cavity, oral cavity, and pharynx, effectively flushing out the anatomical dead space and reducing the carbon dioxide content inhaled by the patient during the next breath, thereby minimizing carbon dioxide rebreathing ^[7].

3.2. Physiological effects of HFNC on patients with acute exacerbation of COPD

3.2.1. Improvement of oxygenation

HFNC effectively improves the oxygenation function of patients with acute exacerbation of COPD by providing high-flow, precisely concentrated oxygen and generating a positive end-expiratory pressure (PEEP) effect. Jiang

Xiuming et al. treated patients with severe pneumonia complicated by respiratory failure using HFNC^[8]. After treatment, the patients' arterial partial pressure of oxygen (PaO₂) increased from (49.56 ± 4.07) mmHg to (78.44 ± 5.12) mmHg, and their oxygen saturation (SaO₂) increased from (82.62 ± 4.83)% to (97.32 ± 1.75)%. The oxygenation index also significantly improved, fully demonstrating the remarkable effect of HFNC in improving oxygenation. The high-flow gas flushes out the dead space, reducing carbon dioxide rebreathing and increasing the oxygen content in the alveoli. The PEEP effect maintains alveolar patency, prevents alveolar collapse, and improves ventilation/perfusion mismatch, enabling more effective diffusion of oxygen from the alveoli into the bloodstream, thereby increasing arterial partial pressure of oxygen and oxygen saturation, lowering the oxygenation index, and reducing the damage caused by hypoxemia to the body^[9].

3.2.2. Reduction of respiratory work

Patients in the acute exacerbation stage of Chronic Obstructive Pulmonary Disease (COPD) experience a significant increase in respiratory muscle workload due to increased airway resistance and pulmonary hyperinflation, making them prone to respiratory muscle fatigue. The high-flow gas provided by High-Flow Nasal Cannula (HFNC) can partially meet the patient's inspiratory demand, reducing the patient's spontaneous inspiratory effort and lowering the respiratory rate. Research by Ren Yuanyuan et al. showed that in the observation group treated with HFNC, the post-treatment respiratory rate decreased from (30.97 ± 4.34) breaths/min to (19.51 ± 2.73) breaths/min, significantly lower than that in the control group treated with non-invasive positive pressure ventilation (NIPPV), which had a post-treatment respiratory rate of 21.57 ± 2.80 breaths/min^[10]. Meanwhile, after the gas is warmed and humidified, patients do not need to perform additional warming and humidification of the inhaled gas, reducing upper airway resistance and energy consumption during respiration, thereby effectively reducing respiratory work and alleviating respiratory muscle fatigue, which helps improve the patient's respiratory status^[11].

3.2.3. Protection of airway mucosa

The gas with appropriate temperature and humidity entering the airway through HFNC can keep the airway mucosa moist, maintain the normal movement of mucociliary, promote the dilution and excretion of sputum, and reduce the risk of airway obstruction caused by thick sputum. Yang Yuhuan found in her study that the incidence of airway-related complications such as nasal bleeding and dry mouth and nose in patients in the HFNC treatment group was only 5.55%, significantly lower than the 22.22% in the NIPPV group, which is closely related to the protective effect of HFNC on the airway mucosa^[12]. At the same time, it avoids the stimulation and damage of dry gas to the airway mucosa, protects the integrity of airway epithelial cells, reduces the risk of respiratory infections, and is conducive to maintaining the normal defensive function of the airway.

4. NIPPV

4.1. Working modes and characteristics of NIPPV

NIPPV mainly includes modes such as continuous positive airway pressure ventilation and bilevel positive airway pressure ventilation. In continuous positive airway pressure ventilation mode, the ventilator provides a continuous positive pressure throughout the respiratory cycle to maintain airway patency and prevent airway collapse, suitable for patients with mild respiratory failure and basically normal respiratory drive^[13]. The bi-level positive

airway pressure (BiPAP) ventilation mode provides different levels of positive pressure during the inspiratory and expiratory phases, respectively. The higher pressure during inspiration assists the patient in inhaling and increases alveolar ventilation, while the lower pressure during expiration maintains airway patency and improves oxygenation. BiPAP can be individually adjusted based on the patient's respiratory rate, inspiratory time, etc., making it more suitable for patients with moderate to severe respiratory failure.

NIPPV can provide a stable high concentration of oxygen, effectively improving the patient's oxygenation function. Jiang Jingzheng et al. used NIPPV to treat COPD patients, and after treatment, the patients' PaO₂ increased from (48.7 ± 9.8) mmHg to (82.1 ± 10.7) mmHg, significantly improving their oxygenation status ^[14]. By setting appropriate pressure levels, alveolar ventilation can be increased, promoting carbon dioxide excretion and correcting hypercapnia. Compared with invasive mechanical ventilation, NIPPV avoids the trauma and related complications caused by tracheal intubation or tracheotomy, such as ventilator-associated pneumonia and airway injury, while preserving the patient's swallowing and coughing functions, facilitating independent sputum expectoration and daily communication.

4.2. Mechanism of action of NIPPV in treating acute exacerbation of COPD

In patients with acute exacerbation of COPD, NIPPV effectively corrects hypoventilation and reduces arterial partial pressure of carbon dioxide by increasing alveolar ventilation. In the study by Huang Guodong et al., in the control group treated with NIPPV, the patients' PaCO₂ decreased from (75.17 ± 7.47) mmHg to (66.54 ± 6.13) mmHg after treatment, while in the observation group combined with HFNC, the patients' PaCO₂ decreased to (60.02 ± 5.25) mmHg, further demonstrating the fundamental role of NIPPV in reducing PaCO₂ ^[15]. The inspiratory pressure can overcome airway resistance, increase tidal volume, and promote carbon dioxide excretion, while the expiratory pressure maintains alveolar patency through the production of positive end-expiratory pressure effect, preventing alveolar collapse during expiration, improving ventilation/perfusion mismatch, and enhancing oxygenation efficiency. NIPPV can also reduce the load on respiratory muscles, allowing fatigued respiratory muscles to rest. By assisting patients in breathing, it reduces the workload of respiratory muscles, decreases their oxygen consumption, and helps alleviate respiratory muscle fatigue and restore their function. In addition, NIPPV can improve patients' breathing patterns, normalize respiratory rates, reduce ineffective ventilation caused by shallow and rapid breathing, and further enhance respiratory efficiency.

5. Comparison of HFNC and NIPPV applications in acute exacerbation of COPD

5.1. Baseline information

To more intuitively compare the efficacy of HFNC and NIPPV, this study conducted baseline data matching and efficacy analysis on two groups of AECOPD patients receiving different respiratory support methods. The general conditions of the two groups of patients are shown in **Table 1** and **2**, with no statistically significant differences ($p > 0.05$) in terms of age, gender, smoking history, and comorbidities, indicating good comparability.

Table 1. Comparison of general conditions between two groups of patients [n(%), $\bar{x} \pm s$]

Group	n	Age	Gender [n (%)]		Smoking status [n (%)]	
			Male	Female	Non-smoker	Smoking history
HNFC Group	15	78.47 \pm 11.59	12(80%)	3(20%)	6(40%)	9(60%)
NIPPV Group	15	77.67 \pm 7.56	12(80%)	3(20%)	9(60%)	6(40%)
t/χ^2		0.236		0.000		1.200
p		0.815		1.000		0.273

Table 2. Comparison of disease between two groups of patients [n(%), $\bar{x} \pm s$]

Group	n	Hypertension [n (%)]		History of endotracheal intubation [n (%)]		Diabetes [n (%)]	
		Yes	No	Yes	No	Yes	No
HNFC Group	15	7(46.67%)	8(53.33%)	1(6.67%)	14(93.33%)	9(60%)	6(40%)
NIPPV Group	15	6(40%)	9(60%)	0	15(100%)	8(53.33%)	7(46.67%)
t/χ^2			0.148		Fisher		0.156
p			0.700		1.000		0.693

Notes: 1. $p < 0.05$ indicates a statistically significant difference.

2. The HNFC group refers to the high-flow oxygen therapy group, and the NIPPV group refers to the non-invasive positive pressure ventilation group.

3. The sample sizes of the two groups were obtained through 1:1 random matching from the original data to ensure baseline comparability.

4. Continuous variables were analyzed using the t-test, while categorical variables were analyzed using the χ^2 test or Fisher's exact test.

5.2. Comparison of therapeutic effects

This study compared the changes in physiological indicators at different time points before and after treatment between the two groups of patients. As shown in **Table 3**, after 24 hours of treatment, the HFNC group showed statistically significant improvements in respiratory rate, pH value, and SpO₂ ($p < 0.05$), while the NIPPV group only showed a trend of improvement. This indicates that in the early stages of treatment, HFNC may have a faster or more significant effect in improving respiratory distress and oxygenation.

Table 3. Comparison of respiratory rate, pH value, and SpO₂ indicators between two groups of patients after 24 hours of treatment ($\bar{x} \pm s$)

Indicator	Group	n	Before treatment	After 24h Treatment	t-value	p-value
Respiratory rate (breaths/min)	HFNC group	15	23.47 \pm 4.12	21.07 \pm 1.94	2.18	0.047
	NIPPV group	15	22.60 \pm 4.72	20.27 \pm 2.96	1.73	0.106
pH value	HFNC group	15	7.33 \pm 0.04	7.37 \pm 0.05	-2.42	0.030
	NIPPV group	15	7.34 \pm 0.06	7.38 \pm 0.07	-1.89	0.080
SpO ₂ (%)	HFNC group	15	88.73 \pm 6.18	92.47 \pm 3.72	-2.24	0.042
	NIPPV group	15	90.07 \pm 5.89	91.80 \pm 4.36	-0.91	0.379

Notes: 1. $p < 0.05$ indicates a statistically significant difference.

2. This table only analyzes and calculates the indicators with complete data at both the “before treatment” and “one day after treatment” time points in the “General Information” worksheet. Indicators such as PaO₂, PaCO₂, and HCO₃⁻ were not included in this analysis due to a significant amount of missing data one day after treatment.

3. Paired t-tests were used for comparisons within groups before and after treatment.

To further evaluate the sustainability of the therapeutic effects, we analyzed the data collected three days after treatment. As shown in **Table 4**, the HFNC group maintained statistical advantages in improvements in respiratory rate, pH value, and SpO₂ ($p < 0.05$), while the improvements in all indicators in the NIPPV group did not reach significant levels. This suggests that for the patient population included in this study, HFNC may have a greater advantage in maintaining stable physiological indicators.

Table 4. Comparison of respiratory rate, pH value, and SpO₂ between two groups three days after treatment ($\bar{x} \pm s$)

Indicator	Group	n	Before treatment	After 3 days treatment	t-value	p-value
Respiratory rate (breaths/min)	HFNC	10	24.20 ± 3.88	21.10 ± 1.91	2.72	0.023*
	NIPPV	10	22.70 ± 5.06	19.60 ± 2.95	2.15	0.059
pH value	HFNC	10	7.32 ± 0.04	7.38 ± 0.05	-3.16	0.011*
	NIPPV	10	7.33 ± 0.07	7.36 ± 0.08	-1.41	0.192
SpO ₂ (%)	HFNC	10	89.10 ± 6.55	93.80 ± 3.88	-2.51	0.033*
	NIPPV	10	90.00 ± 6.15	92.70 ± 4.83	-1.57	0.152

Note: 1. $p < 0.05$ indicates a statistically significant difference.

2. This table only analyzes and calculates the indicators with complete data at both the “before treatment” and “three days after treatment” time points in the “General Information” worksheet. Indicators such as PaO₂, PaCO₂, and HCO₃⁻ were not included in this analysis due to a significant amount of missing data three days after treatment.

3. Paired t-tests were used for comparisons within groups before and after treatment.

4. Continuous variables were analyzed using t-tests, while categorical variables were analyzed using χ^2 tests or Fisher’s exact tests.

The ROX index (SpO₂/FiO₂/respiratory rate) is a sensitive indicator for evaluating early responses to respiratory support. The comparison of ROX indices between the two groups of patients two hours after treatment is shown in **Table 5**. Although the average value in the NIPPV group was slightly higher, the difference between groups was not statistically significant ($p > 0.05$), indicating that in the early stages of treatment, the two methods may be equivalent in terms of their comprehensive effects on alleviating respiratory distress in patients.

Table 5. Comparison of ROX index between the two groups after 2 hours of treatment ($\bar{x} \pm s$)

Group	n	ROX index (2 hours post-treatment, $\bar{x} \pm s$)
HFNC Group	15	10.33 ± 3.87
NIPPV Group	15	11.56 ± 2.89

Note: 1. Independent samples t-test was used for inter-group comparison, with $t = -0.99$ and $p = 0.331$. 2. ROX Index = SpO₂ / (FiO₂ × Respiratory rate). The data in this table is directly sourced from the “ROX Index After 2 Hours of Treatment” column in the “General Information” worksheet. 4. Results Explanation: There was no statistically significant difference in the ROX Index between the two groups after 2 hours of treatment ($p = 0.331$).

When treating patients with acute exacerbation of COPD, both HFNC and NIPPV demonstrate certain efficacy in improving oxygenation and ventilation, albeit with differences in various indicators. For oxygenation improvement, HFNC enhances oxygenation through high-flow flushing of the dead space and positive end-expiratory pressure effects, while NIPPV improves oxygenation by setting appropriate pressure levels to maintain

alveolar patency and increase ventilation volume. Multiple studies have shown that in patients with mild to moderate respiratory failure, HFNC and NIPPV exhibit similar initial improvements in the oxygenation index ^[16]. However, in patients with severe respiratory failure, NIPPV may offer a greater advantage in improving oxygenation due to its ability to provide higher pressure support.

In terms of ventilation improvement, NIPPV directly increases alveolar ventilation volume and significantly reduces arterial partial pressure of carbon dioxide, making it particularly suitable for patients with pronounced hypercapnia ^[17]. Although HFNC can also reduce carbon dioxide rebreathing by flushing the dead space, its effect on reducing arterial partial pressure of carbon dioxide is relatively weaker. Regarding reintubation rate and mortality, analyses indicate that nasal high-flow oxygen therapy can improve sputum characteristics through warming and humidification, making sputum easier to expectorate and creating favorable conditions for sputum evacuation, thereby reducing the risk of tracheal intubation.

5.3. Comparison of patient tolerance and comfort

HFNC offers significant advantages in terms of patient tolerance and comfort. HFNC utilizes a nasal cannula for connection, causing minimal facial pressure and reducing the occurrence of complications such as skin damage and eye irritation. The warmed and humidified gas better meets the physiological needs of the human body, alleviates discomfort in the patient's respiratory tract, and does not affect the patient's ability to eat, drink, or speak, making it more acceptable to patients. In contrast, NIPPV is connected via a mask, which may cause significant pressure on the patient's face and, when worn for extended periods, can easily lead to skin damage, particularly on the bridge of the nose and cheeks. The study by Sun Panbo et al. revealed that the incidence of adverse reactions such as skin injury and claustrophobia in the conventional group receiving standalone NIV treatment was 34.48%, whereas it was only 10.34% in the intervention group treated with HFNC combined with sequential NIV ($p < 0.05$) ^[18]. Masks may also obstruct the patient's field of vision and induce claustrophobia, making them intolerable for some patients. Additionally, discomforts such as oropharyngeal dryness and flatulence may occur during NIPPV treatment, further reducing patient comfort and compliance.

5.4. Comparison of complication incidence rates

The incidence of complications with HFNC is relatively low. Due to its minimal intervention in the airway, the primary complications are nasal mucosa dryness and bleeding. However, these complications can be effectively reduced by appropriately adjusting the temperature, humidity, and gas flow. In the study by Shi Lihong et al., the complication incidence rate in the HFNC group was 4.08% (2/49), with only one case of atelectasis and one case of abdominal distension; in contrast, the NIPPV group had a complication incidence rate of 6.38% (3/47), with two cases of infection and one case of abdominal distension ^[19]. In addition to mask-related complications such as facial skin injury and eye irritation, NIPPV may also cause oropharyngeal dryness, flatulence, aspiration, and other complications. Prolonged use of NIPPV increases water loss in the patient's oropharyngeal region, leading to oropharyngeal dryness; when pressure settings are inappropriate or the patient does not cooperate well, gas may enter the gastrointestinal tract, causing flatulence; when the patient is unconscious or has a weakened cough reflex, there is a risk of aspiration. These complications may affect the patient's treatment outcomes and rehabilitation process.

6. Conclusion

As non-invasive respiratory support methods, HFNC and NIPPV each have distinct characteristics in the treatment of acute exacerbations of COPD. HFNC (High-Flow Nasal Cannula) offers advantages in improving oxygenation, enhancing patient tolerance and comfort, and reducing the incidence of complications, making it particularly suitable for patients with mild to moderate respiratory failure who are intolerant to NIPPV (Non-Invasive Positive Pressure Ventilation). NIPPV, on the other hand, demonstrates significant efficacy in increasing alveolar ventilation and correcting hypercapnia, serving as the preferred option for patients with acute exacerbation of COPD (Chronic Obstructive Pulmonary Disease) complicated by acute hypercapnic respiratory failure. Clinicians should fully consider factors such as the patient's underlying condition, type of respiratory failure, and tolerance to select HFNC, NIPPV, or a combination of both appropriately to achieve the best therapeutic outcomes. Meanwhile, further in-depth research is needed in the future to optimize treatment strategies and improve the management of patients with acute exacerbation of COPD.

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Research Progress on Astaxanthin in Exercise-Induced Fatigue

Guanyinliang Wen

Shanghai University of Sport, Shanghai 200082, China

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Abstract: Exercise-induced fatigue represents a complex physiological response triggered by physical exertion, with its mechanisms primarily originating from central and peripheral systems. Central fatigue arises from neurotransmitter imbalances such as elevated serotonin and reduced dopamine levels, leading to drowsiness and diminished motor performance. Peripheral fatigue occurs at the muscular level, where energy depletion, metabolic waste accumulation, and oxidative stress impair muscle contraction function. Astaxanthin, a potent antioxidant, directly and primarily alleviates peripheral fatigue through its antioxidant, anti-inflammatory, and mitochondrial protective effects. Simultaneously, by improving the peripheral environment and reducing the transmission of fatigue signals to the brain, it indirectly helps alleviate central fatigue. Based on this, this paper reviews the mechanisms of action and related research progress of astaxanthin on exercise-induced fatigue, and discusses its application value and challenges based on the current status.

Keywords: Exercise-induced fatigue; Astaxanthin; Mechanism of action; Oxidative stress; Anti-inflammatory

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1. Introduction

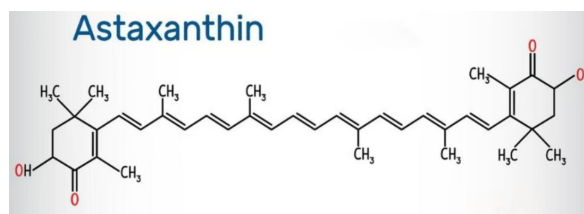
Astaxanthin (AST), specifically 3,3'-dihydroxy-4,4'-diketone- β , β' -carotene, is a multi-target liposoluble ketocarotenoid belonging to the xanthophyll family, which includes β -cryptoxanthin, β -carotene, lycopene, and zeaxanthin ^[1]. Derived from marine organisms, it was first discovered in lobsters and later identified in crabs, salmon, flamingo feathers, certain algae such as *Haematococcus pluvialis*, and fungi ^[2]. Astaxanthin can be obtained through direct extraction or biosynthesis. Due to its potent antioxidant capacity, by exceeding vitamin E by over 100 times and β -carotene by 100 times in antioxidant activity, it finds applications across multiple fields ^[3]. In medicine, research indicates astaxanthin may inhibit cancer cell growth, proliferation, and metastasis through various mechanisms, while also aiding in treating neurodegenerative diseases, such as Parkinson's syndrome and Alzheimer's disease) and preventing atherosclerosis. In skincare, astaxanthin effectively quenches free radicals induced by UV radiation, preventing photoaging and reducing UVA/UVB damage to the skin. Consequently, it is incorporated into various cosmetic products including moisturizers, anti-wrinkle eye creams and face masks ^[4]. Thus, most applications of astaxanthin are based on its unique properties. This paper

comprehensively discussed its application in combating exercise fatigue by focusing on these characteristics.

2. Chemical structure and properties of astaxanthin

Astaxanthin ($C_{40}H_{52}O_4$) has a molecular weight of 596.86 and belongs to the class of terpenoid unsaturated compounds.

Schematic representation of astaxanthin's chemical structure



At its core lies a chain structure composed of 11 conjugated double bonds, with a β-violanone ring at each end. These rings bear a hydroxyl group (–OH) and a ketone group (C=O), respectively. This long-chain conjugated double bond system accounts for astaxanthin's deep pink or red coloration and forms the basis of its potent antioxidant activity. Regarding stereochemistry, astaxanthin possesses two chiral centers (C-3 and C-3'), resulting in three stereoisomers: 3S,3'S, 3R,3'R, and 3R,3'S. Natural astaxanthin primarily originates from *Haematococcus pluvialis*, predominantly in the 3S,3'S configuration, which exhibits the strongest antioxidant activity^[5]. The properties of astaxanthin are largely derived from its structure. Its potent antioxidant capacity stems primarily from its long conjugated double bond system, which stabilizes free radical intermediates, while the terminal hydroxyl and ketone groups also participate in radical quenching. *In vivo*, the reaction between peroxynitrite anion and hydrogen peroxide generates hydroxyl radicals, which can destroy red blood cells and degrade DNA, cell membranes, and polysaccharides. As the number of conjugated double bonds in astaxanthin increases, its ability to quench reactive oxygen species also strengthens. Additionally, the reactivity of the polar hydroxyl configuration in carotenoids is restricted when integrated into the membrane bilayer, hindering reactions between their polyene chains and singlet oxygen. Therefore, astaxanthin, which simultaneously contains hydroxyl and ketone groups, exhibits higher antioxidant activity. The ketone group in astaxanthin activates the hydroxyl group and promotes hydrogen transfer to peroxy radicals, enhancing its antioxidant potency. Ketone groups at positions 4 and 4' further boost astaxanthin's antioxidant properties. By effectively scavenging free radicals and reducing oxidative stress, astaxanthin indirectly suppresses inflammatory responses and enhances immune cell function. In recent years, ongoing research into the structural characteristics of astaxanthin has yielded continuous progress in its application within the field of exercise science. Its antioxidant, anti-inflammatory, and free radical scavenging mechanisms have been progressively validated, with further in-depth studies conducted in related areas.

3. Mechanism of astaxanthin in alleviating exercise fatigue

Exercise-induced fatigue represents a complex physiological response triggered by physical exertion, whose underlying mechanisms can be analyzed at both central and peripheral levels. Central fatigue primarily stems from functional inhibition of motor neurons from the brain to the spinal cord, closely linked to altered neurotransmitter balance: Prolonged exercise increases free tryptophan in the blood, elevating serotonin (5-HT) levels in the

brain, which induces drowsiness and reduces exercise drive. simultaneously, reduced levels of excitatory neurotransmitters like dopamine (DA) further diminish the central nervous system's mobilization capacity ^[6]. Additionally, substances such as ammonia produced by muscle metabolism entering brain tissue may interfere with neural transmission, exacerbating central inhibition. Peripheral fatigue occurs at the neuromuscular junction and within skeletal muscle cells, primarily involving energy depletion and metabolic byproduct accumulation: For instance, excessive depletion of phosphocreatine (CP) and muscle glycogen impairs ATP resynthesis, while the intracellular acidic environment caused by lactic acid accumulation inhibits key enzyme activity (e.g., phosphofructokinase) and disrupts calcium ion release and recycling in the sarcoplasmic reticulum, ultimately reducing muscle contractility ^[7]. Furthermore, oxidative stress resulting from free radical attacks on cell membrane structures damages muscle cell integrity, exacerbating fatigue.

3.1. Antioxidant mechanisms

Astaxanthin regulates oxidative stress (OS) in the body. Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant capacity. Under normal conditions, ROS production and consumption maintain a dynamic equilibrium. During intense exercise-induced oxidative stress, intracellular ROS generation exceeds clearance capacity. Excessive ROS attack critical biomolecules, with lipid peroxidation damage being particularly prominent. This directly compromises the integrity of cell membranes and various organelles, leading to functional impairment ^[8]. Furthermore, excessive ROS disrupts the normal release and recycling of calcium ions (Ca^{2+}) in the sarcoplasmic reticulum and reduces the sensitivity of troponin to Ca^{2+} . The direct consequence is decreased muscle fiber contraction efficiency and reduced maximum voluntary contraction force ^[9]. Simultaneously, ROS accumulation induces vasoconstriction, reducing blood flow to active muscle tissue. This not only limits oxygen (O_2) delivery but also impedes the timely supply of energy substrates like glucose and fatty acids. Consequently, ATP resynthesis rates fail to meet exercise demands, accelerating fatigue onset ^[10]. Astaxanthin possesses potent antioxidant capacity due to its unique molecular structure. Its exceptional antioxidant activity primarily stems from its distinctive molecular composition ($\text{C}_{40}\text{H}_{52}\text{O}_4$). Its long-chain conjugated double bond system and terminal hydroxyl ($-\text{OH}$) and ketone ($-\text{C}=\text{O}$) groups efficiently scavenge large amounts of reactive oxygen species (ROS) generated during exercise and quench singlet oxygen. This terminates free radical chain reactions, protecting muscle cell membranes and mitochondrial structures from oxidative damage while maintaining cellular integrity ^[11]. Furthermore, astaxanthin activates the body's intrinsic "antioxidant defense mechanism" by regulating oxidative stress through the Nrf2 signaling pathway. Under basal conditions, Nrf2 binds to its inhibitory protein Keap1 in the cytoplasm and undergoes continuous degradation, rendering it inactive. Astaxanthin intervention alters Keap1's conformation, causing it to dissociate from Nrf2. The dissociated Nrf2 is then transported into the cell nucleus. Within the nucleus, Nrf2 binds to antioxidant response elements (AREs), initiating transcription and expression of downstream key antioxidant enzyme genes including heme oxygenase-1 (HO-1), superoxide dismutase (SOD), and catalase (CAT) ^[12]. This process activates the cell's intrinsic "antioxidant army", enhancing the body's capacity to scavenge reactive oxygen species (ROS) and mitigate lipid peroxidation damage, ultimately counteracting oxidative stress.

3.2. Anti-inflammatory mechanism

During moderate-to-high-intensity exercise, particularly exhaustive or unaccustomed eccentric movements (e.g., downhill running, strength training), muscle fibers undergo Z-disk rheological changes, and physical tears occur in

the sarcolemma and extracellular matrix ^[13]. Damaged cells immediately release a series of “alarm signals”, pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β). These signals activate vascular endothelial cells, increase vascular permeability, and attract circulating neutrophils (the first immune cells to arrive at the injury site) to rapidly infiltrate the damaged muscle tissue. Subsequently, macrophages are recruited. Initially presenting as pro-inflammatory M1 macrophages, they phagocytose cellular debris and release additional cytokines (e.g., TNF- α , IL-1 β , IL-6), amplifying inflammatory signals to thoroughly clear the injured area. Multiple inflammatory biomarkers have been identified, including cytokines, chemokines, immune-related effectors, acute phase proteins (APPs), reactive oxygen and nitrogen species (RONS), platelet-activating factor (PAF), prostaglandins and cyclooxygenase-related factors (including transcription factors and growth factors), as well as signaling pathways such as NF- κ B, MAPK, and JAK-STAT ^[14]. Studies indicate that astaxanthin suppresses the production of inflammatory mediators in LPS-stimulated BV-2 microglia by inhibiting the induction and proteolytic degradation of iNOS and COX-2 ^[15]. Park et al. found that in streptozotocin-induced diabetic rat models, astaxanthin reduced COX-2, iNOS, and ICAM-1 protein expression levels by alleviating inflammatory responses ^[16]. In a study by Baralic et al., two groups of soccer players were supplemented with astaxanthin or a placebo. Over time, the placebo group exhibited increases in total white blood cell count, neutrophil count, and hs-CRP levels, while no such changes were detected in the supplement group. This further supports the notion that Asx, as a dietary supplement, possesses the ability to suppress mild inflammatory events induced by training ^[17].

3.3. Mitochondrial protection mechanism

The core function of mitochondria is ATP synthesis via oxidative phosphorylation. When mitochondria are damaged, their inner membrane structures, cristae will swell and rupture, leading to uncoupling of oxidative phosphorylation or a sharp decline in its efficiency. This means nutrients are consumed without efficient ATP production. Simultaneously, the activity of the key enzyme responsible for ATP synthesis, the H⁺-ATPase (or F0F1-ATP synthase) also declines ^[18]. Consequently, working muscles cannot obtain a sustained, adequate energy supply, leading to weakened contraction force and rapid onset of fatigue. Cao Xiuming et al. conducted an experiment using astaxanthin to protect mitochondria damaged by hydrogen peroxide in vitro. They observed the activity of mitochondrial Complex I and ATPase; mitochondrial membrane potential, membrane fluidity, and the degree of mitochondrial permeability transition pore (PTP) opening. Results demonstrated that astaxanthin significantly enhanced the activity of H⁺-ATPase (F0F1-ATP synthase) in damaged mitochondria, thereby safeguarding ATP synthesis efficiency ^[19]. Mitochondria serve as cellular powerhouses, primarily functioning through oxidative phosphorylation via the electron transport chain (ETC) to synthesize ATP. During this process, oxygen acts as the final electron acceptor, being reduced to form water. However, some oxygen molecules undergo incomplete reduction, generating byproducts such as reactive oxygen species (ROS) ^[20]. Studies indicate that astaxanthin effectively inhibits lipid peroxidation reactions in biological membranes. Furthermore, experimental evidence demonstrates that exogenously added astaxanthin can be taken up by cells and specifically accumulated within mitochondria. Given that key protein complexes of the electron transport chain are primarily embedded in the inner mitochondrial membrane, this distribution characteristic of astaxanthin enables it to effectively mitigate oxidative damage to mitochondrial membrane structures caused by ROS ^[21]. Astaxanthin effectively mitigates the destructive effects of mitochondrial overload, demonstrating protective effects against oxidative damage across multiple animal models. Studies indicate that in rodents following intense exercise, astaxanthin significantly reduces skeletal muscle damage while decreasing oxidative modification of muscle proteins ^[22]. Furthermore,

under experimental conditions combining a high-fat diet with treadmill exercise, astaxanthin further suppressed the expression of inflammatory markers ^[23]. Collectively, these findings indicate that during physiological stress (such as exercise or metabolic load) leading to mitochondrial overload, astaxanthin exerts its antioxidant effects by inhibiting excessive ROS production, thereby protecting mitochondrial structural and functional integrity.

4. Astaxanthin as a therapeutic approach for exercise-induced fatigue

Multiple studies indicate that daily doses of astaxanthin ranging from 4 to 20 milligrams are well-tolerated with no significant side effects. It effectively scavenges excess free radicals generated during exercise, mitigating oxidative stress damage to muscle cells, thereby aiding fatigue relief and accelerating recovery. Additionally, both short-term higher doses (e.g., 100 mg/day) and long-term moderate doses (8–12 mg/day) are considered safe ^[24–26]. Baralic I et al. demonstrated that astaxanthin supplementation (4 mg/day for 90 days) reduced creatine kinase (CK) release, decreased reactive oxygen species (ROS) production, and enhanced overall antioxidant status in young soccer players ^[27]. Daniel et al. found that 12 mg/day of astaxanthin supplementation in cyclists, for 7 days improved cycling performance while promoting short-term energy metabolism and increasing fat oxidation rates ^[28].

Currently, combined interventions may demonstrate superior effects compared to single-agent astaxanthin applications. Combined interventions represent a research hotspot, exemplified by the combination of astaxanthin and hyperbaric oxygen therapy. A 2024 study on rugby players demonstrated that post-exhaustion exercise, hyperbaric oxygen therapy combined with astaxanthin supplementation (60 minutes of hyperbaric oxygen after oral administration of 16 mg astaxanthin) more effectively promoted recovery of muscle oxygen saturation (SmO₂) and accelerated clearance of blood lactate (Bla) compared to hyperbaric oxygen alone or natural recovery. During hyperbaric oxygen therapy, factors like elevated oxygen concentration may exacerbate oxidative stress. Astaxanthin's potent antioxidant properties counteract this side effect, creating a complementary effect. Animal studies further suggest that the astaxanthin-hyperbaric oxygen combination may enhance the body's intrinsic antioxidant defenses by modulating the Keap1/Nrf2/HO-1 signaling pathway, providing a deeper theoretical basis for the synergistic intervention ^[29].

To date, encapsulation techniques such as spray drying have enabled the production of water-soluble astaxanthin powder, which can be added to sports drinks as a novel approach to alleviating exercise-induced fatigue. By combining electrolytes, vitamins, and other nutrients, this approach integrates nutritional supplementation with anti-fatigue effects. It not only effectively replenishes athletes' fluids, carbohydrates, and electrolytes but also scavenges exercise-induced free radicals, alleviating exercise-induced fatigue and enhancing athletic performance efficiency.

5. Summary and outlook

This paper systematically reviews the mechanisms and application prospects of astaxanthin in alleviating exercise-induced fatigue, based on existing research and its unique chemical structure and biological properties. The onset of exercise fatigue involves complex imbalances in central regulation and peripheral metabolism, where oxidative stress, inflammatory responses, and mitochondrial dysfunction are key factors accelerating fatigue progression. Through a dual mechanism of “directly scavenging reactive oxygen species” and “activating the Keap1/Nrf2 pathway to enhance endogenous antioxidant enzymes”, astaxanthin effectively mitigates exercise-induced oxidative stress. Simultaneously, it suppresses the NF-κB signaling pathway, downregulating the expression of

inflammatory mediators such as TNF- α and IL-1 β to control excessive inflammatory responses. Furthermore, astaxanthin specifically accumulates in mitochondria, stabilizing membrane potential, protecting electron transport chain function, and enhancing ATP synthesis efficiency. This synergistic action across three critical dimensions, the antioxidant defense, anti-inflammation, and energy supply, comprehensively alleviates exercise-induced fatigue. However, despite astaxanthin's promising potential for improving exercise fatigue, several issues warrant further exploration in future studies.

While existing studies have established a general effective dosage range (e.g., 4–20 mg/day), the optimal supplementation dosage and duration for different sports disciplines, intensity levels, and individual variations, such as training status and physical constitution remain unclear. Future studies require more refined clinical trials to establish personalized supplementation protocols. Concurrently, astaxanthin's inherent poor water solubility and low stability remain bottlenecks limiting its bioavailability. While microencapsulation techniques have advanced, developing novel, more targeted, and stable nano-delivery systems, such as liposomes or polymeric nanoparticles will be crucial for enhancing efficacy and improving human utilization rates. Finally, most current research focuses on animal models or small sample populations, lacking large-scale, randomized double-blind, multicenter clinical evidence. Future studies require higher-level clinical data to robustly support the application value and safety of astaxanthin in sports medicine.

Disclosure statement

The author declares no conflict of interest.

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Study on the Distribution Characteristics and Blood Type Analysis of Voluntary Blood Donors in the Linxia Region

Guangzhong La, Anbing Wang, Yan Chang*

Linxia Prefecture Central Blood Station, Linxia 731100, Gansu, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To analyze the distribution and blood type characteristics of unpaid blood donors in Linxia area from 2012 to 2021, provide the basis for the strategy of recruiting safe blood sources in the future, ensure sufficient and safe blood supply, and promote the sustainable development of unpaid blood donation in this area. *Methods:* Collect the data of unpaid blood donors in Linxia area, and make statistics, comparison and analysis based on the query information of the fourth generation safe blood transfusion standardization system and the free blood donation registration form. *Results:* The total number of blood donors was 151131 and the ratio of male to female blood donors was 2.61:1. People aged 18–45 were the main blood donors, accounting for 80.78% of all unpaid blood donors. 37.19% of people with junior high school education or below; Farmers, other professionals and civil servants were the main subjects of blood donation, accounting for 15.74%, 14.98% and 12.12%, respectively. The blood group distribution was O > B > A > AB, and the negative rate was 8.2%. Blood type O was the most common in Hezheng County (34.08%). The distribution of blood type B in Kangle County (31.99%), blood type A in Yongjing County (29.58%), blood type AB in Dongxiang County (10.18%). *Conclusion:* The unpaid blood donors in Linxia area have significant characteristics in terms of gender, age, occupation, education level, etc. to master the distribution characteristics of the unpaid blood donors and blood types in Linxia area is helpful to carry out targeted publicity and recruitment of unpaid blood donation and blood collection, and is of great significance to continuously strengthen the contingent of unpaid blood donors and fully guarantee the clinical blood demand under the new situation.

Keywords: Voluntary blood donation; Population distribution; Blood analysis

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1. Introduction

The Central Blood Station of Linxia Hui Autonomous Prefecture was established in August 2004. Over the past 20 years of steady development, the volume of unpaid blood donations and clinical blood supplies has increased

annually. The prefecture has been honored as a “National Advanced City for Voluntary Blood Donation” four times. In recent years, the work of unpaid blood donation in the Linxia area has made significant progress, with a steady improvement in blood quality and an effective guarantee of clinical blood demand. To conduct an in-depth study on the distribution and blood type characteristics of unpaid blood donors in the Linxia area, relevant data from unpaid blood donors from 2012 to 2021 were analyzed. This study aims to provide scientific data and strategic bases for future publicity and recruitment efforts to secure safe blood sources, ensuring the scientific, reasonable, and efficient use of blood and promoting the healthy and sustainable development of unpaid blood donation work in the region.

2. Materials and methods

2.1. Survey participants

From January 1, 2012, to December 31, 2021, a total of 151,131 voluntary blood donors participated in blood donation at all blood collection sites in Linxia region. These donors met the health consultation and examination requirements specified in the “2019 Edition of Technical Operating Procedures for Blood Stations” after undergoing pre-donation health consultations and preliminary blood tests ^[1].

2.2. Survey method

The registration forms of voluntary blood donors and the Cross Fourth Generation Standardized System for Safe Blood Transfusion were utilized to query and retrieve detailed information on blood donors for data statistics and analysis (each donation counted as one individual).

2.3. Testing methods and reagents

The ABO blood group was determined using the forward and reverse typing method. Forward typing employed anti-A and anti-B blood typing reagents (produced by Beijing Jinhao Pharmaceutical Co., Ltd.), while reverse typing utilized red blood cell reagents (produced by Shanghai Blood Biopharmaceutical Co., Ltd.) ^[2].

RhD blood typing was performed using a specialized cardboard direct agglutination method, where red blood cell suspensions were mixed with anti-RhD serum, and O-type ccdee and CCDee red blood cells were used as negative and positive controls, respectively (produced by Shanghai Blood Biopharmaceutical Co., Ltd.) ^[2].

2.4. Statistical analysis

The SPSS statistical analysis software was used to conduct statistical analysis on relevant data, with counts expressed as n%.

3. Results

3.1. Gender composition

There were 109,239 male donors, accounting for 72.28%, and 41,892 female donors, accounting for 27.72%. The ratio of males to females was 2.61:1. (see **Table 1**)

Table 1. Gender and age distribution

Characteristic	Category	n	Proportion (%)
Gender	Male	109,239	72.28
	Female	41,892	27.72
Age	18–25 years	37,813	25.02
	26–35 years	45,175	29.89
	36–45 years	39,096	25.87
	46–55 years	27,252	18.03
	55–60 years	1,795	1.19

3.2. Age composition

The majority of voluntary blood donors were aged between 18 and 45, accounting for 80.78% of all donors. Specifically, those aged 18–25 accounted for 25.02%, 26–35 accounted for 29.89%, 36–45 accounted for 25.87%, 46–55 accounted for 18.03%, and 55–60 accounted for 1.19%. (**Table 1**)

3.3. Educational attainment distribution

The proportion of donors with a bachelor's degree or higher was 8.19%, those with a junior college degree accounted for 17.33%, those with a high school or technical secondary school education accounted for 14.23%, and those with a junior high school education or below accounted for a significant 37.19%. (**Table 2**)

Table 2. Distribution of educational level and occupation

Characteristic	Category	n	Proportion (%)
Education level	Junior high school or below	56,201	37.19
	High school / Technical secondary school	21,500	14.23
	College	26,186	17.33
	Bachelor's degree or above	12,375	8.19
Occupation	Student	12,800	8.47
	Teacher	8,456	5.60
	Civil servant	18,318	12.12
	Worker	6,572	4.35
	Military personnel	5,981	3.96
	Medical staff	7,609	5.03
	Farmer	23,786	15.74
	Other	22,640	14.98

Other occupations: Includes self-employed individuals, freelancers, migrant workers, and the unemployed.

3.4. Occupational distribution

Farmers, individuals in other occupations, and public officials constitute the main group of voluntary blood

donors, with blood donation rates of 15.74%, 14.98%, and 12.12%, respectively. Students and teachers together account for 14.07%, while workers and military personnel only make up 4.35% and 3.96%, respectively (**Table 2**).

3.5. Blood type distribution

The predominant blood types are A, B, and O, with AB type accounting for 9.64%. The distribution is O > B > A > AB. There was a total of 1,243 RhD-negative blood donors, with an average negativity rate of 0.82%. Among the A, B, O, and AB blood type distributions, the proportion of RhD-negative is 0.72%, 0.81%, 0.81%, and 0.85%, respectively. Statistical analysis using SPSS 25.0 software on the data in **Table 3** yielded an χ^2 value of 30.323 and a *p*-value of 0.00001.

Since the *p*-value is less than 0.05, the difference is statistically significant (**Table 3**). Blood type O is the most prevalent in Hezheng County, accounting for 34.08%; blood type B is the most prevalent in Kangle County, accounting for 31.99%; blood type A is the most prevalent in Yongjing County, accounting for 29.58%; and blood type AB is the most prevalent in Dongxiang County, accounting for 10.18%.

Table 3. Distribution of blood types among voluntary blood donors

ABO blood type	n	Proportion (%)	RhD blood type				χ^2	<i>p</i> -value
			RhD (+) (n)	Constituent ratio	RhD (-) (n)	Constituent ratio		
A	42,904	28.39%	42,595	99.28%	309	0.72%	30.323	< 0.05
B	44,713	29.59%	44,349	99.19%	364	0.81%		
O	48,943	32.38%	48,547	99.19%	396	0.81%		
AB	14,521	9.64%	14,397	99.15%	124	0.85%		
Total	151,131	100%	149,888	99.18%	1,243	0.82%		

3.6. Statistical analysis

Statistical analysis using SPSS 25.0 software on the distribution of A, B, O, and AB blood types in Kangle County, Yongjing County, Hezheng County, and Dongxiang County in the Linxia region yielded an χ^2 value of 63.826. Since the *p*-value is less than 0.05, the difference is statistically significant (see **Table 4**).

Table 4. Distribution of blood types by county and city

County (City)	Blood type and its proportion								Total
	A	Proportion	B	Proportion	O	Proportion	AB	Proportion	
Linxia City	23,965	28.50%	24,439	29.07%	27,539	32.76%	8,131	9.67%	84,074
Kangle County	4,716	27.13%	5,561	31.99%	5,532	31.82%	1,577	9.07%	17,386
Guanghe County	2,542	28.46%	2,725	30.51%	2,823	31.61%	841	9.42%	8,931
Yongjing County	2,634	29.58%	2,572	28.89%	2,862	32.14%	836	9.39%	8,904
Jishishan County	2,434	28.67%	2,504	29.50%	2,735	32.22%	816	9.61%	8,489
Hezheng County	2,063	27.62%	2,151	28.80%	2,546	34.08%	710	9.50%	7,470
Linxia County	1,720	28.01%	1,873	30.50%	1,956	31.86%	591	9.63%	6,140
Dongxiang County	1,693	29.36%	1,664	28.86%	1,822	31.60%	587	10.18%	5,766

4. Discussion

According to statistics, from 2012 to 2021, there were 151,324 instances of voluntary blood donation in the Linxia region. From 2012 to 2021, the average permanent population in Linxia region was 2.0517 million, resulting in a blood donation rate per thousand population of approximately 7.4% in Linxia region^[3]. This rate is lower than the national average of 11.1% in 2020 and significantly lower than the 15.0% recommended by developed countries, China's Hong Kong and Macao regions, and the World Health Organization^[4]. The primary reasons for this disparity include the late establishment, weak foundation, and poor infrastructure of the Central Blood Station in Linxia Prefecture, coupled with relatively low public awareness and acceptance of voluntary blood donation. However, from another perspective, this indicates a vast potential and scope for voluntary blood donation in Linxia region. Strengthening publicity and recruitment efforts in future work will encourage more people to participate in voluntary blood donation.

The gender ratio of voluntary blood donors in Linxia region is 2.61:1, with significantly more male donors than female. This trend is generally consistent with findings reported in other cities within the province, but it differs significantly from the results of a survey conducted by the Gansu Provincial Blood Center^[5,6]. The disparity is primarily attributed to physiological reasons that prevent women from donating blood during pregnancy and childbirth (lasting more than one year), miscarriage (lasting more than six months), lactation (lasting more than one year), and menstruation (three days before and after). Additionally, blood tests reveal a significantly higher rate of unqualified hemoglobin levels in women compared to men^[4]. Therefore, during specific publicity and recruitment campaigns, it is essential to provide appropriate explanations for deferred blood donations based on these reasons. Learning from the good experiences and methods of other blood stations in this regard can help increase the proportion of female blood donors in Linxia region.

The age group primarily engaged in voluntary blood donation in Linxia region is between 18 and 45 years old, which aligns with findings reported in other domestic cities^[7]. This indicates that individuals in this age group are relatively healthy, possess a strong sense of social responsibility, have mature mental development, and exhibit a high level of participation in voluntary blood donation. Targeted publicity and recruitment efforts should be strengthened for this age group to enhance blood donation services. Efforts should be made to develop this age group into regular blood donors. The online reservation service platform for voluntary blood donation should be fully utilized to improve the convenience and efficiency of blood donation services.

From an educational perspective, individuals with junior high school education or below constitute a significant proportion. This trend is related to the fact that the region is a small to medium-sized city in western China, with relatively slow economic and cultural development and a lower average level of education per capita. As socioeconomic development and educational reforms continue to advance, the educational level of voluntary blood donors is expected to rise, leading to a substantial increase in awareness and acceptance of blood donation.

In terms of occupational distribution, individuals in other professions, such as self-employed workers and freelancers, had the highest blood donation rate at 14.98%. The Linxia region has historically been a vital hub for the tea-horse trade and the Tang-Fan Ancient Road, serving as a crucial junction along the Silk Road. As a result, the commerce and logistics industries are relatively well-developed, leading to a large number of people engaged in commercial logistics and service industries^[8]. Comparatively, these groups have more flexible and ample time to participate in blood donations. The blood donation rate among public officials is also relatively high (12.12%), primarily due to the strong emphasis placed on voluntary blood donation by governments at all levels, which has been incorporated into government performance evaluations and spiritual civilization assessments. This is also

attributed to the effective functioning of voluntary blood donation leadership groups and the Red Cross Society at various levels, which actively promote voluntary blood donation efforts ^[9]. In the Linxia region, the rural population accounts for 67.16% of the total population, yet farmers only contribute 15.74% of blood donations. The primary reasons for this include the relatively low educational levels among farmers, leading to low awareness and acceptance of voluntary blood donation. Additionally, their dispersed living conditions make it difficult to promote voluntary blood donation, and most blood collection points are located in bustling urban areas or county seats, making it inconvenient for farmers to donate blood nearby. Moving forward, different recruitment strategies tailored to local conditions, timing, and individuals, and launch a series of “down-to-earth, practical, and effective” promotional activities to strengthen blood donation services should be developed. This will help structurally, holistically, and effectively address the challenge of recruiting voluntary blood donors in rural areas, significantly reversing the situation in the Linxia region where “urban residents donate blood, while rural residents receive blood transfusions” ^[8].

In terms of blood types, the distribution follows the order of $O > B > A > AB$, which is consistent with the blood type distribution characteristics of the Gansu population reported in the literature ^[2]. Based on these blood type distribution characteristics, targeted blood donation recruitment strategies should be developed, with a particular focus on understanding the seasonal variations and clinical application patterns of each blood type to ensure the matching, consistency, and coordination of “blood collection” and “blood utilization,” thereby avoiding clinical blood supply difficulties or blood wastage caused by blood type imbalances. The RHD negative rate is 0.82%, slightly higher than the 0.75% reported in the literature for the Linxia region ^[10]. Compared to other regions, the Linxia region has a relatively abundant supply of RHD negative blood resources ^[11,12]. RHD-negative blood is a scarce and precious blood resource that should be fully utilized by promptly allocating it to blood stations in other regions. Additionally, by applying the technology for preparing frozen red blood cells, red blood cells with rare blood types can be frozen and stored, enabling more rational utilization of this valuable blood resource and more timely transfusions. This effectively mitigates the risk of patients missing the optimal window for rescue due to the inability to locate a blood source promptly.

Currently, the voluntary blood donation program in the Linxia region is progressing smoothly, with an increasing number of individuals participating in voluntary blood donation. Through comprehensive and scientific data analysis, this study can grasp the characteristics of the voluntary blood donor population and blood type distribution in this region. This allows us to formulate corresponding publicity and recruitment strategies, continuously expand the ranks of voluntary blood donors, enhance blood safety standards, effectively safeguard the life and health rights of the people, and robustly ensure medical safety and social stability.

5. Conclusion

Based on the analysis, it can be concluded that the voluntary blood donor population in Linxia region exhibits distinct characteristics in terms of gender, age, occupation, and education level. Understanding the distribution patterns of these donors and their blood types is crucial for developing targeted recruitment strategies and optimizing blood collection efforts. This approach will significantly contribute to strengthening and expanding the voluntary blood donor base, thereby ensuring a stable and sufficient blood supply to meet clinical needs in the evolving healthcare landscape.

Disclosure statement

The authors declare no conflict of interest.

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Real-world Study of the Efficacy and Safety of Idebenone Tablets in the Treatment of Post-stroke Depression

Longteng Liang¹, Pengfei Liu², Guoai Lun³

¹Department of Medical Psychology, Zaozhuang Municipal Hospital, Zaozhuang 277100, Shandong, China

²Department of Neurology, Tai'an Central Hospital, Tai'an 271000, Shandong, China

³Department of Neurology, Qingzhou People's Hospital, Weifang 262500, Shandong, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* This study aimed to systematically evaluate the effect of idebenone tablets in the treatment of post-stroke depression (Post-Stroke Depression, PSD). *Methods:* This study was a single-arm, prospective, observational study that recruited PSD patients who met the inclusion criteria after being assessed by the investigator between January 2022 and June 2023. The demographic characteristics, disease status, treatment status, and medication status of the patients were collected through questionnaires, and the Hamilton depression score of the patients was collected through the Case Report Form (CRF) to evaluate the effectiveness and safety of idebenone tablet treatment. *Results:* A total of 4902 PSD patients were included in this study, of which 2496 were males, accounting for 50.9%, and 2406 were females, accounting for 49.1%. According to the Hamilton Depression Rating Scale (HAMD), 13.9% were no depression at the first visit, 53.0% were mildly depressed, 24.3% were moderately depressed, and 8.8% were severely depressed. After treatment, the proportion of no depression was 26.1%, mild depression accounted for 53.3%, moderate depression accounted for 16.8%, and severe depression accounted for 3.8%, and the difference in the proportion of depression before and after treatment was statistically significant ($P < 0.05$). *Conclusion:* Idebenone tablets can significantly reduce Hamilton's depression score, suggesting that it has a significant therapeutic effect in improving PSD symptoms.

Keywords: Post-stroke depression; Idebenone; Hamilton depression score; Real-world study

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1. Introduction

Post-stroke depression (PSD) is one of the common complications caused by stroke, with a high incidence of 30% to 50%, and a heavy burden of disease, affecting the long-term prognosis of patients. The pathological mechanism of PSD is complex, including inflammatory responses, neurochemical disorders after brain injury, and decreased

neuroplasticity. In view of the complex pathogenesis, the current treatment effect is very limited, and there is an urgent need to find new therapeutic agents to improve the long-term prognosis of patients. Previous studies have suggested that mitochondrial dysfunction affects the synthesis, release, and reuptake of neurotransmitters, which may lead to the development of depressive mood.

The CoQ10 antioxidant Idebenone has a unique anti-inflammatory, antioxidant, and improved mitochondrial function. Studies have shown that idebenone can protect nerve cells, reduce oxidative stress, and promote mitochondrial energy metabolism, thereby playing a therapeutic role in neurological diseases. In recent years, the application of idebenone in stroke rehabilitation has attracted much attention, especially in the treatment of PSD. However, research on the efficacy and safety of idebenone in PSD is still limited, especially with the insufficient real-world study.

Based on this, this study aims to systematically evaluate the efficacy and safety of idebenone tablets in the treatment of PSD through real-world studies. Through a larger sample size. This study hopes to provide strong evidence for the clinical application of idebenone in the treatment of PSD, and further explore its role in improving patients' psychological status and promoting neurorehabilitation. This not only helps to enrich the treatment strategy for PSD but also provides an important reference for clinicians to develop personalized treatment plans.

2. Data and methods

2.1. Study design

This study is a single-arm, prospective, observational study that aims to provide real-world data support for the rational use of idebenone tablets in clinical practice^[1,2]. This study recruited patients with PSD who attended the clinic between January 2022 and June 2023 and met the inclusion and exclusion criteria after being assessed by the investigator. Idebenone tablets were administered orally, with a dose of 30 mg per time, three times daily after meals, for a continuous treatment period of 3 months. Follow-up assessments were conducted at baseline (before treatment) and after 3 months of treatment. The demographic characteristics, disease status, treatment, and medication of the patients were collected through questionnaires, and the Hamilton depression score of the patients was collected through the Case Report Form (CRF) to evaluate the effectiveness and safety of idebenone tablets^[3].

2.2. Study population

The study intends to include PSD patients who have used idebenone tablets, and the specific screening criteria are as follows. Inclusion criteria: (1) Age ≥ 18 years old; (2) History of stroke confirmed as ischemic or hemorrhagic stroke within 6 months to 5 years of onset; (3) Depressive symptoms meet the diagnostic criteria for PSD in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or the International Classification of Diseases (ICD-10); (4) Patients or their family members voluntarily participate in this study and sign the informed consent form^[4].

Exclusion criteria: (1) Presence of other serious neurological diseases, such as Alzheimer's disease, Parkinson's disease, epilepsy, etc.; (2) Patients with serious cardiovascular diseases, such as acute myocardial infarction, severe arrhythmia or heart failure, which may affect the safety evaluation of the study drug; (3) Patients with a history of schizophrenia, bipolar disorder or other serious mental illnesses; (4) Patients with severe abnormalities in liver or kidney function, which affect drug metabolism or may lead to aggravation of adverse reactions; (5) Patients who are participating in other interventional clinical trials or have received other

antidepressant treatments with uncertain efficacy within 3 months before treatment; (6) Patients with a history of allergy to idebenone or its components^[5].

2.3 Evaluation index Hamilton depression score

- (1) Hamilton Depression Score: The Hamilton Depression Rating Scale (HAMD) is a clinical scale compiled by Max Hamilton in 1960 to assess the severity of depression and is widely used in clinical diagnosis, efficacy evaluation and research. This scale is simple and reliable, and is a common tool in clinical research on depression. The scale consists of depressed mood, sensory loss, somatic symptoms, cognitive symptoms, anxiety symptoms, and suicidal ideation, with each item ranging from 0 to 4 points based on severity, with a total score ranging from 0 to 52 points. Typically, higher scores indicate more severe depressive symptoms. In this study, a score of 0–7 was no depression; 8–17 is mild depression; 18–24 indicates moderate depression; A score of 25 and above is severe depression.
- (2) Evaluation of medication adherence: In this study, all patients were surveyed for their compliance with idebenone through a unified questionnaire, and whether the drug was discontinued and the reasons for discontinuation were recorded^[6].

2.4. Statistical methods

Statistical analysis was performed using SAS 9.4 software. The mean and standard deviation of the quantitative data were described, and self-comparison was performed using the paired *t*-test/Wilcoxon signed-rank test or McNemar's test (for categorical variables). Analysis of variance (ANOVA) was used to compare the data among multiple groups. The frequency and rate were described by qualitative data, and the chi-square or McNemar's test was used for comparison between groups. The difference in hypothesis testing with a $P < 0.05$ was statistically significant^[7,8].

3. Results

3.1. General demographic data of patients

A total of 4902 PSD patients were included in this study, including 2496 males (50.9%) and 2406 females (49.1%). More than 80% of the included PSD patients had bad lifestyle habits, as shown in **Table 1**.

3.2. The patient's stroke history and previous treatment methods

The duration of stroke varies, with only 0.1% of patients having been sick for less than 1 year, 49.5% having been sick for 1–2 years old, 24.4% having been sick for 2–3 years old, 18.6% having been sick for 3–5 years old, and 7.4% having been sick for more than 5 years old. More than 90% of the patients were treated with medication, 35.1% of the patients were treated with rehabilitation training, and 11.8% of the patients were treated with surgery, as shown in **Table 2**.

Table 1. General demographic data of patients
[n,(%)]

Variable	Patients with PSD (<i>n</i> = 4902)
Gender	
Male	2496 (50.9)
Female	2406 (49.1)
Age	
< 18 years old	24 (0.5)
18–30 years old	110 (2.2)
31–40 years old	257 (5.2)
41–50 years old	469 (9.6)
51–60 years old	1145 (23.4)
61–70 years old	1371 (28.0)
71–80 years old	1014 (20.7)
> 80 years old	512 (10.4)
Family history	
Yes	681 (16.8)
No	3385 (83.2)
Hypertension	
Yes	2901 (59.2)
No	2001 (40.8)
Diabetes	
Yes	1076 (22.0)
No	3826 (78.0)
Dyslipidemia	
Yes	1353 (27.6)
No	3549 (72.4)
Heart disease	
Yes	588 (12.0)
No	4314 (88.0)
Vasculitis	
Yes	160 (3.3)
No	4742 (96.7)
Bad living habits	
Yes	3995 (81.5)
No	907 (18.5)

Table 2. Stroke history and previous treatment methods
[n,(%)]

Variable	Statistics
Duration of stroke	
< 1 year	7 (0.1)
1–2 years	2423 (49.5)
2–3 years	1193 (24.4)
3–5 years	912 (18.6)
> 5 years	365 (7.4)
Prior medication	
Yes	4617 (94.2)
No	285 (5.8)
Rehabilitation training treatment	
Yes	1719 (35.1)
No	3183 (64.9)
Surgical treatment	
Yes	576 (11.8)
No	4326 (88.2)

3.3. Changes in the distribution of depression before and after treatment

According to the Hamilton Depression Scale, 13.9% had no depression at the first visit, 53.0% were mildly depressed, 24.3% were moderately depressed, and 8.8% were severely depressed. After treatment, the proportion without depression was 26.1%, mild depression accounted for 53.3%, moderate depression accounted for 16.8%, and severe depression accounted for 3.8% and the difference in the proportion of depression before and after treatment was statistically significant ($P < 0.05$) (Table 3).

Table 3. Changes in the distribution of depression before and after treatment [n,(%)]

	No depression	Mild depression	Moderate depression	Severe depression
First diagnosis	682(13.9)	2596(53.0)	1192(24.3)	432(8.8)
After treatment	1279(26.1)	2613(53.3)	824(16.8)	186(3.8)
χ^2			345.462	
P			<0.05	

3.4. Drug adherence analysis

During the treatment, 3.1% of the patients had self-discontinuation, and the reasons for self-discontinuation were: inconvenient follow-up (67 people, accounting for 43.5%), and poor self-perception (55 people, accounting for 35.7%), adverse reactions (17 people, accounting for 11.0%) and others (15 people, accounting for 9.8%) (Table 4).

Table 4. Analysis of drug adherence [n,(%)]

Variable	Statistics
Whether to stop taking the drug	
Yes	154 (3.1)
No	4748 (96.9)
Reasons for drug discontinuation (154 people stopped taking the drug)	
Inconvenient follow-up examination	67 (43.5)
Feeling ineffective	55 (35.7)
Adverse reactions were severe	17 (11.0)
Other	15 (9.8)

4. Discussion

In this study, we evaluated the efficacy of idebenone tablets in patients with PSD, and the results showed that idebenone tablets significantly reduced Hamilton's depression score, suggesting that it had a significant therapeutic effect in improving PSD symptoms. The results of the study further support the use of idebenone as an effective intervention for PSD patients, which not only provides a new option for clinical treatment but also provides a basis for the development of subsequent large-scale and multi-center clinical trials.

In this study, although idebenone tablets had a significant improvement in the Hamilton depression score of post-stroke depressed patients, 3.1% of patients still self-stopped the drug, and the inconvenience of follow-up visits was the largest among patients who stopped taking the drug. This discontinuation rate is relatively low compared to previous studies. In a previous study^[9], the discontinuation rate of antidepressants for PSD was

between 7% and 30%, mainly due to drug infeasibility or more drug side effects. The discontinuation rate in this study was relatively low, which suggests that idebenone is tolerable and safe, indicating that it has better patient compliance and acceptance in practical clinical applications. This result further supports the potential advantages of idebenone in the treatment of PSD.

PSD is a common serious complication that not only increases the mental burden of patients and reduces their quality of life, but also increases the risk of recurrence and death after stroke. Although several drugs are currently used to treat PSD, their efficacy and safety still have certain limitations^[10]. As a drug with strong antioxidant and mitochondrial protective effects, idebenone can promote the recovery of brain tissue by scavenging free radicals, reducing apoptosis, and improving neuronal function, thereby relieving depressive symptoms. In addition, idebenone may further exert its antidepressant effects by regulating the metabolic balance of neurotransmitters, improving cerebral blood flow, and energy metabolism. These mechanisms suggest that idebenone has unique advantages in the treatment of PSD^[11].

Some limitations are inevitable in this study. First, the observation time of this study is short, and the effect of idebenone tablets on the long-term efficacy and safety of post-stroke depressed patients cannot be fully evaluated. In addition, this study did not conduct an in-depth analysis of the reasons for patient self-discontinuation, and future studies should more comprehensively explore patient compliance, especially factors related to drug side effects or individual differences. These limitations suggest that larger, multicenter, long-term follow-up studies are needed before more definitive conclusions can be drawn^[12].

5. Conclusion

In summary, the results of this study verify the effectiveness of idebenone tablets in improving PSD symptoms, especially in reducing Hamilton's depression score. Although this study has some limitations, such as the lack of a control group and short observation time, the results provide a strong basis for further exploring the application value of idebenone in PSD. Future studies should consider expanding the sample size, extending the follow-up time, and exploring the combination of idebenone with other treatments to further optimize the treatment strategy for PSD.

Disclosure statement

The authors declare no conflict of interest.

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Real-world Study on the Effectiveness and Safety of Citicoline Sodium Capsules in the Treatment of Traumatic Brain Injury

Ping Liang¹, Jun Yang², Yuan Lu³, Cheng Du³, Yiqin Yao^{2*}

¹Department of Neurosurgery, Zhongda Hospital, Southeast University, Nanjing 210009, Jiangsu, China

²Department of Neurology, Nanjing Lishui District People's Hospital, Nanjing 211299, Jiangsu, China

³Department of Neurology, Nanjing Jiangning Hospital, Nanjing 210000, Jiangsu, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* This study aimed to evaluate the prognostic impact of citicoline sodium capsules on patients with traumatic brain injury (TBI) and its safety. *Methods:* This study is a multicenter, single-arm, prospective, observational study of brain trauma patients who met the inclusion criteria between March 2023 and June 2024 and who could be treated with citicoline sodium capsules after being evaluated by the investigator. The Glasgow Coma Scale (GCS) and Mini-Mental State Examination (MMSE), the incidence of adverse drug reactions/adverse events during treatment, and the abnormalities of safety tests with clinical evaluation significance were observed at 1 month and 2 months after treatment. *Results:* A total of 2806 patients, 63.1% of whom were male, with an average age of 58.85 years old. The GCS and MMSE scores of the patients at 1 month and 2 months after treatment were significantly improved and were statistically significant, indicating that citicoline sodium had a significant effect on improving the state of consciousness and cognitive function of patients with TBI. Only 8 adverse reactions were reported in the study, all of which were mild gastrointestinal reactions and anaphylaxis, and did not lead to treatment interruption or serious consequences. *Conclusion:* Citicoline sodium has a significant therapeutic effect on patients with TBI and has good safety.

Keywords: Citicoline sodium capsule; Traumatic brain injury; Glasgow Coma Scale; Simple intellectual status check; Safety

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1. Introduction

With the development of domestic transportation and the renewal and increase of production equipment, the incidence of head trauma caused by various injuries is increasing, especially the high order of disability among the working age. Among them, head trauma accounts for 15% of the total trauma in China, and the mortality rate accounts for about 85%. The common clinical types of cranial trauma mainly include scalp trauma, concussion,

intracranial hematoma and other brain contusions and lacerations, and skull fractures. Most types of disease are characterized by complex pathological conditions, rapid disease evolution, and prognosis. Surgery is the necessary and most important means. Common types of poor prognosis are more common, such as total or partial disability of limbs, deterioration of language ability, intellectual deterioration, etc., which cause a huge economic and long-term burden on the families and society of such people, and the quality of life of the patient himself cannot be discussed. Cytidine Diphosphate Choline (CDPCho), also known as citicoline, is a natural endogenous compound involved in the biosynthesis of lecithin in the body. CDPCho can repair the structure of cell membranes after brain cell injury, improve neuronal dysfunction, increase cerebral blood flow, improve retinal function and nerve conduction, improve the simple mental status examination score for mild vascular cognitive impairment, and have a positive impact on patients' mood. A study on citicoline showed that CDPCho can prevent the degradation of choline and ethanolamine phospholipids during cerebral ischemia and prevent leakage of the blood-brain barrier, so it is also used in the treatment of traumatic brain injury (TBI). Data from clinical trials confirm the results of preclinical toxicology studies, showing a good safety profile. This study used a self-controlled method to evaluate the efficacy and safety of citicoline sodium capsules in the treatment of head injury.

2. Data and methods

2.1. General information

This study is a multicenter, single-arm, prospective, observational study^[1]. The target population is patients with TBI who were seen between March 2023 and June 2024 and who were evaluated and could be treated with CDPCho. Inclusion criteria: (1) Age > 18 years old; (2) Exact history of TBI; (3) Awake patients with moderate TBI with a Glasgow Coma Scale (GCS) score of 9–12^[2]. Exclusion criteria: (1) Patients with systemic diseases affecting the nervous system; (2) Unable or unwilling to cooperate with other mental illnesses; (3) Pregnant or lactating women, pregnant women with pregnancy plans during the trial, or unwilling to use effective contraceptive measures^[3].

2.2. Observation indicators

- (1) All patients took the drug orally 3 times a day, with a dose of 200 mg each time.
- (2) Effectiveness observation indicators: GCS and Mini-Mental State Examination (MMSE) scores were monitored at different time points before and after the intervention (pre-intervention, 1 month, and 2 months).
- (3) Safety observation indicators: (A) Truthfully feedback and record the occurrence of adverse drug reactions/adverse events during medication; (B) Abnormal safety examinations with clinical evaluation^[4,5].

2.3. Statistical analysis

The analysis was performed using the Statistics Analysis System (SAS) 9.4. For continuous variables, the descriptive indicators are the number of objects, median, minimum and maximum values, mean, standard deviation, etc., while the indicators for categorical variables are the number and proportion of objects. Continuous variables were compared using paired *t*-tests or ANOVA as appropriate and categorical variables were analyzed using chi-square tests. The test results of the above indicators are two-sided tests, and the judgment of statistical significance is $P < 0.05$ shall prevail. The test of the incidence of adverse events is to compare the indicators

before and after medication, and to grade all adverse events in detail, also describe the pre- and post-(normal/ abnormal) changes in laboratory test results and the relationship to the trial drug when abnormal changes occur^[6].

3. Results

3.1. Demographic characteristics and source distribution of patients

A total of 2809 patients with TBI who were present between March 2023 and June 2024 and could be treated with citicoline sodium capsules were evaluated by the investigator^[7]. Outliers that did not meet the treatment regimen were eliminated, and finally, 2806 patients were included in the analysis. The three provinces with the largest number of people are Shandong, Jiangsu and Hunan, and the specific distribution is shown in Figure 1. The average age of patients was (58.85 + 12.84) years, with 1770 males (63.1%) and 1036 females, accounting for 36.9%. About 60% of patients have an education level of primary and junior high school, as shown in **Table 1**.

Table 1. Demographic characteristics of patients

Variable	Statistics [Mean ± SD, n(%)]
Total number of patients	2806
Age	58.85 ± 12.84
Gender	
Male	1770 (63.1%)
Female	1036 (36.9%)
Education	
No formal education	388 (13.8%)
Primary school education	1012 (36.1%)
Junior high school education	662 (23.6%)
Senior high school education	401 (14.3%)
Associate degree	242 (8.6%)
Bachelor's degree	91 (3.2%)
Postgraduate and above	10 (0.4%)

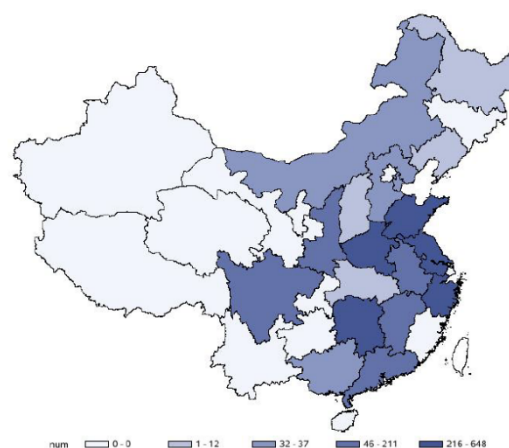


Figure 1. Distribution map of patient sources.

3.2. Patient's disease diagnosis and anamnesis information

Of the 2806 patients, the vast majority were admitted to the hospital due to head injuries and related symptoms caused by car accidents and violent impacts. Among them, 35.2% of the patients had no previous history, and the most common past medical history was that they had been diagnosed with head injury (21.0%), hypertension (18.4%), cerebrovascular disease (5.3%) and diabetes (3.2%) before this visit for head injury. See **Table 2** for details.

Table 2. Diagnosis and history information of patients

Variable	Summary statistic [Mean \pm SD, <i>n</i> (%)]
Past history (not)	988(35.2%)
Head injury	589(21.0%)
Hypertension	516(18.4%)
Cerebrovascular disease	149(5.3%)
diabetes	91(3.2%)

3.3. Information on main research indicators

This study included 2806 patients at baseline, of whom 1602 were followed up at 1 month after treatment and 1112 were followed up at 2 months after treatment. The mean value of GCS in this population was 9.63 ± 1.41 at baseline, 10.18 ± 1.23 at 1 month, and 10.43 ± 1.24 at 2 months after treatment. The mean of MMSE at baseline in this population was 15.31, 16.50 at 1 month, and 17.00 at 2 months after treatment. The above differences are statistically significant. The study found that with the prolongation of time after drug treatment, both GCS and MMSE scores showed an increasing trend, indicating that citicoline sodium capsules are effective in treating TBI. See **Table 3** and **Figure 2** for details.

Table 3. Changes in GCS and MMSE scores before and after treatment

Variable	Before treatment (<i>n</i> = 2806) [Mean \pm SD]	1 month post-treatment (<i>n</i> = 1602) [Mean \pm SD]	2 months post-treatment (<i>n</i> = 1112) [Mean \pm SD]	<i>P</i> -value
GCS score	9.63 ± 1.41	10.18 ± 1.23	10.43 ± 1.24	< 0.001
MMSE score	15.31 ± 7.25	16.50 ± 7.08	17.00 ± 7.69	< 0.001

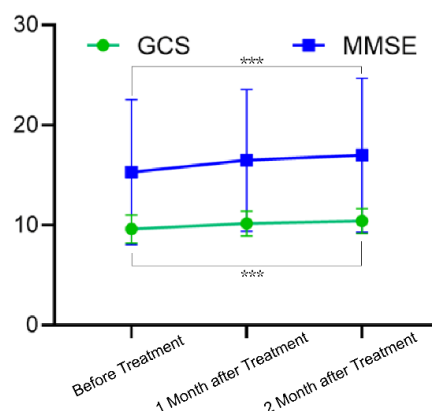


Figure 2. Trend chart of changes in GCS and MMSE scores before and after treatment.

3.4. Adverse reaction information

A total of 8 adverse events occurred in this study, and the overall incidence of adverse events was 0.3%. All incidents are mild to severe. Among them, there were 6 cases of gastrointestinal reactions and 2 cases of allergic reactions, and the above adverse events were finally relieved or cured quickly after timely treatment, and did not cause termination due to adverse reactions or discharge of patients. See **Table 4** for details.

Table 4. Adverse event information

Name of adverse reaction (<i>n</i> = 8)	Severity	Symptoms	Outcome	Whether to terminate or discharge from the hospital
Abnormal laboratory findings	Mild	Abnormal liver and kidney function	Resolved	Not
Gastrointestinal reactions	Mild	other	Resolved	Not
anaphylaxis	Severe	Red dots	Relieved	Not
Gastrointestinal reactions	Mild	Lack of appetite	Resolved	Not
Gastrointestinal reactions	Mild	Other	Resolved	Not
Gastrointestinal reactions	Mild	Other	Resolved	Not
Anaphylaxis	Mild	Other	Outcome	Not

4. Discussion

Moderate to severe TBI poses a significant burden of disease on patients, their families, and society, so it is urgent to explore new ways to potentially treat TBI. Despite advances in the treatment of TBI in recent years, mortality and disability rates remain high. Inflammation, altered cell membrane integrity, and phospholipid metabolism disorders are all involved in the pathophysiological mechanism of TBI. Many studies have shown that citicoline has neuroprotective and neurorepair properties, including the following: repairing damaged neuronal cell membranes (i.e., phospholipid content and function, ion exchange function); Reduce the production of free fatty acids and free radicals; improve neurotransmitter transmission and brain cell metabolism; anti-inflammatory and antioxidant properties; Enhance the integrity of the blood-brain barrier; accelerates the resorption of cerebral edema and reduces the volume of ischemic lesions; inhibits apoptosis; and enhance neurorepair and neuroplasticity properties^[8–10]. Therefore, considering the biochemical, pharmacological and pharmacokinetic properties of citicoline, it may become a potential drug for the treatment of TBI.

The results of this study showed that the incidence of cranial injury was higher in men than in women, with an average age of 58.85 years. Most patients were admitted to the hospital due to head injuries due to external factors such as car accidents or work-related injuries, which is consistent with the results of the analysis of the incidence and prevalence trends of head trauma in China from 2000 to 2019^[11]. In the study, patients were treated with citicoline sodium for an average of about two months, at a dose of 200 mg three times a day. Within 1–2 months after treatment, the GCS and MMSE scores of patients were significantly improved, indicating that citicoline sodium can significantly reduce cognitive impairment secondary to head injury, which is consistent with previous studies^[12].

The study further analyzed the overall situation of 2806 patients. The results showed that the patients were mainly concentrated in three provinces: Shandong, Jiangsu and Hunan, of which 63.1% were males and 36.9%

were females. The average age of the patients was 58.85 years old, and 59.7% had primary and junior high school education, 26.5% had high school education or above, and 13.8% had no education. The most common past medical history is head injury, hypertension, cerebrovascular disease, and diabetes.

The average number of days patients treated with citicoline sodium was 30.12 ± 2.50 days. The mean GCS and MMSE scores of the patients before treatment were 9.63 and 15.31, respectively, and after two months of treatment, the mean scores of these two scores increased to 10.43 and 17.00, respectively. With the prolongation of treatment, the patient's state of consciousness and cognitive function gradually improved, indicating that citicoline sodium has a positive therapeutic effect after head injury.

In this study, only 8 cases of adverse reactions were observed, of which 2 were allergic reactions and 6 were gastrointestinal reactions. The incidence of adverse reactions was low, and the symptoms were mild, and the outcome was good, with no serious adverse events. This indicates that citicoline sodium has good safety and tolerability in the treatment of TBI.

A recent meta-study that included 11 randomised controlled studies and analyzed data from a total of 2771 patients concluded that citicoline treatment was associated with significantly higher ability to live independently (RR, 1.18; 95% CI = 1.05–1.33;) and was associated with citicoline dose or route of administration Independent; In addition, no significant effect of citicoline on mortality was found, and no safety concerns were raised^[13]. It shows that citicoline is safe and effective in treating TBI patients.

5. Conclusion

In summary, the results of this study show that citicoline sodium has a significant effect on the state of consciousness and cognitive function of patients with head injury, and the incidence of adverse reactions is low, and it is well tolerated by patients. Therefore, the application of citicoline sodium in the treatment of TBI has good clinical prospects.

Disclosure statement

The authors declare no conflict of interest.

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Efficacy and Safety Study of Rasagiline Tablets in the Treatment of Parkinson's Disease

Lu Zhang¹, Jin Xu², Ling Liu³, Haiyan Tang⁴

¹Department of Neurology, The First Affiliated Hospital of Zhengzhou University (tertiary hospital), Zhengzhou 450052, Henan, China

²Department of Neurology, Xiangyang Central Hospital, Xiangyang 441000, Hubei, China

³Department of Neurology, Union Medical College Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430000, Hubei, China

⁴Department of Neurology, Huzhou Central Hospital, Huzhou 313000, Zhejiang, China

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Abstract: *Objective:* To evaluate the efficacy and safety of rasagiline tablets in the treatment of Parkinson's disease, in order to provide a more scientific basis for the application of the drug in Parkinson's disease. *Methods:* This study is a single-arm, prospective, observational study. The trial collected patients with primary Parkinson's disease who met the inclusion and exclusion criteria after being assessed by the investigator to evaluate the efficacy and safety of rasagiline tablets in the treatment of Parkinson's disease patients through UPDRSIII and UPDRSII scales, and evaluated the efficacy and safety of rasagiline tablets in the treatment of Parkinson's disease patients. *Results:* A total of 3560 patients were included in this study. 44.1% of patients had early Parkinson's disease, 52.4% had intermediate Parkinson's disease, and 3.5% had advanced Parkinson's disease. The UPDRSIII (exercise capacity) score was 26.76 at baseline, 25.47 at 1 month, 24.18 at 2 months, and 23.39 at 3 months after treatment, and scores significantly improved over time ($P < 0.001$). The UPDRSII (ability to perform daily living) score was an average of 23.60 at baseline, 22.49 at 1 month, 21.53 at 2 months, and 21.09 at 3 months after treatment, with statistically significant differences in scores between months ($P < 0.001$). A total of 18 adverse events/reactions occurred in this study, and adverse symptoms eventually disappeared or resolved, without termination due to adverse events/reactions or patient discharge. *Conclusion:* Rasagiline tablets have significant efficacy in improving daily exercise capacity and living ability in patients with Parkinson's disease, and have a certain safety, which supports the effectiveness of rasagiline as a treatment for Parkinson's disease and provides new evidence for its clinical application.

Keywords: Parkinson's disease; Rasagiline tablets; UPDRS score

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1. Introduction

Parkinson's Disease (PD) is a common degenerative disease of the central nervous system, mainly manifested by symptoms such as resting tremor, muscle rigidity, bradykinesia and postural instability. The pathogenesis of PD is closely related to the gradual loss of dopaminergic neurons in the substantia nigra and the imbalance of related neurotransmitters. Epidemiological surveys show that the prevalence of PD in Europe and the United States reaches 1% for people over 60 years old, more than 4% for those over 80 years old, and the prevalence rate for people aged 65 and above in our country is 1700/100,000. With the progression of the disease, these motor and non-motor symptoms of PD gradually appear and worsen, which, on the one hand, will damage the patient's own daily activities, seriously reduce the patient's quality of life, and, on the other hand, it will also bring a huge economic and care burden to the family and society.

At present, the treatment of PD mainly includes drug therapy, surgical treatment, and rehabilitation treatment, of which drug treatment is the most commonly used method. With the deepening of research on the pathogenesis of PD, monoamine oxidase B (MAO-B) inhibitors can selectively inhibit endogenous and exogenous dopamine breakdown, prolong the action time of dopamine, and improve the clinical symptoms of PD. Rasagiline is a novel, irreversible MAO-B inhibitor that can improve motor and non-motor symptoms in patients. In addition, rasagiline has potential neuroprotective effects, which opens up new possibilities for early intervention in PD.

Studies have shown that rasagiline has shown good efficacy in both monotherapy and combination therapy, but its safety and long-term application effect in different populations still need to be further verified. Therefore, this study aims to evaluate the efficacy and safety of rasagiline tablets in the treatment of PD through a prospective, observational study, to provide more scientific basis for the application of the drug in PD and explore its potential in delaying disease progression. This not only helps optimize the treatment strategy for PD, but also has important implications for improving the quality of life of patients.

2. Data and methods

2.1. Study design

This study is a single-arm, prospective, observational study that collects patients with primary PD who met the inclusion criteria after being assessed by the investigator between January 2023 and June 2024, and evaluated the efficacy and safety of rasagiline in the treatment of PD patients through UPDRSIII, UPDRSII, and adverse reactions^[1,2]. Rasagiline mesylate tablets were administered at a dose of 1 mg once daily orally. The treatment duration was 3 months for all enrolled patients. Medication adherence was assessed through patient diaries and pill counts at each follow-up visit.

2.2. Study population

The target population of this study is PD patients who are seen between January 2023 and June 2024 and who can be treated with rasagiline tablets after being evaluated by the investigator in the case of basic treatment. Inclusion criteria: (1) Patients with a clinical diagnosis of primary PD; (2) Receiving a relatively stable dose of antiparkinsonian drugs during the study period; (3) Age \geq 18 years old; (4) Patients or their legal representatives sign the informed consent form and are willing to participate in this study and complete the survey as required. Exclusion criteria: (1) PD caused by encephalitis or metabolic diseases; (2) Accompanied by severe mental illness; (3) Patients with severe heart, liver, and kidney function impairment; (4) Patients with severe cognitive

dysfunction; (5) Patients with allergy to rasagiline tablets; (6) Unable to cooperate and complete the researcher.

2.3. Research indicators

- (1) Evaluation of patients' motor function: UPDRSIII (Unified Parkinson's Disease Rating Scale Part III) is the third part of the Unified PD rating scale to evaluate the motor function of patients. The evaluation of this part includes limb resting tremor, limb stiffness, bradykinesia, standing balance, and gait^[3,4].
- (2) Evaluation of patients' ability to perform daily living: UPDRSII (Unified Parkinson's Disease Rating Scale Part II) is the second part of the Unified PD rating scale to evaluate patients' ability to live in daily living. This score mainly examines the patient's ability to perform activities in daily life, such as eating, writing, dressing, washing, walking, and getting up. The higher the score, the greater the difficulty the patient encounters in daily life.
- (3) Adverse reaction evaluation: Adverse reaction evaluation is used to monitor various adverse reactions that patients have during rasagiline, including but not limited to nausea, headache, insomnia, hypotension, hallucinations, etc.^[5,6]

2.4. Statistical analysis

Statistical analysis was performed using SAS 9.4 software. The quantitative data were described as the number of cases, mean, standard deviation, median and interquartile range according to whether they conformed to or were approximately normally distributed. For continuous variables, the changes from baseline to post-treatment were analyzed using a paired t-test (after confirming normality of the differences with the Shapiro-Wilk test). For categorical variables, changes in function status were assessed using the Wilcoxon signed-rank test. The frequency and rate were described by qualitative data, and the chi-square test was used for comparison between groups. The difference in hypothesis testing with a $P < 0.05$ was statistically significant^[7,8].

3. Results

3.1. Demographic characteristics and disease diagnosis of patients

A total of 3560 patients with primary PD who attended the clinic between January 2023 and June 2024 and met the inclusion exclusion criteria after being assessed by the investigator were collected in this study. 44.1% of patients had early PD, 52.4% had intermediate PD, and 3.5% had late PD. The results are shown in **Table 1**.

3.2. Changes in UPDRSIII (Motor Examination) score before and after treatment

The UPDRSIII (Motor Examination) score was 26.76 at baseline, 25.47 at 1 month, 24.18 at 2 months, and 23.39 at 3 months after treatment, with statistically significant differences in scores between months ($P < 0.001$). The results are shown in **Table 2**.

3.3. Changes in UPDRSII (ability of daily living) before and after treatment

The UPDRSII (ability to perform daily living) score was an average of 23.60 at baseline, 22.49 at 1 month, 21.53 at 2 months, and 21.09 at 3 months after treatment, with statistically significant differences in scores between months ($P < 0.001$). The results are shown in **Table 3**.

Table 1. Demographic characteristics and disease diagnosis of patients

Variable	Statistics [Mean \pm SD,n(%)] (N = 3560)
Age	64.0 \pm 9.8
Gender	
Male	2016 (56.6)
Female	1544 (43.4)
Clinical staging diagnosis	
Early-stage (Hoehn-Yahr 1-2 stage)	1569 (44.1)
Mid-stage (Hoehn-Yahr 2.5-3stage)	1865 (52.4)
Advanced-stage (Hoehn-Yahr 4-5stage)	126 (3.5)
The duration of the disease from illness to this visit	
Less than 1 year	769 (21.6)
1–5 years	2226 (62.5)
5–10 years	516 (14.5)
More than 10 years	49 (1.4)

Table 2. Changes in UPDRSIII (Motor Examination) score before and after treatment

	Before treatment	Treatment for 1 month	Treatment for 2 months	Treatment for 3 months	<i>P</i>
The mean \pm standard deviation	26.76 \pm 13.92	25.47 \pm 13.03	24.18 \pm 12.02	23.39 \pm 11.82	< 0.001
Median (Q1–Q3)	25 (16–38)	24 (15–36)	23 (15–33)	23 (14–33)	

Table 3. Changes in UPDRSII (ability of daily living) before and after treatment

	Before treatment	Treatment for 1 month	Treatment for 2 months	Treatment for 3 months	<i>P</i>
The mean \pm standard deviation	23.60 \pm 11.36	22.49 \pm 10.90	21.53 \pm 10.22	21.09 \pm 10.46	< 0.001
Median (Q1–Q3)	23 (15–34)	22 (14–32)	21 (14–30)	21 (13–29)	

3.4. Evaluation of adverse reactions of patients

A total of 18 adverse events/reactions occurred in this study, including neurologic abnormalities, digestive system abnormalities, metabolic and nutritional abnormalities, ocular, ear, and labyrinth abnormalities, cardiac or vascular abnormalities, and muscular, skeletal, and connective tissue abnormalities of mild severity. Among them, 6 cases were in the first cycle, 3 cases in the second cycle, 5 cases in the third cycle, and 4 cases in the fourth cycle. Adverse symptoms eventually disappeared or resolved without termination of adverse events/reactions or discharge of the patient.

4. Discussion

The results of the study showed that rasagiline tablets had significant efficacy in improving motor function (UPDRS III score) and daily living ability (UPDRS II score) in PD patients. Compared with baseline, patients experienced significant reductions in both scores after receiving rasagiline, indicating effective improvements in patients' quality of life and motor function. This is similar to the results of a study in Taizhou, Jiangsu Province, where the UPDRSII score and UPDRSIII score of PD patients were significantly reduced after 12 weeks of treatment with levodopa preparations combined with rasagiline^[9]. Our findings further support the effectiveness of rasagiline as a treatment for PD and provide new evidence for its clinical application.

In addition, the results of this trial showed that only 18 adverse events/reactions occurred in 3560 patients treated with rasagiline for PD, with mild severity and good outcomes. A meta-analysis published in 2013 found that the most commonly reported adverse events/reactions of rasagiline as monotherapy were headache, dizziness, and insomnia by searching the literature from 1990-2012; When treated in combination with other drugs, depression, dizziness, drowsiness, and other sleep disturbances can occur^[10].

As a progressive neurodegenerative disease, PD not only seriously affects the quality of life of patients but also brings a heavy economic and nursing burden to society and families. The core pathological mechanism of PD is the loss of dopaminergic neurons in the substantia nigra, leading to a decrease in dopamine levels in the brain. Rasagiline tablets, as a selective and irreversible monoamine oxidase B (MAO-B) inhibitor, reduce the degradation of dopamine in the brain by inhibiting the activity of MAO-B, thereby increasing dopamine levels and improving motor symptoms in patients^[11]. In addition, rasagiline also has antioxidant and anti-apoptotic effects, which may provide some protection to neurons and help delay disease progression. Therefore, rasagiline tablets can not only improve the clinical symptoms of PD but also reduce the long-term burden of the disease.

5. Conclusion

In summary, this study verified the effectiveness and safety of the drug in improving daily living ability and motor function by evaluating the effect of rasagiline tablets on the UPDRSII and UPDRSIII scores of PD patients. Future studies should further explore its long-term effects and potential neuroprotective mechanisms to provide a more comprehensive plan for the treatment of PD.

Disclosure statement

The authors declare no conflict of interest.

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In-Depth Exploration of the Efficacy of Hook Plate-Double Ligament Dynamic Fixation for HACD

Jun Ge*

Taizhou City Hospital of Traditional Chinese and Western Medicine, Taizhou 225300, Jiangsu, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To evaluate the therapeutic effect of dynamic fixation with a hook plate-double loop plate internal fixation system for high-energy acromioclavicular joint complex dislocation (denoted as HACD, i.e., Rockwood type III-V dislocation). *Methods:* Fifty-eight patients with HACD were selected and evenly divided by drawing lots. The experimental group underwent ligament reconstruction treatment, while the reference group received hook plate fixation treatment. The efficacy and other indicators were compared between the groups. *Results:* The overall effective rates between the groups were similar ($P > 0.05$). The experimental group had a longer surgical duration, lower pain scores at 6 months postoperatively, higher shoulder joint function scores, and a lower complication rate, with $P < 0.05$ when compared between groups. *Conclusion:* The effectiveness of the double loop plate internal fixation system ligament reconstruction treatment for patients with HACD is comparable to that of hook plate fixation treatment. Although the surgical duration is slightly longer, postoperative pain is milder, facilitating the recovery of shoulder joint function in patients and offering higher safety.

Keywords: Hook plate-double loop plate internal fixation system; HACD; In-depth efficacy; Shoulder joint function score; Complications

Online publication: Dec 10, 2025

1. Introduction

HACD, namely Rockwood type III-V dislocation, is a common type of acromioclavicular joint dislocation caused by external violence, resulting in the rupture of the coracoclavicular ligament or acromioclavicular ligament and complete dislocation of the acromioclavicular joint. Immediate surgical treatment is required to prevent adverse events such as joint deformity^[1]. Hook plate fixation is a basic treatment for this condition, allowing direct exposure of the affected area with a relatively simple operational procedure and effective reduction. However, it has a high incidence of postoperative pain and can lead to restricted joint movement, thus presenting surgical

limitations. The treatment of ligament reconstruction using a double-loop plate internal fixation system, namely coracoclavicular and acromioclavicular ligament reconstruction, can maintain joint stability, eliminate the need for a second surgery, cause minimal trauma, and significantly improve long-term outcomes ^[2]. Therefore, this study enrolled 58 patients with HACD to evaluate the treatment differences of hook plate-double ligament dynamic fixation.

2. Materials and methods

2.1. General information

Fifty-eight patients with HACD admitted between October 2019 and October 2024 were selected and evenly divided by drawing lots. The basic data between the groups are as follows (**Table 1**).

Table 1. Basic data comparison between groups (*n*/%, mean \pm SD)

Group	n	Gender		Age (years)	Injury-to-treatment (days)	Location		Rockwood classification		
		Male	Female			Left	Right	Type III	Type IV	Type V
Experimental	29	18 (62.07)	11 (37.93)	42.19 \pm 4.95	4.45 \pm 0.84	13 (44.83)	16 (55.17)	11 (37.93)	10 (34.48)	8 (27.59)
Control	29	17 (58.62)	12 (41.38)	42.28 \pm 4.91	4.49 \pm 0.81	14 (48.28)	15 (51.72)	10 (34.48)	12 (41.38)	7 (24.14)
χ^2/t	-	0.072	0.070	0.185	0.069	0.296				
<i>P</i> -value	-	0.788	0.945	0.854	0.792	0.862				

2.2. Methods

The experimental group received ligament reconstruction treatment using a double-loop plate internal fixation system: General anesthesia or cervical plexus and brachial plexus nerve block were selected to position the patient in a beach chair position. An arc-shaped incision was made at the outer one-third of the clavicular midline to expose the coracoid process and acromioclavicular joint, thereby revealing the coracoclavicular and acromioclavicular ligaments. Free blood clots or soft tissues were cleared, and the existing cartilage disc within the acromioclavicular joint space was preserved. A Kirschner wire was used to drill a tunnel through the coracoid process, and a loop plate was placed at the base of the coracoid process. A guidewire was then introduced, and Kirschner wires (2 mm) were placed at the cortical area of the posterior clavicle margin (5 mm away) and the distal clavicle (35 mm away), following the residual ends of the ligaments and opening the bone tunnel towards the base of the coracoid process. A self-made wire guide (with a hook) was used to pull the tail wire through the bone tunnel, and a loop plate was pressed onto the clavicle. The shoulder joint was abducted, and the anterior and posterior aspects of the distal clavicle were reduced. The tail wire was tied, and the conoid and trapezoid ligaments were reconstructed, followed by reconstruction of the acromioclavicular ligament. After hemostasis of the incision, the incision was sutured.

The reference group was treated with clavicular hook plate fixation; the anesthesia and positioning methods were the same as above. The curved incision was located at the outer one-third of the clavicular midline, exposing the distal clavicular joint and acromioclavicular joint. After clearing away necrotic tissue and blood clots, a clavicular hook plate was placed below the acromion, adhering to the clavicle, and the dislocation of the

acromioclavicular joint was reduced. Drilling was performed on the clavicle, and screws were inserted and fixed. Postoperative drainage and incision suture procedures were the same as above.

2.3. Observation indicators

- (1) Surgical indicators: Indicators such as surgical duration and intraoperative blood loss were recorded. The pain level from 1 to 6 months postoperatively was assessed using the Visual Analog Scale, with a total score of 10 points, where higher scores indicated greater pain.
- (2) Shoulder joint function score: The Constant-Murley scoring criteria were selected, including strength testing (25 points), daily activities (20 points), pain (15 points), and range of motion (40 points), with higher scores indicating better function.
- (3) Complication rate: The incidence of complications such as acromioclavicular joint pain and subacromial bursitis was recorded.

2.4. Efficacy evaluation criteria

Excellent results were defined as no shoulder pain, normal range of motion and joint strength, and no impact on work and daily life; good results were defined as mild shoulder pain, a range of motion less than 180°, slightly decreased joint strength, and mild interference with work and daily life; poor results were defined as significant joint pain, abnormal range of motion and strength, and severe interference with work and daily life.

2.5. Statistical analysis

Data processing was completed using SPSS 28.0 software. Continuous variables were compared and tested using *t*-tests, while categorical variables were compared and tested using chi-square tests. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of overall effectiveness rates between groups

The overall effective rate of the experimental group was close to that of the reference group (*P* > 0.05) (Table 2).

Table 2. Comparison of overall effective rates between groups (n/%)

Group	n	Excellent	Good	Poor	Total effective rate
Experimental group	29	17 (58.62)	11 (37.93)	1 (3.45)	96.55 (28/29)
Control group	29	12 (41.38)	13 (44.83)	4 (13.79)	86.21 (25/29)
χ^2					5.220
<i>P</i> -value					0.022

3.2. Comparison of surgical indicators between groups

The experimental group had a longer surgical duration and lower pain scores at 6 months postoperatively, with *P* < 0.05 in the intergroup comparison (Table 3).

Table 3. Comparison of surgical indicators between groups (mean \pm SD)

Group	n	Operative time (min)	Intraoperative blood loss (mL)	Hospital stay (days)	Pain score		
					1 month after surgery	3 months after surgery	6 months after surgery
Experimental group	29	80.39 \pm 7.94	55.21 \pm 5.36	5.15 \pm 0.97	5.44 \pm 0.91	4.76 \pm 0.41	1.48 \pm 0.24
Control group	29	52.55 \pm 5.38	54.75 \pm 5.40	5.20 \pm 0.94	5.49 \pm 0.88	4.82 \pm 0.45	3.40 \pm 0.39
<i>t</i> -value		15.632	0.326	0.199	0.213	0.531	22.579
<i>P</i> -value		< 0.001	0.746	0.843	0.832	0.598	0.000

3.3. Comparison of shoulder joint function scores between groups

Before surgery, there was no significant difference in shoulder joint function scores between the groups, with $P > 0.05$ in all comparisons. At 6 months postoperatively, the experimental group had higher shoulder joint function scores, with $P < 0.05$ in the intergroup comparison (Table 4).

Table 4. Comparison of shoulder joint function scores between groups (mean \pm SD, points)

Group	n	Strength test		Daily activity		Pain		Range of motion	
		Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
Experimental group	29	10.95 \pm 1.79	16.75 \pm 2.53	6.29 \pm 1.78	15.97 \pm 2.05	5.09 \pm 0.97	12.57 \pm 2.95	16.45 \pm 2.97	35.22 \pm 3.75
Control group	29	10.99 \pm 1.83	14.02 \pm 2.34	6.32 \pm 1.81	13.14 \pm 2.02	5.11 \pm 0.94	10.09 \pm 2.82	16.49 \pm 3.02	31.91 \pm 3.70
<i>t</i> -value		0.084	4.266	0.064	5.295	0.080	3.273	0.051	3.384
<i>P</i> -value		0.933	0.000	0.949	0.000	0.937	0.002	0.960	0.001

3.4. Comparison of complication rates between groups

The experimental group had a lower complication rate, with $P < 0.05$ in the intergroup comparison (Table 5).

Table 5. Comparison of complication rates between groups (*n*/%]

Group	n	AC Joint Pain	Subacromial Bursitis	Joint Stiffness	Subacromial Osteolysis	Reduction Loss	Incision Infection	Re-dislocation	Total Incidence
Experimental group	29	1 (3.45)	0	1 (3.45)	0	0	0	0	6.90 (2/29)
Control group	29	2 (6.90)	1 (3.45)	1 (3.45)	1 (3.45)	1 (3.45)	1 (3.45)	1 (3.45)	27.59 (8/29)
χ^2 value									4.350
<i>P</i> -value									0.037

4. Discussion

HACD mostly involves Rockwood type III-V dislocations, caused by significant damage to the coracoclavicular ligaments at the distal end of the clavicle, including the trapezoid and conoid ligaments, primarily presenting

as ruptures. This leads to an upward tilt of the distal end of the clavicle, resulting in dislocation. The primary intervention for this condition is surgery, mainly involving internal fixation procedures such as clavicular hook plate fixation or Kirschner wire tension band fixation^[3]. The clavicular hook plate allows for a small range of motion in the acromioclavicular joint and provides excellent fixation for dislocations. It utilizes leverage to generate stable and long-lasting pressure around the acromioclavicular joint, creating a tension environment that facilitates ligament reconstruction, promotes bone and muscle healing, and shortens the time to initiate postoperative functional exercises. However, this surgical approach requires plate removal, which can lead to shoulder pain or improper reduction of the coracoclavicular distance and increases the risk of postoperative complications, thus presenting certain surgical limitations.

The double-loop plate internal fixation system can effectively reduce joint dislocation, and its strength is similar to the normal physiological characteristics of the coracoclavicular ligament. Fixation and suture treatment of the clavicle and coracoid process can ensure the natural adherence of the coracoclavicular ligament, thereby enhancing its tensile resistance^[4]. Additionally, during the incision healing process, the fixation sutures are non-absorbable, providing a long-lasting stabilizing effect on the acromioclavicular joint. Moreover, this procedure does not require a secondary operation, as the internal fixation device can be directly retained in the body, resulting in lower surgical risks. Furthermore, its relatively simple operation method contributes to high surgical feasibility.

The results showed that the total effective rate of the experimental group was close to that of the reference group ($P > 0.05$). The experimental group had a longer surgical duration but a lower pain score at 6 months postoperatively, with a statistically significant difference between the groups ($P < 0.05$). The reason for this is that both the double-loop plate internal fixation system and hook plate fixation surgery can improve the horizontal and vertical stability of the acromioclavicular joint by utilizing anatomical reduction and stabilizing the shoulder joint. The hook plate, with its rigid fixation, can significantly resist dislocation forces, thus providing strong short-term fixation effects. In contrast, the double-loop plate internal fixation system reconstruction can restore the dynamic stability of the acromioclavicular ligament and coracoid ligament, improving their physiological load-bearing function and achieving better therapeutic outcomes^[5]. The reconstruction of two ligaments using the double Endobutton plate internal fixation system requires highly accurate separation of the two ligaments, along with bone tunnel positioning, threading, and fixation wire placement, which consequently increases the surgical duration. Compared to the placement of the hook plate and screw insertion in hook plate fixation, the procedure for the double Endobutton plate internal fixation system ligament reconstruction is relatively complex and technically challenging. During the surgery, it is necessary to avoid the nerves and vascular tissues beneath the clavicle, thus requiring a longer operative time. However, double ligament reconstruction can restore the natural tension of the ligaments around the shoulder joint, prevent the mechanical irritation in the subacromial space caused by hook plate fixation, and thereby avoid pain symptoms due to factors such as plate foreign body. Moreover, double ligament reconstruction involves a smaller dissection area, adequately preserves tissues such as the cartilaginous disc, and does not involve extensive manipulation of the clavicle or acromion region, thus reducing the degree of muscle attachment point injury and similarly facilitating pain improvement^[6]. The postoperative shoulder function score of the experimental group was higher, with a between-group comparison of $P < 0.05$. The reason for this is that the double Endobutton plate internal fixation system ligament reconstruction allows the placement of the stabilization device at a mutually horizontal position of the acromioclavicular joint, which can prevent clavicular rotation. In the reconstruction of the coracoclavicular ligament using the double Endobutton plate internal fixation system, the fixation wires of the plate can effectively repair the nearby acromioclavicular ligament, significantly

enhancing the stability of the acromioclavicular joint.

Additionally, double ligament reconstruction fully considers the physiological characteristics of the patient. For instance, if the coracoid process is small, the space for screw placement is relatively limited. Therefore, in this study, only one anchor screw was placed to prevent coracoid fracture. The coracoclavicular ligament consists of the trapezoid and conoid ligaments, which have significantly different clavicular insertion points. Thus, during surgery, drilling is performed separately at the remnants of the conoid and trapezoid ligaments, and the two bundles of ligaments are reconstructed using the tail lines of the anchor screws. This restores the biomechanical characteristics of the joint area, enabling early postoperative rehabilitation training and thereby improving the patient's shoulder function^[7]. The complication rate in the experimental group was low, with a between-group comparison of $P < 0.05$. The reason for this is that the double Endobutton plate internal fixation system ligament reconstruction prevents the irritation caused by implants such as the hook plate, reducing complications like incision infection or subacromial bursitis. Moreover, a second surgery is not required, so cases of reduction loss are rare. Furthermore, the double Endobutton plate internal fixation system ligament reconstruction allows physiological micromotion of the acromioclavicular joint and is not a rigid fixation method, resulting in a lower incidence of postoperative joint stiffness. More importantly, this technique protects the soft tissues around the shoulder joint, preventing significant damage to the fascial attachment points of muscles such as the deltoid or trapezius, thus resulting in milder symptoms such as acromioclavicular joint pain postoperatively^[8]. Additionally, the double Endobutton plate internal fixation system ligament reconstruction utilizes both vertical and horizontal stabilization to restore the biomechanical characteristics of the natural ligaments, making it less likely to cause stress concentration and other issues, thereby reducing the risk of re-dislocation.

5. Conclusion

In conclusion, the overall effectiveness of using the double-looped plate internal fixation system for ligament reconstruction in the treatment of patients with HACD is nearly equivalent to that of hook plate fixation. However, the double-ligament approach typically results in milder postoperative pain, better recovery of shoulder joint function, and fewer postoperative complications, thus offering greater surgical advantages.

Disclosure statement

The author declares no conflict of interest.

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Research on Synergistic Regulation of Sleep-Emotion-Behavior Based on SLS Magnesium Glycinate Complex Liquid Supplement

Li Jing, Veira Kwok, Rachel Chung, Jade Cooper, Jacob Kwok

Auckland Molecular Biosciences Innovation Center, Auckland 2104, New Zealand

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Abstract: Hyperactivity and tic symptoms in children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) have a bidirectional association with sleep disorders, while magnesium deficiency is a key nutritional factor exacerbating this vicious cycle. The SLS Magnesium Glycinate Complex Liquid Supplement formula adopts the core logic of “sleep improvement - mood stabilization - behavioral regulation” and enhances the neuromodulatory effects of magnesium ions through multi-component synergy. Tailored to the developmental needs of different stages aged 4-16 years, the formula features a child-friendly dosage design, forming a closed-loop regulation in aiding sleep, reducing tics, and maintaining daytime functioning. A 3-month clinical trial showed that the formula improved sleep efficiency by 15%-23%, reduced tic frequency by 21%-32%, and enhanced emotional stability scores by 24%-30% across all age groups with ADHD, with good safety and tolerability. This study provides a targeted nutritional intervention solution for ADHD, and its age-stratified design concept offers scientific reference for precise nutritional support during different developmental stages of children and adolescents.

Keywords: SLS Magnesium Glycinate; ADHD; Sleep disorder; Emotional stability; Behavioral regulation; Age-specific intervention

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1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders in children and adolescents, characterized by core symptoms of inattention, hyperactivity, and impulsivity, often accompanied by comorbid tic disorders, emotional lability, and sleep disturbances, which has a significant impact on academic performance, social interaction, and psychological development.

Nutritional is a crucial mediating role in this circumstance, with magnesium deficiency being identified as a key risk factor. However, existing nutritional interventions for ADHD often lack targeted design: most magnesium supplements adopt a single-component formula with low bioavailability, ignore age-specific developmental needs of children and

adolescents, and fail to address the multi-dimensional problems of sleep, emotion, and behavior simultaneously.

To fill this gap, this study developed the SLS Magnesium Glycinate Complex Liquid Supplement, based on the core logic of “sleep improvement - mood stabilization - behavioral regulation.” The formula integrates multiple synergistic components to enhance neuromodulatory efficacy, and adopts an age-stratified dosage design. Through a 3-month multicenter, randomized, double-blind, placebo-controlled trial, this study verified the formula’s efficacy in improving sleep, reducing tics, and stabilizing mood, and evaluated its safety and tolerability. The results aim to provide a targeted, age-adapted nutritional intervention solution for ADHD, and offer scientific reference for precise nutritional support in children and adolescents at different developmental stages.

2. Bidirectional Association Mechanism Between ADHD Symptoms (Hyperactivity and Tics) and Sleep

2.1. Exacerbating Effects of Sleep Disorders on ADHD Symptoms

The incidence of sleep disorders in children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) is significantly higher than in healthy populations, with 50%-70% of patients experiencing difficulty falling asleep, sleep maintenance disorders, or abnormal sleep structure ^[1]. Sleep deprivation directly impairs prefrontal cortex function, which is responsible for attention regulation, impulse inhibition, and behavioral planning. Diminished neural activity in this brain region following sleep loss exacerbates the core manifestations of ADHD.

Sleep disorders and tic symptoms exhibit a synergistic deterioration effect: nocturnal sleep fragmentation reduces the brain’s inhibitory control over subcortical motor circuits ^[2], potentially increasing daytime tic severity. Meanwhile, sleep insufficiency induces neurotransmitter imbalance, characterized by decreased synthesis of serotonin and γ -aminobutyric acid (GABA), and disrupted dopamine metabolism ^[3], which further aggravates hyperactivity, impulsivity, and emotional lability, forming a vicious cycle of “poor sleep - severe symptoms - worse sleep” ^[4].

2.2. Reverse Interference of ADHD Symptoms on Sleep Quality

The core features of ADHD directly disrupt sleep homeostasis: hyperactivity leads to excessive physical activity before bedtime, maintaining high nervous system excitability and prolonging sleep latency ^[5]; impulse control deficits cause frequent nocturnal awakenings, resulting in sleep efficiency (total sleep time/bedtime) below 75% (compared to over 85% in healthy children) ^[6]. Sleep deprivation impairs brain metabolic waste clearance and neural repair, not only reducing sleep recovery efficacy but also further weakening neural regulatory capacity, exacerbating next-day hyperactivity and impulsivity (Figure 1).

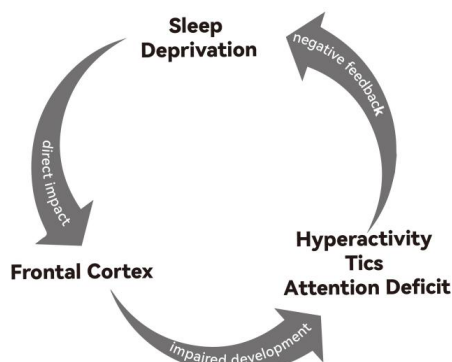


Figure 1: Correlation Between Sleep Deprivation and ADHD

2.3. Mediating Role of Nutritional Factors in the Association

Nutritional imbalance is an important mediator linking ADHD symptoms and sleep disorders, with magnesium deficiency being particularly critical. Magnesium is an essential macromineral involved in over 300 enzymatic reactions, playing a vital role in neurotransmitter synthesis, neural signal transmission, and sleep-wake cycle regulation^[7].

Children with ADHD often exhibit insufficient magnesium intake and metabolic abnormalities: studies have shown that serum magnesium levels in ADHD populations are 15%-20% lower than in healthy children. Magnesium deficiency directly inhibits GABA synthetase activity, reducing central inhibitory neurotransmitter levels, which both exacerbates hyperactivity and tic symptoms^[8] and disrupts sleep homeostasis. Additionally, magnesium deficiency enhances hypothalamic-pituitary-adrenal (HPA) axis activity, leading to disrupted cortisol secretion rhythms and elevated nocturnal cortisol levels, further deteriorating sleep quality^[9]. Furthermore, gut microbiota imbalance and intestinal mucosal barrier impairment can interfere with central nervous system function via the “gut-brain axis.” L-glutamine, a key energy source for intestinal epithelial cells, repairs the intestinal mucosa and reduces neural interference from inflammatory factors^[10].

3. Design Concept and Child-Friendliness of the SLS Magnesium Glycinate Formula

3.1. Core Design Logic: Multi-Target Synergistic Regulation

The SLS Magnesium Glycinate formula is designed around the concept of “magnesium as the core, multi-component synergy,” focusing on four core needs of ADHD populations: 1. Sleep support: Synergy between magnesium glycinate and lemon balm extract regulates sleep rhythms, shortens sleep latency, and improves sleep structure; 2. Mood stabilization: Central inhibitory effects of magnesium glycinate and L-theanine reduce nervous system excitability and emotional fluctuations; 3. Tic reduction: Magnesium’s neuromuscular regulatory effects, combined with the metabolic synergy of vitamin B6, alleviate involuntary tics; 4. Daytime function maintenance: The combination of L-theanine and magnesium glycinate achieves “calming without drowsiness,” avoiding daytime fatigue associated with sleep improvement and ensuring learning and activity efficiency^[11].

3.2. Scientific Basis for Component Combination

Magnesium glycinate (600 mg): An organic chelated form with 30%-50% higher bioavailability than inorganic magnesium and minimal gastrointestinal irritation, providing dual active components (glycine, a neuroprotective amino acid, and magnesium ions)^[12];

L-theanine (30 mg): A unique non-essential amino acid in green tea that promotes cerebral alpha wave production, relieving anxiety and improving sleep without impairing daytime cognitive function^[11];

Vitamin B6 (0.5 mg): A key coenzyme for neurotransmitter synthesis that facilitates intracellular transport and utilization of magnesium ions^[13], enhancing its neuromodulatory efficacy;

L-glutamine (300 mg): A critical nutrient for intestinal mucosal repair that regulates gut-brain axis function and reduces neural interference from inflammatory factors^[10];

Lemon balm extract (50 mg): Contains active components such as rosmarinic acid and luteolin, exerting a mild sedative effect and synergizing with magnesium ions to improve sleep quality.

4. Logic and Adaptability of Age-Stratified Intervention

4.1. 4-8 Years: School-Age Correction Period—Early Intervention to Block Progression

Ages 4-8 mark the initial stage of formal education, with relatively light learning tasks and unconsolidated behavioral patterns. This period is a golden window for early identification and intervention of ADHD symptoms. During this stage, children's brain development is still in a rapid shaping phase with high neural circuit plasticity, making abnormal behaviors more effectively correctable through nutritional supplementation and behavioral intervention.

4.2. 8-12 Years: Golden Remodeling Period—Nutritional Enhancement for Functional Repair

Learning tasks gradually increase for children aged 8-12, requiring improved cognitive functions such as attention and memory to meet specific learning goals and examinations. This stage is critical for brain development, with rapid maturation of cognitive regulatory regions such as the prefrontal cortex. Adequate nutrition is an important guarantee for neural function repair.

4.3. 12-16 Years: Behavioral Optimization Period—Precision Targeting for Functional Improvement

Adolescents aged 12-16 enter puberty, undergoing significant physical and psychological changes. Behavioral patterns are basically established, and ADHD symptoms may be accompanied by exacerbated emotional issues. This stage involves high academic pressure and increased social needs, requiring precise nutritional intervention to optimize existing behavioral patterns and enhance adaptability.

5. Clinical Trial Results and Evidence-Based Support

5.1. Trial Design

This was a multicenter, randomized, double-blind, placebo-controlled trial involving 60 ADHD patients in each of three age groups (4-8 years, 8-12 years, 12-16 years), randomly assigned to the SLS formula group or placebo group at a 1:1 ratio for a 3-month intervention. The intervention protocol was: 1 sachet of the SLS formula daily for the SLS group, and sachets with identical appearance and taste but no active ingredients for the placebo group. Efficacy was evaluated through sleep indicators (sleep latency), behavioral indicators (tic frequency), emotional indicators (anxiety scores, emotional stability scores), and safety indicators (hepatic and renal function, incidence of gastrointestinal reactions).

5.2 . Age-Stratified Trial Results

(1) 4-8 Years: School-Age Correction Period

Sleep indicators: Sleep latency shortened by 18 minutes (32.5%) compared to baseline, significantly superior to the placebo group ($P<0.01$);

Behavioral indicators: Tic frequency reduced by 21.3% ($P<0.01$);

Emotional indicators: Anxiety scores decreased by 24.1%, and emotional fluctuation frequency reduced by 28.3% ($P<0.05$).

(2) 8-12 Years: Golden Remodeling Period

Sleep indicators: Sleep latency shortened by 22 minutes (38.6%), significantly superior to the placebo group ($P<0.001$);

Behavioral indicators: Tic frequency reduced by 27.5% ($P<0.001$);

Emotional indicators: Anxiety scores decreased by 27.8%, and emotional stability scores increased by 29.6% ($P<0.001$).

(3) 12-16 Years: Behavioral Optimization Period

Sleep indicators: Sleep latency shortened by 25 minutes (41.7%), significantly superior to the placebo group ($P<0.001$);

Behavioral indicators: Tic frequency reduced by 31.8% ($P<0.001$);

Emotional indicators: Anxiety scores decreased by 29.9%, and emotional stability scores increased by 28.8% ($P<0.001$).

5.3. Safety and Evidence-Based Support

Safety results showed that the incidence of gastrointestinal discomfort (diarrhea, abdominal distension) in the SLS formula group was only 2.8%, with no significant difference from the placebo group ($P>0.05$). No abnormal changes in hepatic/renal function or electrolyte levels were observed during the intervention, and no cumulative toxicity was noted.

6. Conclusion and Future Perspectives

Based on the bidirectional association mechanism between ADHD symptoms (hyperactivity and tics) and sleep disorders, the SLS Magnesium Glycinate formula constructs an intervention system of “sleep improvement - mood stabilization - behavioral regulation” with magnesium ions as the core, synergized by L-theanine, vitamin B6, L-glutamine, and lemon balm extract.

Its age-stratified design precisely adapts to the developmental needs of children in three different age stages. The child-friendly dosage and formulation enhance intervention feasibility and adherence. A 3-month clinical trial confirmed that the formula exhibits significant effects in improving sleep, stabilizing mood, and optimizing behavior in ADHD populations aged 4-16 years (Figure 2), with excellent safety.

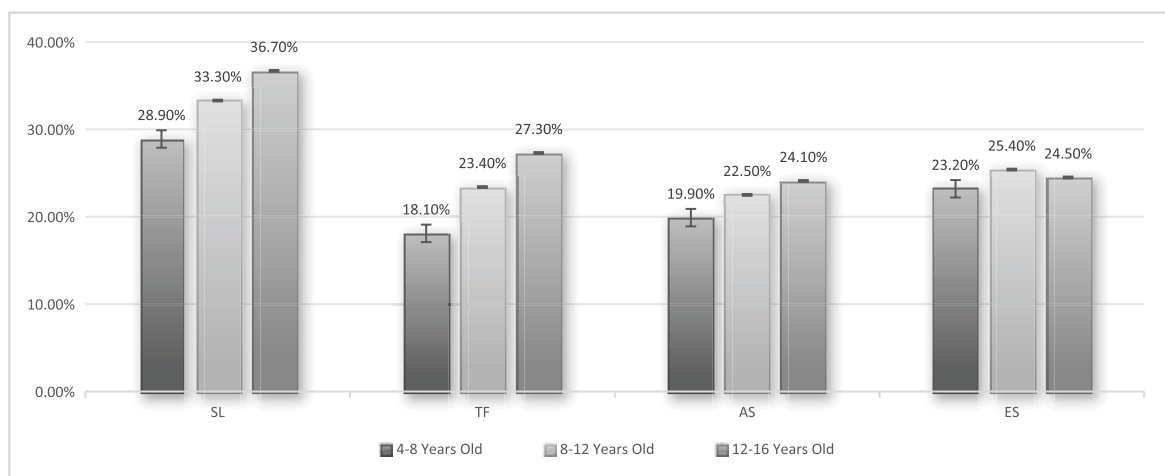


Figure 2. Changes in Sleep Indicators After 3 Months of SLS Magnesium Glycinate Supplement in Children of Different Age Groups. The figure indicates the changes between experimental group and placebo group (percentage change in the experimental group minus percentage change in the placebo group). SL (Sleep Latency) and ES (Emotional Stability) values indicate increased percentages; TF (Tic Frequency) and AS (Anxiety Scores) values indicate decreased percentages.

Of course, data may be affected by individual differences (e.g., children aged 4-6 may have insufficiently clear descriptions of feelings, leading to inaccurate scale-based data due to question wording). Future research should further explore: the improvement effects of different dosage gradients on specific symptoms to provide a basis for individualized intervention; the impact of long-term intervention (over 6 months) on cognitive development and social adaptability in ADHD patients; and the combined effects with non-pharmacological interventions such as behavioral therapy and cognitive training to construct a more comprehensive integrated management plan for ADHD.

Disclosure statement

The authors declare no conflict of interest.

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Research on the Mechanism of the lncRNA DLX6-AS1/miR-26a/PTEN Axis in Regulating the Activation of Hepatic Stellate Cells in Post-hepatitis Liver Fibrosis: An Analysis Based on Systematic Validation and Clinical Translation Methods

Yan Wang, Chao Gao, Dongqin Fei, Fang Zhang, Qi Zhang*

People's Hospital of Liuhe District, Nanjing, Affiliated to Medical College of Yangzhou University, Nanjing, Jiangsu 211500, China

**Author to whom correspondence should be addressed.*

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Abstract: *Objective:* To elucidate the role and clinical potential of the lncRNA DLX6-AS1/miR-26a/PTEN axis in liver fibrosis. *Methods:* Systematic studies were conducted using cellular and animal models through causal validation, bivariate experiments, single-cell sequencing, ROC analysis of clinical samples, and humanized mouse models. *Results:* LncRNA DLX6-AS1 inhibited PTEN by adsorbing miR-26a, promoting hepatic stellate cell activation in a dose/time-dependent manner; the axis demonstrated excellent diagnostic performance (AUC > 0.9), and its inhibitors effectively reversed fibrosis in vivo. *Conclusion:* This study provides new biomarkers and targeted therapeutic strategies for liver fibrosis.

Keywords: Liver fibrosis; lncRNA DLX6-AS1; miR-26a; PTEN; Hepatic stellate cells; Competing endogenous RNA

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1. Introduction

Liver fibrosis is the core pathological process in the progression of chronic liver diseases, characterized by excessive deposition of extracellular matrix, ultimately leading to cirrhosis and hepatocellular carcinoma^[1-3]. The activation of hepatic stellate cells is a central event in this process. Recent studies have indicated that long non-coding RNAs, acting as competing endogenous RNAs, can participate in disease regulation by adsorbing microRNAs. LncRNA DLX6-AS1 exhibits abnormally high expression in various tumors (hereinafter referred to as DLX6-AS1); miR-26a plays a protective role in fibrotic diseases; PTEN, as an important tumor suppressor

gene, is also involved in the regulation of fibrosis^[4-6]. Although a few studies have suggested potential regulatory connections among the three, the specific mechanism of action and clinical value of the DLX6-AS1/miR-26a/PTEN axis in liver fibrosis remain unclear. This study aims to systematically elucidate the role of this molecular axis in liver fibrosis and provide new targets for diagnosis and treatment.

2. Materials and methods

2.1. Cell culture and transfection

The human hepatic stellate cell line LX-2 (purchased from ATCC) was cultured in DMEM medium containing 10% fetal bovine serum (FBS) at 37°C with 5% CO₂. The regulatory axis model was constructed using Lipofectamine 3000 transfection reagent, with transfection of DLX6-AS1 overexpression plasmid, empty plasmid (negative control), miR-26a mimics/inhibitors, and PTEN overexpression plasmid, along with corresponding empty vector controls. Cells were collected 48 hours after transfection for verification experiments such as qRT-PCR and Western blot.

2.2. Three-step verification of the causal chain in the “Mechanism Axis”

To clarify the upstream-downstream causal relationship of the DLX6-AS1/miR-26a/PTEN axis, the study designed the following three-step functional experiments.

2.2.1. Correlation verification

The expression levels of DLX6-AS1, miR-26a, and PTEN mRNA were detected by qRT-PCR, and the protein expression of PTEN and the HSC activation marker α -SMA was analyzed by Western blot to determine the correlation between DLX6-AS1 and downstream molecules.

2.2.2. Mediation effect verification (Rescue experiment)

miR-26a mimics were co-transfected on the basis of DLX6-AS1 overexpression to observe whether the restoration of miR-26a could reverse the inhibition of PTEN and HSC activation (α -SMA/COL1A1 expression) by DLX6-AS1.

2.2.3. Functional endpoint validation

Co-transfect PTEN overexpression plasmid into cells with DLX6-AS1 overexpression, and detect α -SMA, COL1A1, and cell proliferation indicators to verify the direct regulatory effect of PTEN restoration on HSC activation.

2.3. “Dose gradient + time gradient” bivariate experimental design

To dynamically reveal the regulatory pattern of this axis, the study subjected LX-2 cells transfected with DLX6-AS1 overexpression plasmid to bivariate treatment:

- (1) Dose Gradient: Three plasmid transfection doses were set: low (1.0 μ g), medium (2.0 μ g), and high (4.0 μ g).
- (2) Time Gradient: Three time points were set after transfection: 24, 48, and 72 hours.
- (3) Cells were collected at each time point, and the expression changes of DLX6-AS1, miR-26a, PTEN, and

α -SMA were detected by qRT-PCR and Western Blot.

2.4. Establishment and intervention of animal models

All animal experimental procedures were approved by the Animal Ethics Committee of our institution. Eight-week-old male C57BL/6 mice were selected to establish a liver fibrosis model by intraperitoneal injection of 20% CCl₄ (dissolved in olive oil, 2 mL/kg body weight) twice a week for 8 consecutive weeks. The control group was injected with an equal amount of olive oil.

To conduct in vivo intervention, successfully modeled mice were randomly divided into the following groups ($n = 10$ per group):

- (1) Model Group: Injected with blank control reagent via the tail vein.
- (2) DLX6-AS1 Inhibitor Group: Injected with an antagonist oligonucleotide targeting DLX6-AS1 via the tail vein.
- (3) miR-26a Mimic Group: Injected with miR-26a agomir via the tail vein.
- (4) PTEN Overexpression Group: Injected with PTEN overexpression adeno-associated virus (AAV) via the tail vein.
- (5) After 4 weeks of intervention, mouse serum and liver tissues were collected for subsequent analysis.

2.5. Single-cell RNA sequencing (scRNA-seq) analysis

Liver tissues were harvested from mice in the above-mentioned model group, and primary hepatocytes and non-parenchymal cells were isolated using the collagenase perfusion method. Single-cell RNA sequencing libraries were constructed and sequenced from the obtained cell suspensions using the 10x Genomics platform. Data quality control, dimensionality reduction, clustering, and cell subpopulation annotation were performed using the CellRanger and Seurat R packages. The focus was placed on the hepatic stellate cell (HSC) population, and the expression characteristics of DLX6-AS1, miR-26a, and PTEN in different HSC subpopulations were compared through differential gene expression analysis and gene expression visualization.

2.6. Clinical sample analysis and diagnostic performance evaluation

Liver biopsy tissue samples and serum samples were collected from 120 patients each (30 patients per stage) at different stages of liver fibrosis as confirmed by clinical pathology (according to the METAVIR scoring system: F0-F1, F2, F3, F4), with all patients providing informed consent. The expression levels of DLX6-AS1, miR-26a, and PTEN mRNA in the tissues were detected using quantitative real-time polymerase chain reaction (qRT-PCR). The diagnostic value of each molecule and their combined model for significant liver fibrosis (\geq F2) and cirrhosis (F4) was analyzed using receiver operating characteristic (ROC) curves, and the area under the curve (AUC), sensitivity, and specificity were calculated.

2.7. Humanized mouse model validation

To enhance clinical relevance, we further constructed a humanized mouse model. Human hematopoietic stem cells were transplanted into immunodeficient NSG mice, and after the reconstruction of the human immune system, a liver fibrosis model was established by induction with carbon tetrachloride (CCl₄). The mice were also treated with a DLX6-AS1 inhibitor, and the effects on serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, Ishak fibrosis scores in liver tissues, and collagen deposition areas were evaluated.

3. Statistical analysis methods

All experiments were independently repeated at least three times. Data are presented as mean \pm standard deviation. Statistical analysis was performed using SPSS 25.0 software. Comparisons between two groups were conducted using Student's t-test, while comparisons among multiple groups were performed using one-way analysis of variance (ANOVA), with post-hoc tests conducted using the LSD method. Diagnostic efficacy was evaluated through ROC curve analysis. A *P*-value of less than 0.05 was considered statistically significant.

4. Results

4.1. Three-step verification logic for constructing the causal chain of the “Mechanism Axis”

To clarify the causal relationship of the DLX6-AS1/miR-26a/PTEN axis, the study conducted the following three-step verification (Table 1–3 and Figure 1).

Table 1. Effect of DLX6-AS1 overexpression on the molecular axis in hepatic stellate cells

Treatment group (<i>n</i> = 3)	DLX6-AS1 Expression (Fold change)	miR-26a Expression (Fold change)	PTEN Protein Expression (Relative value)	α -SMA Expression (Relative value)
Control group	1.000 \pm 0.051	1.000 \pm 0.062	1.000 \pm 0.083	1.000 \pm 0.054
DLX6-AS1 overexpression group	3.567 \pm 0.312*	0.421 \pm 0.035*	0.453 \pm 0.041*	2.154 \pm 0.203*

Note: Data are presented as mean \pm SD. **P** < 0.001 vs. control group.

Table 2. Causal verification: DLX6-AS1/miR-26a rescue experiment

Treatment group (<i>n</i> = 3)	DLX6-AS1 expression (Fold change)	miR-26a expression (Fold change)	PTEN protein expression (Relative value)	α -SMA expression (Relative Value)
Control	1.000 \pm 0.051	1.00 \pm 0.062	1.00 \pm 0.04	1.00 \pm 0.05
DLX6-AS1 Overexpression	3.567 \pm 0.312*	0.42 \pm 0.04*	0.45 \pm 0.04*	2.15 \pm 0.20*
miR-26a Mimic	0.987 \pm 0.045	3.26 \pm 0.29#	1.62 \pm 0.15#	0.49 \pm 0.03#
DLX6-AS1 OE + miR-26a Mimic	2.88 \pm 0.254*	1.15 \pm 0.12#	0.98 \pm 0.09#	1.12 \pm 0.11#

Note: **P** < 0.001 vs. control group; #*P** < 0.001 vs. DLX6-AS1 overexpression group.

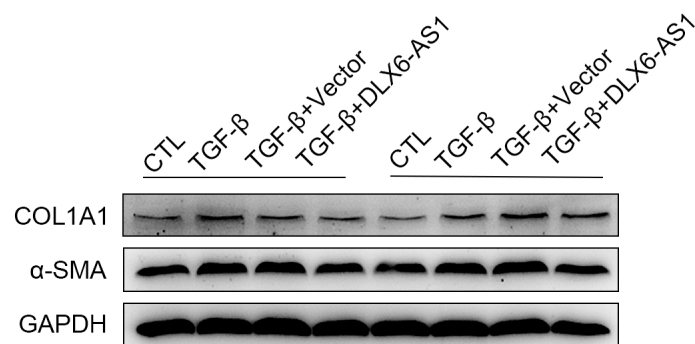


Figure 1. DLX6-AS1 inhibits TGF- β -induced COL1A1 and α -SMA expression. Western blot results suggest that DLX6-AS1 can inhibit TGF- β -induced fibrosis.

Table 3. Functional verification: Reversal of DLX6-AS1-induced fibrosis by PTEN overexpression

Treatment group (<i>n</i> = 3)	PTEN Protein expression (Relative value)	α -SMA expression (Relative value)	COL1A1 expression (Relative value)	Cell proliferation rate (%)
Control	1.00 \pm 0.04	1.00 \pm 0.05	1.00 \pm 0.03	100.2 \pm 5.23
DLX6-AS1 Overexpression	0.45 \pm 0.04*	2.11 \pm 0.20*	2.52 \pm 0.21*	180.5 \pm 15.13*
PTEN Overexpression	2.88 \pm 0.25#	0.42 \pm 0.03#	0.31 \pm 0.02#	55.2 \pm 4.34#
DLX6-AS1 OE + PTEN OE	1.15 \pm 0.12#	1.12 \pm 0.10#	1.21 \pm 0.11#	110.5 \pm 8.77#

Note: **P** < 0.001 vs. control group; #**P** < 0.001 vs. DLX6-AS1 overexpression group.

4.2. Introduction of a bivariate experimental design combining “Dose gradient + Time gradient”

The study dynamically monitored the regulatory effects of the DLX6-AS1/miR-26a/PTEN axis through a bivariate experimental design (Table 4).

Table 4. The impact of DLX6-AS1 overexpression on the expression of α -SMA, PTEN, and miR-26a in Hepatic Stellate Cells (HSCs)

Treatment group (<i>n</i> = 3)	DLX6-AS1 fold overexpression	Time point (hours)	α -SMA relative expression	miR-26a relative expression	PTEN relative expression
Control	1.00 \pm 0.05	24	1.00 \pm 0.05	1.00 \pm 0.06	1.01 \pm 0.04
DLX6-AS1 OE (Low Dose)	2.06 \pm 0.12	24	1.35 \pm 0.10*	0.82 \pm 0.07*	0.77 \pm 0.06*
DLX6-AS1 OE (Medium Dose)	4.12 \pm 0.22	24	1.88 \pm 0.15*	0.65 \pm 0.05*	0.62 \pm 0.08*
DLX6-AS1 OE (High Dose)	8.01 \pm 0.35	24	2.57 \pm 0.21*	0.45 \pm 0.03*	0.46 \pm 0.04*
Control	1.00 \pm 0.05	48	1.00 \pm 0.05	1.00 \pm 0.06	1.00 \pm 0.04
DLX6-AS1 OE (Medium Dose)	4.09 \pm 0.20	48	2.46 \pm 0.20*	0.58 \pm 0.05*	0.54 \pm 0.04*
Control	1.00 \pm 0.05	72	1.00 \pm 0.05	1.00 \pm 0.06	1.00 \pm 0.04
DLX6-AS1 OE (Medium Dose)	4.15 \pm 0.21	72	3.12 \pm 0.26*	0.49 \pm 0.04*	0.41 \pm 0.08*

Note: **P** < 0.001 vs. the control group at the corresponding time point. The relative expression levels of α -SMA and PTEN are set to 1 based on the control group.

4.3. Role of the DLX6-AS1/miR-26a/PTEN axis in an animal model of liver fibrosis

To validate the role of this molecular axis in an in vivo setting, the study established a CCl₄-induced mouse model of liver fibrosis (Table 5).

Table 5. Results of the animal model: Impact of the DLX6-AS1/miR-26a/PTEN axis on the fibrotic process

Group	DLX6-AS1 expression (Fold change)	miR-26a Expression (Fold change)	PTEN level (% of control)	Collagen deposition area (%)	Ishak fibrosis score (0–6)
Normal control (<i>n</i> = 10)	1.00 \pm 0.05	1.00 \pm 0.06	100.01 \pm 4.53	5.31 \pm 0.81	0.00 \pm 0.00
CCl ₄ fibrosis model (<i>n</i> = 10)	4.02 \pm 0.35*	0.32 \pm 0.07*	40.21 \pm 3.46*	45.1 \pm 5.24*	4.51 \pm 0.53*
CCl ₄ + miR-26a mimic (<i>n</i> = 10)	2.53 \pm 0.27#	2.85 \pm 0.23#	120.3 \pm 9.86#	18.3 \pm 2.68#	2.04 \pm 0.32#
CCl ₄ + PTEN overexpression (<i>n</i> = 10)	3.51 \pm 0.31*	0.41 \pm 0.05*	180.11 \pm 15.13#	12.1 \pm 1.89#	1.56 \pm 0.24#
CCl ₄ + DLX6-AS1 inhibitor (<i>n</i> = 10)	0.81 \pm 0.09#	1.86 \pm 0.14#	150.78 \pm 12.35#	15.2 \pm 2.06#	1.81 \pm 0.28#

Note: **P** < 0.001 vs. the normal control group; #**P** < 0.001 vs. the CCl₄-induced fibrosis group.

4.4. Validation of cellular heterogeneity using single-cell RNA-seq technology

To elucidate cellular heterogeneity during HSC activation, the study performed single-cell RNA sequencing analysis on liver tissue from the mouse model of liver fibrosis (Table 6).

Table 6. Single-cell RNA-seq analysis: Identification of HSC subpopulations and their gene expression characteristics

Cell subset (based on scRNA-seq clustering)	Proportion (%)	Key Marker genes	DLX6-AS1 relative expression	miR-26a relative expression	PTEN relative expression
Subset 1 (Quiescent HSC)	65.234	Lrat, Pdgfra	0.87 ± 0.05	2.15 ± 0.13	1.86 ± 0.13
Subset 2 (Early Activated HSC)	20.123	Coll1a1, Acta2, Tgfβ	3.57 ± 0.21*	0.43 ± 0.02*	0.51 ± 0.04*
Subset 3 (Pro-apoptotic HSC)	10.567	Bax, Caspase-3	1.24 ± 0.07	1.57 ± 0.11	3.23 ± 0.14#
Subset 4 (Other)	4.076	-	-	-	-

Note: * $P^* < 0.001$ vs. subpopulation 1; # $P^* < 0.001$ vs. subpopulation 2. Relative expression data are normalized to the mean value of subpopulation 1 (quiescent HSCs), which is set to 1.

4.5. Potential of the DLX6-AS1/miR-26a/PTEN axis as a biomarker for liver fibrosis

The study conducted stratified analysis on clinical samples and validated the diagnostic potential of this molecular axis using ROC curves (Table 7 and Figure 2).

Table 7. Clinical sample analysis: Relationship between DLX6-AS1/miR-26a/PTEN expression and liver fibrosis staging

Group ($n = 30/\text{group}$)	DLX6-AS1 (Relative expression)	miR-26a (Relative expression)	PTEN (Relative EXPRESSION)	Mean FibroScan value (kPa)	Liver fibrosis stage (F0–F4)
Mild Fibrosis (F0-F1)	1.25 ± 0.32	2.45 ± 0.41	1.57 ± 0.33	6.58 ± 1.25	F0-F1
Moderate Fibrosis (F2)	2.59 ± 0.53*	1.06 ± 0.28*	0.81 ± 0.23*	10.87 ± 2.06*	F2
Severe Fibrosis (F3)	3.85 ± 0.62*	0.58 ± 0.13*	0.42 ± 0.11*	15.54 ± 2.45*	F3
Cirrhosis (F4)	5.78 ± 0.81*	0.24 ± 0.03*	0.27 ± 0.05*	22.42 ± 3.19*	F4

Note: * $P^* < 0.001$ vs. the mild fibrosis (F0-F1) group.

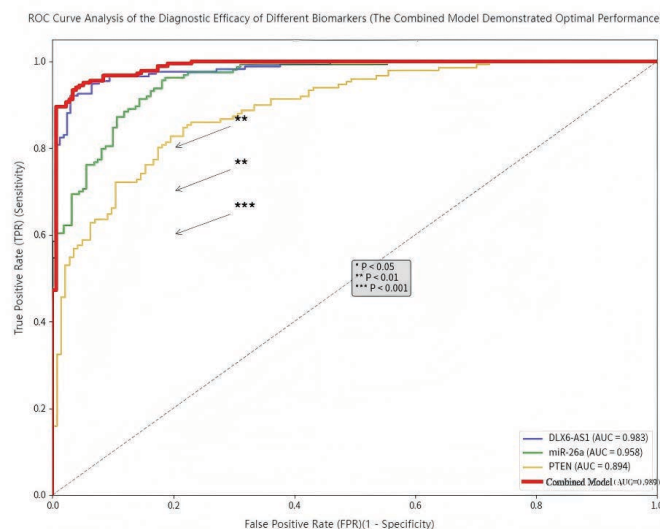


Figure 2. Diagnostic performance evaluation using ROC curves. AUC: Area under the curve. The combined model was constructed using logistic regression analysis of DLX6-AS1, miR-26a, and PTEN. The AUC of the multi-marker combined model reached 0.988, significantly higher than that of any single marker ($P < 0.05$).

4.6. Establish humanized mouse models to provide reliable in vivo validation

In a humanized mouse model of liver fibrosis, DLX6-AS1 inhibitors effectively reversed the abnormal expression of this molecular axis and significantly improved liver function and the degree of fibrosis (**Table 8**).

Table 8. Therapeutic effect of DLX6-AS1 inhibitors on liver fibrosis in humanized mouse models

Group (<i>n</i> = 10/group)	DLX6-AS1 (Relative expression)	miR-26a (Relative expression)	PTEN (Relative expression)	Serum ALT (U/ L)	Serum AST (U/ L)	Ishak fibrosis score (0–6)
Normal Control	1.00 ± 0.05	1.00 ± 0.06	1.00 ± 0.04	25.13 ± 2.67	30.45 ± 3.41	0.00 ± 0.00
Humanized Fibrosis Model	3.86 ± 0.32*	0.31 ± 0.07*	0.37 ± 0.35*	185.45 ± 15.13*	210.46 ± 18.35*	4.86 ± 0.53*
DLX6-AS1 Inhibitor	1.23 ± 0.11#	1.86 ± 0.14#	1.53 ± 0.13#	55.46 ± 5.87#	65.79 ± 6.23#	1.56 ± 0.24#

Note: **P** < 0.001 vs. normal control group; #**P** < 0.001 vs. humanized fibrosis group.

5. Discussion

The occurrence and development of liver fibrosis are closely related to the activation of hepatic stellate cells (HSCs), but the underlying molecular mechanisms remain to be elucidated [7–9]. This study systematically confirmed for the first time the key regulatory role of the DLX6-AS1/miR-26a/PTEN molecular axis in the activation process of HSCs.

At the molecular mechanism level, we clarified the regulatory relationship of this axis through a three-step verification method [10]: DLX6-AS1 inhibits PTEN expression by adsorbing miR-26a, ultimately driving HSC activation. This finding echoes the ceRNA regulatory mechanism proposed by Liang et al. Notably, introducing miR-26a mimics or overexpressing PTEN can effectively block the pro-fibrotic effect of DLX6-AS1, demonstrating the good intervenability of this pathway.

Further dynamic studies revealed that the regulatory effect of this molecular axis exhibits significant dose- and time-dependency. As the expression level of DLX6-AS1 increases, its inhibitory effect on downstream molecules and pro-activation effect synchronously enhance, indicating that this axis plays the role of a dynamic regulator in the fibrotic process, which is consistent with the clinical characteristics of the progressive development of liver fibrosis.

Using single-cell sequencing technology, we found that the expression of DLX6-AS1 exhibits obvious cell subset specificity, with significantly high expression in early-activated HSCs. This finding not only deepens the understanding of the fibrotic mechanism from the perspective of cellular heterogeneity but also provides important clues for the development of precise targeted therapeutic strategies.

In terms of clinical value, this molecular axis demonstrates promising translational prospects. Clinical sample analysis reveals a close correlation between its expression levels and fibrotic staging, with the combined diagnostic model exhibiting superior diagnostic efficacy. Animal experiments further validate the therapeutic potential of targeting this axis, particularly noting the significant anti-fibrotic effects of DLX6-AS1 inhibitors in humanized mouse models, providing robust support for subsequent clinical research [11].

From the perspective of clinical nursing, the discovery of this molecular axis offers new insights into the holistic management of patients with liver fibrosis. Risk assessment tools based on this biomarker facilitate early identification of high-risk populations [12]; its well-defined molecular mechanisms provide a theoretical basis for

formulating individualized health education programs^[13]; and it also points the way for optimizing symptom management strategies. As targeted therapies advance, nurses will play an increasingly important role in treatment monitoring, medication guidance, and adverse reaction management.

It should be noted that this study has some limitations. DLX6-AS1 may participate in fibrotic regulation through other signaling pathways, and the optimal usage regimen and long-term safety of its inhibitors still require in-depth exploration. These issues will be the key directions for our future research.

6. Conclusion

In conclusion, the discovery of the DLX6-AS1/miR-26a/PTEN axis not only deepens our understanding of the pathogenesis of liver fibrosis but also provides new targets for its diagnosis and treatment. Integrating this molecular biomarker into clinical practice will help advance precise prevention and treatment of liver fibrosis, ultimately improving patient outcomes.

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Disclosure statement

The authors declare no conflict of interest.

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Skeleton–Silhouette Complementary Perception: Toward Robust Gait Recognition

Xiaokai Liu*, Luyuan Hao

Information Science and Technology College, Dalian Maritime University, Dalian 116026, Liaoning Province, China

*Corresponding author: Xiaokai Liu, xkliu@dlmu.edu.cn

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Abstract: Gait, the unique pattern of how a person walks, has emerged as one of the most promising biometric features in modern intelligent sensing. Unlike fingerprints or facial characteristics, gait can be captured unobtrusively and at a distance, without requiring the subject's awareness or cooperation. This makes it highly suitable for long-range surveillance, forensic investigation, and smart environments where contactless recognition is crucial. Traditional gait-recognition systems rely either on silhouettes, which capture the outer appearance of a person, or on skeletons, which describe the internal structure of human motion. Each modality provides only a partial understanding of gait. Silhouettes emphasize shape and contour but are easily distorted by clothing or carried objects; skeletons describe motion dynamics and limb coordination but lose discriminative details about body shape. This article presents the concept of Complementary Semantic Embedding (CSE), a unified framework that merges silhouette and skeleton information into a comprehensive semantic representation of human walking. By modeling the complementary nature of appearance and structure, the approach achieves more robust and accurate gait recognition even under challenging conditions.

Keywords: Complementary perception; Gait recognition; Feature fusion

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1. Introduction: Why Gait Matters

Among all biometric traits, gait occupies a special position^[1]. It can be observed at a distance, through ordinary video cameras, without any physical contact. Every individual walks with a distinctive rhythm and spatial pattern, shaped by anatomy, age, and lifestyle. For security systems, this means people can be recognized even when their faces are hidden or when they move through crowded environments. For healthcare applications, changes in gait can reveal early signs of neurological or muscular disorders.

Yet, identifying a person by the way they walk is far from trivial^[2]. Human walking involves a highly complex coordination of limbs and joints, influenced by countless factors such as clothing, footwear, walking speed, load carrying, and camera perspective. Two video sequences of the same person may look entirely

different simply because of lighting or attire.

Early computer-vision systems focused primarily on silhouette analysis: extracting the outline of a walking person from each video frame, aligning the silhouettes over time, and using them as dynamic templates for classification. These silhouettes contain detailed information about body shape, but can change drastically when a person wears a long coat or carries a backpack. Later, with the progress of human pose estimation technology, another representation emerged-the skeleton graph, composed of discrete key joints such as shoulders, hips, knees, and ankles. This abstraction captures the geometry and motion of the human body, largely independent of appearance. It provides robustness against clothing variation but discards subtle cues about physique that help distinguish individuals. Each of these representations tells part of the story; neither alone can fully describe the individuality of gait. The key question therefore, becomes: how can we combine the strengths of both silhouettes and skeletons to form a complete picture of human walking?

2. From silhouettes to skeletons: Principles of gait recognition

To understand how gait can serve as a biometric, it helps to visualize the process. Imagine a sequence of video frames showing a person walking across a corridor. A typical gait recognition system performs three major steps:

- (1) Detection and Preprocessing: The person is isolated from the background. Silhouette extraction methods produce binary masks outlining the figure; pose-estimation algorithms detect skeletal joints.
- (2) Feature Representation: These dynamic signals are transformed into numerical features. For silhouettes, this might be a Gait Energy Image, an averaged image summarizing a walking cycle. For skeletons, features include joint coordinates and limb angles over time.
- (3) Classification and Recognition: Machine-learning models analyze these features to identify the person or verify identity.

Silhouette-based methods capture appearance dynamics, providing information about limb shape and proportion. They are powerful when the subject's clothing and lighting conditions remain consistent. However, they fail when visual cues change. Skeleton-based methods capture structural dynamics, tracking relative motion between joints. These are invariant to external appearance but sometimes ambiguous - two individuals of different builds may share very similar skeleton patterns. The challenge, then, is how to merge these two complementary views so that the system understands both what a person looks like and how they move.

3. The idea of complementary semantic embedding

The Complementary Semantic Embedding (CSE) framework begins with a simple but profound observation: silhouette and skeleton data describe the same physical event - a person walking - but from two different perspectives. Like two languages describing the same story, they each express unique semantics. Integrating them can reveal meaning that is hidden when either is viewed in isolation. The CSE model treats silhouettes and skeletons as homologous isomerism data - two forms of signals derived from the same source. It then aligns and fuses them at a high semantic level rather than at the raw data or feature level. This semantic fusion allows the system to learn correlations between external shape and internal structure.

In essence, the method aims to capture three key complementarities:

- (1) Robustness compensation: When silhouettes are distorted by clothing or accessories, skeletons provide invariant structural cues.
- (2) Appearance compensation: When skeletons lack discriminative body-shape details, silhouettes restore identity-related information.
- (3) Dynamic compensation: When self-occlusion hides part of a silhouette, skeleton motion data recover missing dynamics. By combining these aspects, the framework achieves a more balanced understanding of gait - one that is both structurally consistent and appearance-aware.

4. How the framework works

4.1. Concept overview

The Complementary Semantic Embedding system consists of three major components:

- (1) Data preprocessing: Converts raw videos into synchronized silhouette and skeleton streams.
- (2) Dual feature extraction: Uses specialized neural networks to process each modality.
- (3) Complementary fusion and classification: Merges the two streams into a unified representation for final recognition.

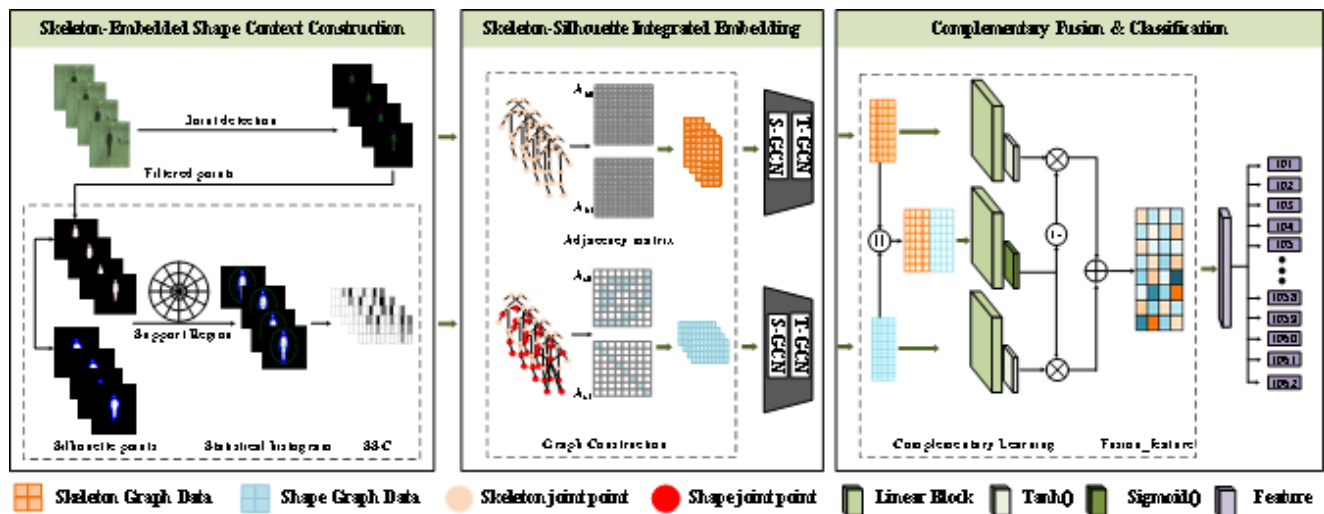


Figure 1. The Complementary Semantics Embedded Framework includes three modules: Data preprocessing, Specific convolution network, and Complementary feature fusion for classification.

4.2 Skeleton-Embedded Shape Context (SSC)

At the heart of the method lies the Skeleton-Embedded Shape Context (SSC), a representation that connects key skeletal joints with their surrounding silhouette regions. Imagine tracing the outline of a person's silhouette and marking the location of key joints like knees or elbows. Around each joint, a set of local regions is defined to describe how the body shape extends outward. These regions act like a "field" linking internal bones with external appearance. This hybrid representation allows the model to learn, for example, how the curvature of a leg silhouette relates to the bending angle of the knee joint. Through such correspondences, the network develops a deeper physical understanding of motion, capturing what moves and how it moves simultaneously.

4.3. Complementary Semantic Embedding

Once both streams, silhouette features and skeleton features, are extracted, the system employs an attention-based fusion mechanism. This module evaluates, dimension by dimension, which modality contributes more discriminative information and assigns adaptive weights accordingly. In regions where silhouette information is reliable (for instance, the outline of a leg), it dominates; where skeleton data are more stable (like under occlusion), the system leans on structural cues.

Mathematically, this corresponds to a weighted combination of nonlinear transformations, guided by learned importance scores. Conceptually, it resembles a conversation between two experts: one describing outer form, the other internal mechanics. The attention unit ensures their opinions combine intelligently into a single judgment.

4.4. Intuitive flow of the framework

Video frames enter two parallel paths, silhouette analysis and skeleton analysis, each producing a stream of high-level features. These converge within a fusion module that learns to integrate complementary semantics. The resulting vector represents a person's gait identity in a compact, discriminative form.

5. Experimental validation and key findings

To evaluate this approach, researchers tested it on a major benchmark datasets: CASIA-B - collected by the Chinese Academy of Sciences, containing 124 subjects walking under three conditions: normal, with a bag, and with a coat, from 11 camera angles. In This case, skeletons were extracted using OpenPose ^[3], and silhouettes were preprocessed from video frames. The experiments compared the proposed framework with well-known baseline models relying on single modalities.

5.1. Robustness and accuracy

Across all conditions, the complementary framework significantly outperformed traditional methods, including SPAE GV ^[4], GaitGANv1 ^[5], GaitGANV2 ^[6], MGANs ^[7], PoseGait ^[8]. In the normal walking scenario, accuracy improved to above 90 percent; in more challenging carrying-bag or wearing-coat cases, the improvement margin exceeded 20 percent over silhouette-only models. The results confirm that skeleton cues help maintain identity consistency even when appearance changes. Conversely, silhouettes enhance recognition when skeleton extraction is uncertain due to occlusion or camera angle.

Table 1. Comparison of identification accuracy with comparable methods

Gallery NM 1-4		0-180										Mean
Prob												
SPAE GV ^[4]	50.0	58.6	61.1	63.3	64.0	62.1	62.3	66.3	64.4	54.5	46.7	62.8
GaitGANv1 ^[5]	41.9	53.6	63.0	64.5	63.2	58.2	61.7	65.7	62.7	54.1	40.6	61.0
GaitGANV2 ^[6]	48.1	61.9	68.7	71.7	66.7	64.8	66.1	70.2	71.6	56.8	46.1	66.2
MGANs ^[7]	54.9	65.9	72.1	74.8	71.1	65.7	70.0	75.6	76.2	68.6	53.8	68.1
PoseGait ^[8]	49.7	61.6	67.0	66.7	60.8	59.0	62.5	61.4	67.3	62.0	62.0	63.7
Ours	87.2	91.7	94.0	92.6	87.9	87.0	88.4	91.9	91.7	88.4	83.2	90.1

5.2. Feature distribution insights

Using dimensionality-reduction visualization (t-SNE), the fused representations formed compact clusters for each identity, with clear separation between individuals. This pattern indicates that the model learned an effective embedding space where people are easily distinguishable despite covariate variations.

6. Applications and broader implications

The implications of robust multimodal gait recognition extend far beyond identification tasks.

6.1. Security and surveillance

In public security, gait recognition enables continuous monitoring without violating privacy, since it relies on motion rather than facial details. Systems deployed in airports, subways, or public buildings could detect known individuals or abnormal behaviors automatically. The fusion approach described here makes such systems more reliable in real-world conditions where people wear different clothes or carry personal items.

6.2. Healthcare and rehabilitation

Gait is a sensitive indicator of human health. Neurological disorders such as Parkinson's disease, stroke, or muscular dystrophy manifest early in walking irregularities. By combining structural and appearance cues, the complementary perception model can detect subtle changes in movement patterns that might escape the human eye. Integrating such models into wearable or ambient sensors could revolutionize preventive healthcare.

6.3. Beyond vision: Toward multimodal human sensing

The principles behind complementary perception extend naturally to other sensing modalities - radar, infrared, sonar, and wireless radio. Each captures different physical aspects of human motion. Integrating them could lead to general multimodal perception networks capable of understanding human activity in almost any environment, day or night.

7. Outlook: Toward intelligent human sensing

The Complementary Semantic Embedding framework represents a step toward holistic human understanding. Future research will likely focus on three directions:

- (1) Cross-modal generalization: Extending the framework to incorporate non-visual data such as millimeter-wave radar or depth sensors. These can penetrate clothing or operate in darkness, complementing visual modalities.
- (2) Lightweight deployment: Optimizing the architecture for edge computing and embedded AI chips so that gait recognition runs in real time on mobile or IoT devices.
- (3) Explainable perception: Interpreting what the fused features mean physically, which aspects of motion define identity, and how they relate to biomechanics or emotion.

Ultimately, the goal is to build intelligent sensing systems that can perceive and reason about human behavior comprehensively - not merely as pixels or coordinates, but as expressions of identity, health, and intention. The fusion of silhouette and skeleton perception provides a tangible example of how AI can integrate

heterogeneous information to achieve a deeper level of understanding.

Disclosure statement

The authors declare no conflict of interest.

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Investigation on the Current Situation of Missed Nursing Care and Analysis of Its Influencing Factors Among 1,476 Nurses in Southern Xinjiang

Hui Chen, Xiangtao Chen, Hefang Wang

Kashi Prefecture Second People's Hospital, Kashi Prefecture 844000, Xinjiang Uygur Autonomous Region, China

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Abstract: *Objective:* To investigate the current situation of nurses' lack of nursing care in southern Xinjiang and analyze its influencing factors. *Methods:* A convenient sampling method was used to select 1476 nurses from two tertiary hospitals in Kashi from May 2022 to December 2022 as the subjects of a cross-sectional survey. The nurses in southern Xinjiang were investigated by general information questionnaire and nursing deficiency scale-nurse version. *Results:* A total of 1476 valid questionnaires were collected in this study. The score of nurses' lack of care in southern Xinjiang was (56.05 ± 9.36) , which was above the middle level. Among them, the scores of timely responses to call bells, view patient medical records, fully understand their own patient's condition, and provide emotional support for patients and/or family members were relatively low. Univariate analysis showed that there were significant differences in the scores of nurses' age, nurses' level, nursing career satisfaction and nursing job satisfaction ($p < 0.05$). Multivariate analysis showed that the occupational satisfaction and nursing job satisfaction of nursing staff were the main factors affecting the lack of nursing work ($p < 0.05$). *Conclusion:* The lack of nursing care of nurses in southern Xinjiang is at the upper middle level. The younger the age, the lower the satisfaction of nursing profession and the lower the satisfaction of nursing position, the more serious the lack of nursing care. In order to solve this problem, nursing managers should actively respond to the influencing factors of nursing absence and actively seek effective management measures to reduce the incidence of nursing absence and ensure the safety of patients.

Keywords: Xinjiang; Nurse; Lack of care; Nursing management

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1. Introduction

Missed Nursing Care refers to the failure of nursing staff to provide appropriate care and attention in the healthcare sector, which negatively impacts patients' health and recovery. This phenomenon not only poses a threat to patients' safety and prognosis but also directly affects the efficiency and sustainable development of the healthcare system ^[1]. According to research, 66.16% to 71.9% of nurses have engaged in missed nursing care behaviors ^[2].

The occurrence of missed nursing care may lead to prolonged hospital stays, pressure ulcers, physical disabilities, and other adverse outcomes for patients, as well as negatively impacting the hospital's reputation ^[3]. Therefore, addressing this issue fundamentally is crucial for ensuring the quality of healthcare and patient safety. However, as one of the remote regions in China, southern Xinjiang faces complex geographical conditions, inconvenient transportation, relatively backward economic development, and a scarcity of medical resources, making missed nursing care one of the severe challenges confronting healthcare services in the area ^[4]. Hence, this study aims to explore the current situation of missed nursing care in nursing work in southern Xinjiang from the perspective of nurses through a cross-sectional survey and analyze its attributes. Based on these attributes, this study provides nursing managers with a focal point for management to improve the current situation of missed nursing care in southern Xinjiang, enhance nursing quality, and increase patient satisfaction.

2. Objects and methods

2.1. Survey objects

Using a convenience sampling method, 1,476 nurses from two tertiary hospitals in Kashi Prefecture from May 2022 to December 2022 were selected as the research objects for the cross-sectional survey. This study has been approved by the Medical Ethics Committee of Kashi Prefecture Second People's Hospital.

2.1.1. Inclusion criteria

- (1) Practicing nurses who have obtained professional qualification certificates and have worked in the Kashi region for at least one year
- (2) Nurses who have provided informed consent and voluntarily agreed to participate in this study

2.1.2. Exclusion criteria

- (1) Nurses undergoing standardized training or further education
- (2) Nurses working in non-clinical positions
- (3) Nurses who leave their jobs or give birth during the intervention period

2.2. Methods

2.2.1. General information questionnaire

Based on the objectives of this study, relevant literature was reviewed, and a general information questionnaire was designed based on previous experience. It mainly includes the nurse's gender, age, educational background, whether the time spent working in the current department is the longest, professional title, nurse competency level, work schedule type, average number of hours worked overtime per day, job satisfaction in nursing, job position satisfaction, and the adequacy of nurse staffing in the department.

2.2.2. Nursing omission scale-nurse version (MISSCARE survey)

This scale was proposed by foreign scholar Kalisch and translated and localized by Chinese scholar Si Fei ^[5]. The scale consists of two parts: Part A, the Missed Nursing Care subscale, which is primarily used to evaluate the omission of nursing activities within the hospital. It contains 24 items and uses a Likert 5-point scale. A higher score indicates more frequent omissions in nursing work, with a test-retest reliability of 0.87. Part B, the Reasons

for Missed Nursing Care subscale, mainly assesses the reasons for nursing omissions. It is divided into three dimensions: manpower, material resources, and communication, with 19 items. A Likert 4-point scale is used, and a higher score indicates that the item is a significant reason for nursing omissions. The Cronbach's α coefficient for this scale ranges from 0.64 to 0.86, with a test-retest reliability of 0.86.

2.3. Survey method

Based on the intentions and collaboration requests, this study fully communicated with the nursing departments of two tertiary-level hospitals and established WeChat groups. Research subjects who met the inclusion criteria and provided informed consent were invited to join the WeChat groups. The researchers provided unified training on the survey objectives, related concepts, content, questionnaire completion methods, and precautions to ensure that participants understood how to fill out the questionnaire and emphasized confidentiality commitments. To ensure the authenticity and reliability of the survey results, character limits were set in the questionnaire, and participants were required to complete the survey using only one mobile phone or computer for a single submission. The questionnaire could only be submitted after being fully completed. A total of 1,476 valid questionnaires were collected, with a response rate of 98.40%.

2.4. Statistical methods

Data were processed using SPSS 22.0 statistical software. When measurement data conformed to a normal distribution, they were expressed as mean \pm standard deviation ($\bar{x} \pm s$), and independent sample t-tests were used. Count data were expressed as rates, and comparisons between the two groups were made using the χ^2 test. In univariate analysis, factors with significant differences in univariate analysis were included in multivariate stepwise regression analysis. A *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. General information of nurses in Southern Xinjiang

A total of 1,476 nurses in Southern Xinjiang were surveyed, including 50 males and 1,426 females, aged 19–59 years with an average age of (32.05 ± 6.01) years.

3.1.1. Educational qualifications

36 with secondary vocational education, 648 with junior college education, and 792 with bachelor's degree or above.

3.1.2. Professional titles

672 nurses, 616 nurse practitioners, and 188 chief nurses or above.

3.1.3. Nurse competency levels

369 at N0–1 level, 693 at N2 level, 367 at N3 level, and 47 at N4 level.

3.1.4. Work experience

215 with 1 to < 3 years, 765 with 3 to < 5 years, 323 with 5 to < 10 years, 173 with 10–20 years, and 215 with over 20 years.

3.1.5. Work shift types

350 on regular day shifts, 120 on regular night shifts, 154 on auxiliary shifts, and 852 on APN rotation shifts. Average daily overtime hours: 140 with 0 hours, 527 with > 0 to 0.3 hours, 596 with > 0.3 to 1 hour, and 213 with > 1 hour.

3.2. Comparison of nursing omission scores among nurses with different demographic characteristics

The results of this study showed that the nursing omission score for nurses in Southern Xinjiang was (56.05 ± 9.36) points. The items with lower scores were “responding promptly to call bells”, “reviewing patient medical records to fully understand the conditions of patients under their care”, and “providing emotional support to patients and/or their families”. There were significant differences ($p < 0.05$) in the score of ages, nurse competency level, satisfaction with nursing profession, and satisfaction with nursing position. See **Table 1**.

Table 1. Comparison of scores for nursing omissions among nurses with different demographic characteristics

Category	n	Score	F/t value	p-value
Gender			-1.792	0.073
Male	50	30.56 ± 6.08		
Female	1426	32.11 ± 6.01		
Age (years)			6.189	0.000
≤ 25	188	57.26 ± 8.99		
25 to ≤ 35	739	56.48 ± 9.43		
35 to < 45	282	54.72 ± 8.64		
≥ 45	267	46.46 ± 9.85		
Education Level			1.293	0.276
Technical Secondary School	36	55.11 ± 8.10		
College	648	56.72 ± 9.44		
Bachelor's Degree or Above	792	55.35 ± 9.41		
Longest Tenure in Current Department			1.640	0.102
Yes	750	58.97 ± 4.26		
No	726	58.28 ± 5.26		
Professional Title			0.996	0.409
Nurse	672	56.74 ± 9.60		
Senior Nurse	616	55.71 ± 9.07		
Nurse-in-charge or above	188	54.85 ± 9.41		
Nurse Rank (N-level)			3.020	0.029
N0–1	369	56.61 ± 9.32		
N2	693	56.66 ± 11.93		
N3	367	54.11 ± 8.91		
N4	47	53.17 ± 9.65		

Table 1 (Continued)

Category	n	Score	F/t value	p-value
Years of Experience			2.197	0.054
1 to < 3	215	52.86 ± 6.01		
3 to < 5	765	58.29 ± 9.18		
5 to < 10	323	57.17 ± 9.53		
10 to 20	173	55.56 ± 9.28		
> 20	215	59.38 ± 10.53		
Work Shift Type			1.676	0.171
Day Shift	350	56.62 ± 9.08		
Night Shift	120	59.27 ± 10.14		
Support Shift	154	55.63 ± 9.36		
APN Rotation	852	55.44 ± 9.52		
Average Daily Overtime (hours)			0.904	0.406
0	140	56.54 ± 9.48		
> 0 to 0.3	527	54.38 ± 8.90		
> 0.3 to 1	596	55.57 ± 9.24		
> 1	213	56.06 ± 9.36		
Satisfaction with Nursing Profession			6.241	0.000
Satisfied	417	49.11 ± 6.60		
Somewhat Satisfied	436	50.04 ± 9.91		
Neutral	342	57.54 ± 9.43		
Somewhat Dissatisfied	193	56.17 ± 9.26		
Dissatisfied	88	56.40 ± 8.88		
Satisfaction with Current Position			2.486	0.043
Satisfied	516	50.75 ± 6.83		
Somewhat Satisfied	613	52.00 ± 9.99		
Neutral	134	55.73 ± 9.65		
Somewhat Dissatisfied	115	56.21 ± 9.31		
Dissatisfied	98	57.40 ± 9.11		
Perceived Staffing Level in Department			1.486	0.205
Adequate	529	56.75 ± 9.11		
Fair	442	56.69 ± 9.88		
Basic	357	56.29 ± 9.15		
Less than Ideal	94	54.11 ± 9.06		
Inadequate	54	55.28 ± 9.40		

3.3. Results of multiple linear regression analysis on nursing omissions

Using the total score of nursing omissions among nurses in southern Xinjiang as the dependent variable, and age, nurse competency level, satisfaction with nursing profession, and satisfaction with nursing position as independent variables, a multiple linear regression analysis method was employed to further analyze the independent factors contributing to nursing omissions among nurses in southern Xinjiang. The assignment of independent variables is shown in **Table 2**. The results revealed that age, satisfaction with nursing profession, and satisfaction with nursing position were independent factors influencing nursing omissions among nurses ($p < 0.05$). See **Table 3**.

Table 2. Variable assignment table

Variable	Assignment method
Age	1 = ≤ 25 years, 2 = 25 to ≤ 35 years, 3 = 35 to < 45 years, 4 = ≥ 45 years
Nurse rank	1 = N0-1, 2 = N2, 3 = N3, 4 = N4
Satisfaction with nursing profession	1 = Satisfied, 2 = Somewhat satisfied, 3 = Neutral, 4 = Somewhat dissatisfied, 5 = Dissatisfied
Satisfaction with current position	1 = Satisfied, 2 = Somewhat satisfied, 3 = Neutral, 4 = Somewhat dissatisfied, 5 = Dissatisfied

Table 3. Analysis of multiple linear regression results for nursing omissions among nurses in Southern Xinjiang

Variable	β	S.E.	<i>t</i> -value	<i>p</i> -value	95% CI
Age	-4.665	1.058	-4.409	0.000	-6.743 -2.587
Nurse rank	-0.213	0.630	-0.339	0.735	-1.450 - 1.023
Satisfaction with nursing profession	1.323	0.635	2.083	0.038	0.076 - 2.570
Satisfaction with current position	2.464	0.699	3.525	0.000	1.091 - 3.837

4. Discussion

4.1. The phenomenon of nursing omissions among nurses in Southern Xinjiang is relatively severe

The results of this study indicate that the score for nursing omissions among nurses in southern Xinjiang was (56.05 ± 9.36), suggesting that the phenomenon of nursing omissions among nurses in this region is relatively severe, and hospital administrators should pay attention to this issue. In this study, the three items with the lowest scores on the nursing omissions scale were “responding promptly to call bells”, “reviewing patient medical records to fully understand the conditions of patients under their care”, and “providing emotional support to patients and/or their families”. The analysis suggests that there may be a shortage of nurses in southern Xinjiang, leading to each nurse being responsible for a larger number of patients. When multiple patients require care simultaneously or emergencies arise, nurses may be unable to respond promptly to call bells. In response to these circumstances, it is recommended that hospitals increase the number of nurses to reduce their workload and ensure that each nurse can better respond to call bells ^[6].

In this study, it was found that the scores for reviewing patients’ medical records and fully understanding the conditions of patients under one’s care were relatively low. This may be due to a lack of sufficient awareness among nursing staff regarding this task, coupled with the belief that it is a simple operation, leading to a lack of emphasis on it. In response to the aforementioned situation, managers should emphasize the importance of

this operation and its impact on patient safety and the quality of care. They should also randomly select patient cases for nurses to review, implement a reward and punishment system, and enhance nurses' work efficiency and understanding of patient conditions ^[7].

Finally, providing emotional support to patients and/or their families requires nurses to possess strong empathy, enabling them to understand patients' inner feelings. However, due to the relatively tedious nature of nurses' daily work and the influence of external factors, nurses may not be able to concentrate on listening to patients' feelings, thereby affecting their empathy with patients and reducing the effectiveness of emotional support. To address this issue, it is recommended to establish different "emotional support rooms" in different wards and hang "do not disturb" warning signs at the doors to ensure that emotional support is provided without interruption, thereby offering better emotional support to patients ^[8].

4.2. Factors influencing nursing omissions among nurses in Southern Xinjiang

The results of this study indicate that the younger the age, the more severe the nursing omissions. This finding is similar to the survey results of Zhang Jing and others on nurses ^[9]. The reasons for this may include the following: young nurses may have just graduated or started their nursing careers, lacking practical work experience and having not fully received professional training or practice. Therefore, they may feel confused or uncertain when facing complex nursing tasks or emergencies, leading to nursing omissions ^[10]. Secondly, young nurses may not have fully mastered skills in time management, task allocation, and priority setting, resulting in an inability to effectively organize and arrange nursing tasks in a busy work environment, thus leading to nursing omissions ^[11]. This suggests that nursing managers should provide young nurses with ample training opportunities, including the cultivation of theoretical knowledge and practical skills, to help them acquire the necessary professional knowledge and skills and improve the quality of care.

The findings of this study indicate that nurses with lower job satisfaction in nursing are more likely to experience instances of missed nursing care. The reasons for this are as follows: Salary and benefits are crucial to nurses' satisfaction. If nurses' efforts in nursing do not match their income, or if there is a lack of appropriate welfare and incentive mechanisms, it can lead to dissatisfaction among nurses at work. In such cases, nurses may lack motivation and enthusiasm, resulting in missed nursing care ^[12]. Secondly, most nurses hope to have opportunities for continuous learning and growth in their careers. If hospitals fail to provide sufficient opportunities for nurses to enhance their skills and career development, it can lead to frustration and disappointment among nurses, causing a decline in their commitment and interest in work, and subsequently resulting in missed nursing care ^[13]. To address these issues, management should support the development of nurses by providing necessary training and resources, while encouraging nurses to participate in the decision-making process to enhance their job satisfaction and sense of involvement. Additionally, implementing appropriate patient allocation and workload management strategies can ensure that nurses can allocate their time and resources reasonably. Furthermore, providing regular training and learning opportunities enables nurses to continuously update their knowledge and skills and stay abreast of the latest nursing practices ^[14].

The survey results also show that nurses with higher job satisfaction in nursing positions tend to experience fewer instances of missed nursing care. This may be because nurses with higher satisfaction are usually passionate about their profession, and they are more focused on patients' needs in nursing work. They are more willing to invest time and effort to meet patients' needs, establish good relationships with patients, and thereby reduce the likelihood of missed nursing care ^[15]. On the other hand, nurses with lower job satisfaction in nursing positions

may face higher emotional and mental health issues, such as anxiety, emotional fatigue, and job burnout caused by work stress. These issues may interfere with nurses' attention and concentration, increasing the risk of missed nursing care^[16]. This suggests that nurses' mental health and work-life balance are crucial for improving job satisfaction and reducing missed nursing care. Management should pay attention to nurses' mental health conditions and provide psychological support and resources, such as psychological counseling services and stress management training. At the same time, encouraging and supporting nurses to maintain a good work-life balance can help alleviate work stress and enhance the quality of nursing care.

5. Conclusion

In summary, the level of nursing omission among nurses in southern Xinjiang is above average, with younger nurses and those with lower job satisfaction and lower satisfaction with their nursing positions experiencing more severe nursing omissions. To address this issue, nursing administrators should actively respond to the factors influencing nursing omissions and seek effective management measures to reduce the incidence of nursing omissions and ensure patient safety.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Study on Acupoint Injection Combined with Intrapapinal Anesthesia for Labor Analgesia in Primiparas

Shuaihui Zeng†, Zesen Zhan†, Zijing Zhang*

Department of Obstetrics, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

† These authors contributed equally to this work and share the first authorship.

*Corresponding author: Zijing Zhang, zhangzj53@mail2.sysu.edu.cn

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Abstract: *Objective:* To investigate the effects of intrapapinal anesthesia combined with acupoint injection at Zusanli (ST36) and Sanyinjiao (SP6) on labor progression and delivery outcomes in full-term primiparas. *Methods:* A retrospective analysis was conducted on 303 full-term primiparas who delivered between July and December 2023. According to the analgesic method, the participants were divided into an observation group ($n = 110$) and a control group ($n = 193$). Maternal general characteristics, mode of delivery, duration of each labor stage, incidences of uterine inertia, urinary retention, and intrapartum fever, as well as neonatal outcomes, were compared between the two groups. *Results:* The rate of vaginal delivery in the observation group was significantly higher than that in the control group ($p < 0.05$). The duration of the first stage of labor was significantly shorter ($p < 0.05$). The incidences of uterine inertia and urinary retention were both significantly lower in the observation group than in the control group ($p < 0.05$). There were no significant differences in neonatal Apgar scores or neonatal intensive care unit (NICU) transfer rates between the two groups ($p > 0.05$). *Conclusion:* Intrapapinal anesthesia combined with acupoint injection at Zusanli and Sanyinjiao can increase the rate of vaginal delivery, shorten the first stage of labor, and reduce obstetric interventions in full-term primiparas, without increasing adverse maternal or neonatal outcomes.

Keywords: Acupoint injection; Intrapapinal anesthesia; Primiparous women; Labor outcomes

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1. Introduction

Childbirth is a natural physiological process for women of reproductive age, while labor pain is one of the most intense and unforgettable pains experienced during vaginal delivery ^[1]. The physiological basis of labor pain mainly involves neuro-reflex pain caused by uterine contractions, cervical dilation, and fetal descent ^[2]. For primiparous women, the labor process is usually longer and cervical dilation progresses more slowly, resulting in more prolonged pain. The effectiveness of analgesic management is therefore crucial for both maternal and

neonatal safety as well as for improving the childbirth experience.

Epidural analgesia (EA) is currently the most widely used and effective method of labor analgesia in clinical practice. However, potential adverse effects such as prolonged labor and urinary retention remain major clinical concerns^[3–5]. Consequently, developing multimodal analgesic strategies that ensure adequate pain relief while promoting smooth labor progression and minimizing intervention has become a focus of current research.

Acupoint stimulation, a key component of traditional Chinese medicine, regulates body functions through the neuro–endocrine–immune network, exerting multi-target and holistic regulatory effects. Studies have shown that acupuncture may participate in the regulation of labor through multiple mechanisms, including activating the hypothalamic–pituitary–adrenal (HPA) axis to promote the release of endogenous opioid peptides such as β -endorphin and enkephalin, thereby relieving pain; regulating autonomic nervous system function to reduce sympathetic excitability and improve the maternal stress response during labor; and stimulating oxytocin secretion to enhance the coordination of uterine contractions^[6–9]. Zusanli (ST36) and Sanyinjiao (SP6) are commonly used acupoint combinations in obstetrics and gynecology. Acupoint injection uses the continuous mechanical stimulation of hypotonic injection water to prolong and enhance the effect of acupuncture^[10].

Based on these theoretical foundations, this study aimed to investigate the effects of epidural analgesia combined with acupoint injection at Zusanli and Sanyinjiao on labor progression and delivery outcomes in full-term primiparous women, in order to provide clinical evidence for optimizing perinatal analgesic management.

2. Materials and methods

2.1. Study population

This retrospective cohort study consecutively collected data from women who delivered in the Department of Obstetrics at the Third Affiliated Hospital of Sun Yat-sen University between July and December 2023 using the hospital's electronic medical record system.

The study was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University, and all procedures adhered to the principles of medical ethics. Patient information was anonymized during data collection, management, and analysis to ensure confidentiality and privacy protection.

2.1.1. Inclusion criteria

- (1) Full-term pregnancy (37–42 weeks of gestation)
- (2) Singleton pregnancy with cephalic presentation in primiparas
- (3) Willingness to undergo vaginal delivery with spontaneous onset of labor
- (4) Administration of epidural labor analgesia after cervical dilation ≥ 1 cm

2.1.2. Exclusion criteria

- (1) Severe pregnancy complications or comorbidities (such as severe preeclampsia, serious cardiopulmonary disease, or diabetic ketoacidosis)
- (2) Cesarean delivery performed before the onset of labor due to social reasons, fetal distress, or other medical indications
- (3) Incomplete clinical data or missing key variables
- (4) Analgesic method was changed or analgesia failed during labor

2.2. Grouping and analgesic methods

According to the analgesic regimen, the participants were divided into a control group ($n = 193$) and an observation group ($n = 110$). The control group received epidural analgesia (EA) only. When regular uterine contractions occurred and the cervix was dilated to approximately 1 cm, puncture was performed at the L2–3 or L3–4 intervertebral space. A 1 mL dose of sufentanil citrate injection (batch No. 21A09171A2; Yichang Humanwell Pharmaceutical Co., Ltd., China) was first administered intrathecally. The epidural catheter was then inserted cephalad and secured with 4 cm retained in the epidural space, followed by connection to an electronic patient-controlled analgesia (PCA) pump. The pump parameters were set as follows: total volume 120 mL, containing ropivacaine 75 mg and sufentanil 45 μg ; background infusion rate 6 mL/h; bolus dose 8 mL; and lockout interval 15 minutes. In the observation group, within 30 minutes after confirming effective analgesia with the same EA procedure as in the control group, acupoint injection was performed bilaterally at Zusanli (ST36, located one finger-breadth lateral to the anterior crest of the tibia) and Sanyinjiao (SP6, located 3 cm above the tip of the medial malleolus). After routine skin disinfection, the needle was inserted vertically and rapidly and 1 mL of sterile water was slowly injected at each acupoint, for a total of 4 mL across four sites.

2.3. Outcome measures

This study included both primary and secondary outcome measures. The primary outcome was the mode of delivery (vaginal delivery or cesarean section). Secondary outcomes included four aspects.

- (1) Duration of labor, including the first, second, and third stages, determined according to Obstetrics and Gynecology (9th edition) ^[11].
- (2) Incidence of epidural anesthesia-related adverse events, including uterine inertia and urinary retention. Uterine inertia was defined as insufficient uterine contractions requiring oxytocin administration to assist labor, and urinary retention referred to difficulty in urination or the need for indwelling catheterization during labor.
- (3) Neonatal outcomes, including birth weight, Apgar scores at 1, 5, and 10 minutes, and NICU transfer rate.
- (4) Maternal baseline characteristics, including gestational age, height, pre-delivery weight, maternal age, history of abortion or induced labor, educational level, employment and marital status, as well as the presence of gestational diabetes mellitus (GDM) and gestational hypertension.

2.4. Statistical analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Measurement data conforming to a normal distribution were expressed as mean \pm standard deviation (SD), and comparisons between groups were performed using the independent-samples t test. Categorical data were expressed as counts and percentages [n (%)], and comparisons between groups were performed using the chi-square (χ^2) test. A p value of < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general clinical characteristics between the two groups

There were no statistically significant differences between the two groups in terms of gestational age, maternal age, height, pre-delivery weight, educational level, occupation, marital status, number of abortions or induced

labors, gestational diabetes mellitus, or gestational hypertension ($p > 0.05$). These results indicate that the baseline characteristics of the two groups were balanced and comparable (**Table 1**).

Table 1. Comparison of general data between the two groups of parturients

Variable	Observation group (n = 110)	Control group (n = 193)	t/χ^2	p
Gestational week	39.53 (0.93)	39.42 (0.93)	-0.915	0.361
Height (cm)	158.75 (5.00)	159.69 (5.28)	-1.533	0.126
Pre-delivery weight (kg)	65.14 (8.94)	66.37 (8.44)	-1.149	0.251
Maternal age (years)	28.57 (3.12)	28.86 (3.41)	0.726	0.468
Inductions or abortion times			0.679	0.712
None	92 (83.6%)	154 (79.8%)		
Once	13 (11.8%)	28 (14.5%)		
Twice or more	5 (4.5%)	11 (5.7%)		
Education level			0.077	0.994
High school or below	18 (16.4%)	30 (15.5%)		
College	35 (31.8%)	64 (33.2%)		
Bachelor	52 (47.3%)	90 (46.6%)		
Master or above	5 (4.5%)	9 (4.7%)		
Employed	98 (88.3%)	164 (85.0%)	0.650	0.420
Married	105 (95.5%)	185 (95.9%)	0.027	0.869
Gestational diabetes	15 (13.6%)	28 (14.5%)	0.044	0.834
Gestational hypertension	3 (2.7%)	4 (2.1%)	0.133	0.715

Note: Values are presented as mean (SD) or n (%). Independent samples t -test and chi-square test were used for group comparisons. $p < 0.05$ indicates statistical significance.

3.2. Comparison of delivery modes between the two groups

The vaginal delivery rate in the observation group was 90.9%, which was significantly higher than that in the control group (82.4%) ($p < 0.05$), indicating that epidural anesthesia combined with acupoint injection helped improve the vaginal delivery rate among primiparous women. The duration of the first stage of labor in the observation group was 584.19 ± 266.52 minutes, significantly shorter than that in the control group (744.66 ± 256.53 minutes, $p < 0.05$), whereas no significant differences were found between the two groups in the duration of the second and third stages of labor ($p > 0.05$). These findings suggest that the combined use of acupoint injection can effectively shorten the first stage of labor and promote labor progression. Regarding anesthesia-related adverse events, the incidence of uterine inertia in the observation group was 60.0%, lower than that in the control group (73.0%, $p < 0.05$), and the incidence of urinary retention was also lower in the observation group (64.0% vs. 79.4%, $p < 0.05$). Overall, these results indicate that epidural anesthesia combined with acupoint injection not only increases the rate of vaginal delivery and shortens the first stage of labor but also reduces the risk of anesthesia-related adverse events (**Table 2**).

Table 2. Comparison of labor outcomes between groups

Variable	Observation group (n = 110)	Control group (n = 193)	t/χ^2	<i>p</i>
Vaginal delivery	100 (90.9%)	159 (82.4%)	4.103	0.043
First stage of labor (min)	584.19 (266.52)	744.66 (256.53)	-2.446	0.015
Second stage of labor (min)	67.16 (56.86)	78.02 (51.05)	-1.555	0.121
Third stage of labor (min)	10.27 (2.42)	10.53 (3.78)	-0.673	0.502
Oxytocin augmentation	60 (60%)	116 (73%)	4.720	0.030
Urinary retention	64 (64%)	150 (79.4%)	8.034	0.005

Note: Values are presented as mean (SD) or n (%). Independent samples *t*-test and chi-square test were used for group comparisons. *p* < 0.05 indicates statistical significance.

3.3. Comparison of neonatal outcomes

There were no statistically significant differences between the two groups in neonatal birth weight, Apgar scores at 1, 5, and 10 minutes, or the rate of neonatal transfer to the NICU (*p* > 0.05). These results indicate that epidural anesthesia combined with acupoint injection can improve delivery outcomes without increasing the risk of adverse neonatal outcomes (Table 3).

Table 3. Comparison of neonatal outcomes between groups

Variable	Observation group (n = 110)	Control group (n = 193)	t/χ^2	<i>p</i>
Neonatal weight (kg)	3.17 (0.29)	3.10 (0.33)	-1.841	0.067
1-min Apgar score	9.94 (0.37)	9.92 (0.34)	-0.339	0.735
5-min Apgar score	9.97 (0.286)	10 (0.00)	1.326	0.320
10-min Apgar score	9.98 (0.191)	10 (0.00)	1.326	0.186
Transfer to NICU	13 (11.8%)	29 (15%)	0.604	0.437

Note. NICU: neonatal intensive care unit. Values are presented as mean (SD) or n (%). Independent samples *t*-test and chi-square test were used for group comparisons. *p* < 0.05 indicates statistical significance.

4. Discussion

The results of this study showed that epidural anesthesia combined with acupoint injection of sterile water at Zusanli (ST36) and Sanyinjiao (SP6) significantly increased the vaginal delivery rate in full-term primiparous women, shortened the duration of the first stage of labor, and reduced the incidence of anesthesia-related adverse events such as uterine inertia and urinary retention. There were no statistically significant differences between the two groups in neonatal birth weight, Apgar scores, or the rate of neonatal transfer to the neonatal intensive care unit (NICU), suggesting that this combined analgesic approach can improve maternal delivery outcomes without increasing the risk of adverse neonatal outcomes.

The results of this study showed that the cesarean section rate in the observation group was significantly lower than that in the control group (9.1% vs. 17.6%), and the duration of the first stage of labor was also notably shorter. These findings are consistent with the meta-analysis conducted by Shui Linhui et al., which reported that acupuncture combined with epidural analgesia significantly reduced the risk of conversion to cesarean section (OR

= 0.45)^[12]. In addition, the present study further observed smoother labor progression in the observation group compared with the control group. Previous studies have suggested that epidural analgesia may delay cervical dilation to some extent^[13]. However, the combined analgesic protocol used in this study not only reduced the cesarean section rate but also shortened the duration of labor, suggesting that the addition of acupoint injection may help alleviate or even counteract the potential delaying effect of pharmacological analgesia on labor progression. The underlying mechanism may be related to the synergistic stimulation of Zusanli (ST36) and Sanyinjiao (SP6), which can promote the synthesis and release of endogenous oxytocin and prostaglandins through neurohumoral pathways, thereby enhancing the coordination and efficiency of uterine contractions and facilitating cervical dilation and fetal descent^[6,7,14]. Therefore, while maintaining effective analgesia, this combined approach not only avoids interference with normal labor but may also promote its physiological progression.

This study found that the incidences of uterine inertia and urinary retention were significantly lower in the observation group than in the control group, demonstrating the potential clinical advantages of the combined analgesic approach. The reduced incidence of uterine inertia supports the aforementioned hypothesis that acupoint injection may enhance the intensity and rhythmicity of uterine contractions, thereby promote labor progression and lowering the risk of uterine inertia, which is consistent with previous findings^[6,15,16]. The decreased incidence of urinary retention may be attributed to two factors. On the one hand, the shorter duration of labor in the observation group reduced bladder distension and voiding difficulty associated with prolonged labor; on the other hand, acupoint stimulation may partially counteract the inhibitory effects of epidural anesthesia on bladder sensation and function, thereby improving maternal spontaneous urination and comfort^[17]. The reduction in these adverse reactions not only helps optimize the delivery process and lower the risk of infection but also enhances the overall childbirth experience, reflecting a patient-centered approach to obstetric care.

The results of this study showed no significant differences between the two groups in neonatal Apgar scores, the rate of neonatal transfer to the NICU, further confirming the good maternal and neonatal safety of the combined analgesic regimen. The sterile water used for acupoint injection has a simple composition and contains no heterologous proteins; it exerts its effects solely through local physical stimulation, which ensures a high level of safety^[7,18]. These findings are consistent with the review by Zheng Xiaoying et al., which emphasized that acupuncture and related techniques for labor analgesia offer the advantages of minimal invasiveness and fewer side effects^[8].

The innovation of this study lies in its systematic evaluation of the clinical value of combining acupoint injection of sterile water at Zusanli (ST36) and Sanyinjiao (SP6) with epidural analgesia. This method is simple to perform and provides a sustained “needling sensation” at the acupoints, requiring less manpower than traditional acupressure or electrostimulation, making it well suited for implementation in delivery rooms. However, as a retrospective study, the present research cannot completely eliminate selection bias and the influence of potential confounding factors. In addition, data on maternal analgesic satisfaction (e.g., VAS scores) and total analgesic drug consumption were not collected, preventing a comprehensive assessment of the analgesic efficacy and cost-effectiveness of the combined method. Future studies should include prospective, large-sample randomized controlled trials and dynamically monitor serum hormone levels such as oxytocin and prostaglandins to further elucidate the mechanisms and clinical value of this combined analgesic strategy.

5. Conclusion

This study demonstrates that epidural anesthesia combined with acupoint injection of sterile water at Zusanli (ST36) and Sanyinjiao (SP6) is a safe and effective adjunctive method for labor analgesia in full-term primiparous women. This approach can increase the rate of vaginal delivery, shorten the first stage of labor, and reduce the need for interventions such as oxytocin administration and catheterization, without increasing the risk of adverse neonatal outcomes. Overall, this combined analgesic technique helps optimize the labor process and improve maternal and neonatal outcomes, and it merits further clinical application and validation.

Disclosure statement

The authors declare no conflict of interest.

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Research on the Impact of Health Education Nursing Based on the Transtheoretical Model of Behavior Change on Self-Efficacy in Osteoporosis Patients with Low Bone Mass

Fenglai Hu

Beijing Aerospace General Hospital, Beijing 100076, China

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Abstract: *Objective:* To investigate the impact of health education nursing based on the Transtheoretical Model of Behavior Change on self-efficacy in osteoporosis patients with low bone mass. *Methods:* A total of 91 osteoporosis patients with low bone mass admitted to our hospital from June 2000 to the end of June 2023 were selected and randomly divided into an observation group and a control group using the envelope method, with 46 and 45 cases in each group, respectively. The control group received routine nursing care, while the observation group received health education nursing based on the Transtheoretical Model of Behavior Change. Bone mineral density (lumbar spine L1–L4, femoral neck), disease awareness (Osteoporosis Knowledge Test Questionnaire, OKT-Q), and self-efficacy (Adult Health Self-Management Skills Rating Scale, AHSMSRS) were compared between the two groups. *Results:* After the intervention, bone mineral density levels, disease awareness levels, and self-efficacy levels significantly increased in both groups, with the observation group showing greater improvements in all indicators compared to the control group ($p < 0.05$). *Conclusion:* Interventions based on the Transtheoretical Model of Behavior Change effectively enhance patient self-efficacy and bone health by precisely matching behavioral stages, strengthening social support, and regulating neurobehavioral factors.

Keywords: Transtheoretical model of behavior change; Osteoporosis; Low bone mass population; Self-efficacy; Health education nursing; Bone mineral density

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1. Introduction

Osteoporosis has emerged as a significant global public health challenge, with its associated fracture risk significantly reducing patients' quality of life and life expectancy^[1]. Statistics indicate that approximately 200 million people worldwide are affected by this disease, with individuals with reduced bone mineral density constituting a high-risk group^[2]. However, in China, the awareness, diagnosis, and treatment rates of osteoporosis

are generally low, with patients often exhibiting key issues such as insufficient disease understanding, weak self-management abilities, and poor intervention compliance, severely limiting the effectiveness of prevention and control efforts^[3].

Traditional health education methods mostly focus on the one-way transmission of knowledge, lacking systematic intervention in the dynamic process of individual behavioral change, making it difficult to effectively stimulate patients' intrinsic motivation and facilitate sustained behavioral transformation. The theory of behavior change emphasizes that behavioral change is a staged, dynamically evolving continuous process, typically including the pre-intentional stage, intentional stage, preparation stage, action stage, and maintenance stage. This theory advocates for matching corresponding intervention strategies according to the characteristics of different stages, thereby more effectively guiding and maintaining the establishment of healthy behaviors^[4].

Therefore, this study explored the intervention effect of health education nursing based on the theory of behavior change on osteoporosis patients with low bone mass by implementing it among patients admitted to our hospital from June 2000 to the end of June 2023, and provided evidence for clinical selection plans. The specific report is as follows.

2. Data and methods

2.1. General information

A total of 91 patients with osteoporosis with low bone mass admitted to our hospital from June 2000 to the end of June 2023 were selected and randomly divided into an observation group and a control group using the envelope method, with 46 and 45 cases in each group, respectively. There were no statistically significant differences in the basic information between the two groups ($p > 0.05$), as shown in **Table 1**. This study was approved by the hospital ethics committee and complied with the relevant ethical principles of the Declaration of Helsinki.

Table 1. Comparison of general information between the two groups ($\bar{x} \pm s/n$)

Characteristic	Observation group (n = 46)	Control group (n = 45)	t/χ^2	p -value
Gender (Male/Female)	16 / 30	17 / 28	0.088	0.766
Age (years)	54–74	53–74	0.012	0.990
	63.15 ± 3.84	63.16 ± 3.91		
Education level [n]			0.478	0.787
High school or below	13	14		
College	21	22		
Bachelor's degree or above	12	9		

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Patients aged 45 to 75 years
- (2) Diagnosed with low bone mass osteoporosis by QCT examination
- (3) Able to independently complete the OKT-Q and AHSMSRS scale assessments
- (4) No contraindications to long-term calcium or vitamin D medication

- (5) Willing to accept a 6-month intervention

2.2.2. Exclusion criteria

- (1) Secondary osteoporosis caused by hyperparathyroidism, long-term glucocorticoid use, etc.
- (2) Comorbid with malignant tumors, severe heart, liver, or kidney failure, etc.
- (3) Unhealed lower limb fractures or limited mobility due to rheumatoid arthritis
- (4) Dementia, schizophrenia, etc., affecting cognitive assessment
- (5) Participation in other osteoporosis clinical trials within the past 3 months

2.3. Methods

Patients in the control group received routine care: Standardized health education was provided by responsible nurses, which included distributing brochures on osteoporosis knowledge, explaining basic disease information, and daily precautions. Routine medication guidance was also provided, detailing the usage and precautions for drugs such as calcium carbonate D3 tablets and calcitriol. Monthly telephone follow-ups were conducted to understand the patients' basic conditions and answer simple questions.

Patients in the observation group received health education nursing based on the Transtheoretical Model of Behavior Change

- (1) An interdisciplinary intervention team was formed, consisting of orthopedic surgeons, specialist nurses, and rehabilitation therapists, who commenced their work after undergoing unified training.
- (2) Prior to intervention, patients' behavioral stages were assessed: For those in the pre-contemplation stage, the focus was on elucidating the hazards of osteoporosis and the benefits of proactive intervention through case analysis. For patients in the contemplation stage, the motivational interviewing technique was employed to identify barriers to behavior change, including exercise-related fears and nutritional misconceptions, and personalized health education brochures were used to correct biased perceptions. For patients in the preparation and action stages, stage-specific goals were jointly established, such as gradually increasing sun exposure time (from 15 minutes to 30 minutes daily) and incorporating resistance training exercises (increasing the frequency of elastic band exercises from twice a week to four times a week), and a behavioral commitment contract was signed to reinforce a sense of responsibility.
- (3) The family support system was integrated into the intervention: Family members were guided to participate in monitoring dietary calcium intake (ensuring a daily intake of dairy products ≥ 300 mL) and medication adherence.
- (4) A digital management file was established, with weekly reminders sent via the WeChat platform to encourage behavior compliance (such as step count tracking and calcium supplement check-ins). Specialist nurses conducted 15–20 minutes video follow-ups every two weeks, using the teach-back method to confirm knowledge retention and adjusting intervention strategies in a timely manner.
- (5) For patients entering the maintenance stage, monthly peer support exchange meetings were organized, where successful cases shared their experiences of behavior change to consolidate long-term healthy behaviors.

The entire process lasted for six months, with an emphasis on staged feedback and positive reinforcement.

2.4. Observation indicators

2.4.1. Bone mineral density

Observe and compare the volumetric bone mineral density (vBMD) of the two groups of patients before and after the intervention. Bone mineral density was measured using Quantitative Computed Tomography (QCT). The subjects were asked to lie supine on the CT scanning table, with the body's midline aligned with the center of the scanning gantry and both knees flexed and placed on a specialized pillow to reduce the physiological curvature of the lumbar spine. The scanning range covered the mid-sections of the lumbar vertebrae L1–L4 and both femoral necks, utilizing a spiral CT mode (with a tube voltage of 120 kV and a tube current of 80–100 mAs). During the scanning process, a calibration phantom needed to be placed simultaneously between the subject's lower back and the scanning table, ensuring that the phantom and the spine/femur regions were imaged simultaneously to correct for CT value drift and convert it into absolute bone mineral density values.

2.4.2. Disease cognition

Observe and compare the levels of disease cognition in the two groups of patients before and after the intervention. Cognition levels were measured using the Osteoporosis Knowledge Test Questionnaire (OKT-Q). This questionnaire consists of 22 items, with each correct answer scoring 1 point and incorrect or unknown answers scoring 0 points, resulting in a total score range of 0 to 22 points. Based on the total score, cognition levels were classified into three grades: excellent (≥ 16 points), moderate (11 to 15 points), and inadequate (≤ 10 points).

2.4.3. Self-efficacy

Observe and compare the levels of self-efficacy in the two groups of patients before and after the intervention. Self-efficacy was measured using the Rating Scale of Health Self-Management Skill for Adults (AHSMSRS). This scale comprises 38 items and employs a Likert 5-point rating scale (1 = never, 5 = always), with a total score range of 38 to 190 points. Based on the total score, self-efficacy was classified into three levels: high (141 to 190 points), moderate (90 to 140 points), and low (38 to 89 points). Higher scores indicate higher self-efficacy.

2.5. Statistical methods

Our hospital analyzed the study using the SPSS 21.0 statistical software package. Measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$) and conformed to a normal distribution. Comparisons between groups were made using the *t*-test. Count data were expressed as relative numbers, and comparisons between groups were conducted using the chi-square (χ^2) test. Clinical efficacy comparisons were made using the rank-sum test, with a *p*-value < 0.05 indicating statistically significant differences.

3. Results

3.1. Comparison of bone density level between the two groups

Before the intervention, there was no significant difference in bone density levels between the two groups ($p > 0.05$). After the intervention, bone density levels in both groups significantly increased, with the observation group showing greater improvement in all indicators compared to the control group ($p < 0.05$). See **Table 2**.

Table 2. Comparison of bone density level between the two groups before and after intervention ($\bar{x} \pm s$, mg/cm³)

Group	n	Lumbar spine (L1–L4)		Femoral neck	
		Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Observation group	46	112.15 \pm 3.45	134.15 \pm 3.51*	238.15 \pm 4.91	283.15 \pm 8.22*
Control group	45	112.34 \pm 3.54	125.91 \pm 3.61*	239.41 \pm 5.08	261.15 \pm 8.36*
<i>t</i> -value		0.259	11.040	1.203	12.658
<i>p</i> -value		0.796	< 0.001	0.232	< 0.001

Note: Compared with the same group before intervention, * $p < 0.05$

3.2. Comparison of disease cognition level between the two groups

Before the intervention, there was no significant difference in disease cognition levels between the two groups ($p > 0.05$). After the intervention, disease cognition levels in both groups significantly increased, with the observation group showing greater improvement in all indicators compared to the control group ($p < 0.05$). See **Table 3**.

Table 3. Comparison of disease cognition level between the two groups before and after intervention ($\bar{x} \pm s$)

Group	n	Pre-intervention	Post-intervention
Observation group	46	8.15 \pm 1.33	16.25 \pm 1.48*
Control group	45	8.12 \pm 1.29	13.94 \pm 1.53*
<i>t</i> -value		0.109	7.416
<i>p</i> -value		0.913	< 0.001

Note: Compared with the same group before intervention, * $p < 0.05$

3.3. Comparison of self-efficacy level between the two groups

Before the intervention, there was no significant difference in self-efficacy levels between the two groups ($p > 0.05$). After the intervention, self-efficacy levels in both groups significantly increased, with the observation group showing greater improvement in all indicators compared to the control group ($p < 0.05$). See **Table 4**.

Table 4. Comparison of self-efficacy level between the two groups before and after intervention ($\bar{x} \pm s$)

Group	n	Pre-intervention	Post-intervention
Observation group	46	54.15 \pm 8.15	161.29 \pm 7.84*
Control group	45	55.08 \pm 8.21	150.94 \pm 7.93*
<i>t</i> -value		0.542	6.261
<i>p</i> -value		0.589	< 0.001

Note: Compared with the same group before intervention, * $p < 0.05$.

4. Discussion

Osteoporosis is characterized by a reduction in bone mass and damage to the bone microstructure, with the core pathology being a dynamic imbalance between bone formation mediated by osteoblasts and bone resorption

dominated by osteoclasts. With the intensification of population aging, the prevalence of osteoporosis among individuals aged 50 and above in China has reached 19.2%, while the proportion of those with low bone mass exceeds 46.4%. These patients face a significantly increased risk of fractures. Traditional health education methods, such as distributing knowledge booklets, conducting group lectures, and monthly telephone follow-ups, have become commonly used clinical approaches due to their simplicity and low cost ^[5]. However, this model fails to address the core contradiction of low bone mass individuals who “know but do not believe, and believe but do not act”. Data from the control group show that although both lumbar spine bone density and OKT-Q scores improved, the increases plateaued, reflecting the limitations of this approach in overcoming patients’ insufficient intrinsic motivation and barriers to behavior maintenance.

The intervention program based on the Theory of Behavior Change is designed to address the aforementioned bottlenecks. This theory views behavior change as a dynamic process of “pre-intention–intention–preparation–action–maintenance” and precisely activates behavior transformation mechanisms through stage-matched strategies: For patients in the pre-intention stage, visual presentations of cases of disability caused by fractures can stimulate risk perception and reconstruct patients’ cognitive perception of long-term health value; for those in the intention stage, motivational interviewing techniques expose barriers such as fear of exercise and nutritional misconceptions through open-ended inquiries, while personalized educational booklets simultaneously correct cognitive biases regarding the relationship between calcium absorption and bone metabolism; when patients enter the preparation and action stages, the setting of stepped goals provides a continuous sense of accomplishment through the achievement of small goals, and the signing of behavioral commitment letters strengthens executive control functions ^[6,7].

Additionally, family collaboration and digital management are incorporated to provide dual safeguards for maintaining patients’ behavioral adherence. Family members oversee dietary calcium intake and medication compliance; the WeChat platform facilitates step count recording and calcium supplement check-ins, compensating for the decline in executive function among elderly patients. Specialist nurses conduct biweekly video follow-ups using the teach-back method, enabling effective and timely strategy adjustments to prevent behavioral regression ^[8]. The continuous implementation of various strategies resulted in the observation group achieving an OKT-Q score of 16.25 and a self-efficacy score of 161.29, both higher than those of the control group. Notably, the immediate positive feedback in digital management consistently reinforces patients’ behavioral patterns, while peer support during the maintenance phase strengthens their treatment confidence through successful case studies ^[9].

5. Conclusion

In summary, interventions based on the Transtheoretical Model of Behavior Change effectively enhance patients’ self-efficacy and bone health by precisely matching behavioral stages, strengthening social support, and regulating neurobehavioral factors.

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Current Application Status and Evidence-Based Medicine Review of Herbal Medicine in the Treatment of Functional Dyspepsia in Internal Medicine with Integrated Traditional Chinese and Western Medicine

Chunxiao Wang

Department of Integrated Traditional Chinese and Western Medicine, Dongzhou Internal Medicine Clinic of Hangzhou Fuyang Size Health Management Co., Ltd., Hangzhou, Zhejiang 310000, China

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Abstract: Functional Dyspepsia (FD) is a common functional gastrointestinal disorder in internal medicine, characterized by a protracted course and high recurrence rate, significantly affecting patients' quality of life. Western medical treatment primarily focuses on symptomatic relief, with limitations such as limited long-term efficacy and a high likelihood of adverse reactions. Traditional Chinese Medicine (TCM) herbal treatment for FD, based on syndrome differentiation and treatment, offers advantages of holistic regulation and fewer side effects. With the development of integrated traditional Chinese and Western medicine, the application of herbal medicine in FD treatment has gradually shifted from a single syndrome-based approach to a synergistic model of "herbal medicine + conventional Western medical regimen". This review summarizes the application of herbal medicine under the guidance of TCM theory, the practice of herbal medicine in integrated traditional Chinese and Western medical settings, and the grading and evaluation of evidence-based medicine. Through analysis, the aim is to further promote the standardized and evidence-based application of herbal medicine in the integrated treatment of FD.

Keywords: Functional Dyspepsia; Herbal medicine; Integrated traditional Chinese and Western medicine; Evidence-based medicine; Syndrome differentiation and treatment; Gastrointestinal disorders

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1. Introduction

Functional Dyspepsia (FD) refers to a group of clinical syndromes originating from the gastroduodenal region, lacking evidence of organic lesions, and primarily manifesting as postprandial fullness, early satiety, upper abdominal pain, or burning sensation^[1]. Its diagnosis requires compliance with the Rome IV criteria and exclusion

of organic diseases such as peptic ulcers and gastric cancer. The pathogenesis of FD is complex, currently believed to be associated with gastrointestinal motility disorders, visceral hypersensitivity, intestinal dysbiosis, psychosomatic factors, and abnormal central nervous system regulation. A single factor is insufficient to fully explain its pathophysiological process ^[2]. Western medical treatment for FD primarily focuses on symptomatic treatment, with commonly used medications including proton pump inhibitors (PPIs), prokinetic drugs, *Helicobacter pylori* eradication drugs, and central nervous system regulators. However, clinical efficacy is limited, approximately 40% of patients respond poorly to PPIs, and long-term use may lead to adverse reactions such as intestinal dysbiosis and vitamin B12 deficiency. In Traditional Chinese Medicine (TCM), FD is classified under the categories of “distension and fullness”, “epigastric pain”, and “abdominal discomfort”, with the core pathogenesis being “dysfunction of the spleen and stomach and stagnation of Qi flow”. Treatment emphasizes “syndrome differentiation and treatment”, utilizing herbal remedies to regulate organ function and improve Qi circulation, offering the advantages of holistic regulation and fewer side effects. With the development of integrated traditional Chinese and Western medicine, the collaborative treatment model of “herbal remedies + conventional Western medical protocols” has gradually become a research hotspot in FD treatment. This approach leverages the rapid symptom relief characteristic of Western medicine while improving the patient’s overall physical condition and reducing recurrence rates through herbal remedies. However, there is currently a lack of systematic reviews on the current application status, strength of evidence-based research, and clinical standardization of herbal remedies in the integrated treatment of FD. Based on this, a comprehensive review of the current application status and evidence-based research on herbal remedies is necessary.

2. Current application status of herbal remedies in integrated traditional Chinese and Western medicine for FD treatment

2.1. Common syndromes of FD and corresponding herbal remedies guided by TCM theory

The core of TCM treatment for FD lies in “syndrome differentiation and medication according to the syndrome”. Common clinical syndromes include liver-stomach disharmony, spleen-stomach deficiency cold, spleen-stomach damp-heat, and food stagnation. The corresponding herbal remedies and formulas for each syndrome have clear theoretical foundations.

Liver-stomach disharmony is the most common syndrome in FD, often caused by emotional distress, liver Qi stagnation, and counterflow Qi affecting the stomach. The main symptoms include epigastric distension and pain, frequent belching, and exacerbation of symptoms with emotional fluctuations. Treatment follows the principle of “soothing the liver and regulating Qi, harmonizing the stomach and relieving pain”. The classic formula commonly used is Chaihu Shugan San (*Bupleurum*, *Cyperus rotundus*, *Aurantii fructus immaturus*, *Paeoniae radix alba*, *Ligusticum chuanxiong*, and *Glycyrrhizae radix preparata*), with clinical modifications often made: for pronounced belching, add *Citri sarcodactylis fructus* and *Inulae flos*; for acid reflux, add *Sepiae endoconcha* and *Concha ostreae calcinata*; for emotional depression, add *Albiziae cortex* and *Curcumae radix* ^[3]. Modern pharmacological studies have shown that saikosaponins in *Bupleurum* can regulate central neurotransmitters (such as serotonin and dopamine), alleviate anxiety, and improve gastrointestinal motility; volatile oil components in *Cyperus rotundus* can inhibit gastrointestinal smooth muscle spasms and relieve epigastric distension and pain.

The syndrome of spleen-stomach deficiency-cold is mostly caused by insufficient Yang Qi in the spleen and stomach, weak warming and nourishing ability, and abnormal transportation and transformation. Its main

symptoms include vague pain in the gastric region, preference for warmth and pressure, abdominal distension after eating, and loose stools. The treatment approach is to “warm the middle-jiao and invigorate the spleen, harmonize the stomach and relieve pain”. The representative formula is Fuzi Lizhong Pill (*Aconite*, ginseng, prepared ginger, licorice, and fried *Atractylodes macrocephala*)^[4]. Among them, Fuzi Lizhong Pill has a strong ability to warm Yang and disperse cold, making it suitable for patients with obvious chills and cold extremities. Cinnamon and *Evodia rutaecarpa* can be added according to symptoms to enhance the warming Yang effect. Huangqi Jianzhong Pill, on the other hand, takes into account both tonifying Qi and building the middle-jiao to alleviate urgency, making it more suitable for patients with fatigue and vague pain in the gastric region. Those with poor appetite can add fried malt and endothelium *Corneum gigeriae galli* to aid transportation and transformation.

The syndrome of spleen-stomach damp-heat is caused by the accumulation of damp-heat in the middle-jiao, which obstructs the transportation and transformation function of the spleen and stomach^[5]. Its main symptoms include burning sensation in the gastric region, bitter and sticky taste in the mouth, poor appetite, and sticky and uncomfortable stools. The treatment requires “clearing heat and resolving dampness, regulating Qi and harmonizing the middle-jiao”. Commonly used formulas include Lianpu Yin (coptis, magnolia bark, *Acorus gramineus*, *Pinellia ternata*, reed rhizome, gardenia, and fermented soybean) or Qingzhong Decoction (coptis, gardenia, *Pinellia ternata*, *Poria cocos*, tangerine peel, licorice, and *Alpinia katsumadai*)^[6]. Berberine in coptis can inhibit the activity of *Helicobacter pylori* and reduce gastric mucosal inflammation; magnolol in magnolia bark can regulate gastrointestinal motility and relieve abdominal distension symptoms.

The syndrome of food stagnation is mostly caused by improper diet, overeating, and food accumulation in the gastric region. Its main symptoms include fullness in the gastric region, belching with foul odor and sour regurgitation, and loss of appetite. The treatment mainly focuses on “promoting digestion and removing food stagnation, harmonizing the stomach and reversing Qi”. The representative formula is Baohe Pill (hawthorn, medicated leaven, *Pinellia ternata*, *Poria cocos*, tangerine peel, *Forsythia suspensa*, and radish seed). If food accumulation is severe, *Citrus aurantium* and areca nut can be added. Hawthorn acid in hawthorn can promote fat digestion, and raphanin in radish seed can enhance gastrointestinal motility and accelerate the elimination of food accumulation.

2.2. Application scenarios of herbal medicine in the integrated traditional Chinese and Western medicine treatment of FD

2.2.1. Combining herbal medicine with Western symptomatic drugs to enhance efficacy and reduce adverse reactions

For the common symptoms of “upper abdominal pain and burning sensation” in FD patients, Western medicine often uses PPIs (such as omeprazole and rabeprazole). However, some patients may experience “PPI resistance” or side effects from long-term use. Clinical studies have shown that combining PPIs with herbal remedies for the “liver-stomach disharmony syndrome” (such as Chaihu Shugan San) can enhance the symptom relief rate through a dual mechanism of “inhibiting gastric acid secretion + regulating gastrointestinal motility”. Research by Chen Shiwan et al. found that in the treatment of FD in children, the combination of Chaihu Shugan San and omeprazole enteric-coated capsules can effectively improve gastrointestinal digestive function and increase gastric emptying rate^[7]. For patients primarily experiencing “postprandial fullness and early satiety”, Western medicine commonly uses prokinetic drugs (such as mosapride) in combination with herbal remedies for the “spleen-stomach deficiency-cold syndrome” (such as Xiangsha Liujunzi Decoction) to further improve gastrointestinal motility:

Mosapride promotes acetylcholine release by stimulating 5-HT₄ receptors, while Xiangsha Liuqunzi Decoction synergistically enhances gastrointestinal smooth muscle contractility. Compared to the single-treatment group, patients in the combined treatment group showed more significant improvement in dyspepsia symptoms and more pronounced therapeutic effects ^[8].

2.2.2. Combination of herbal remedies and *Helicobacter pylori* eradication therapy to improve post-eradication FD symptoms

Helicobacter pylori infection is a significant risk factor for FD, with approximately 60% of FD patients also having *Helicobacter pylori* infection. Although Western medical *Helicobacter pylori* eradication regimens (such as bismuth-based quadruple therapy) can eliminate *Helicobacter pylori*, FD symptoms persist in some patients after eradication. At this juncture, combining herbal remedies can alleviate symptoms by regulating the gastric mucosal microenvironment and improving gastrointestinal function.

A study indicates that the combination of bismuth-based quadruple therapy with Wenzhong Hewei Decoction (composed of roasted licorice, dried ginger, *Atractylodes macrocephala*, *Citrus aurantium*, costus root, white cardamom, tangerine peel, magnolia bark, *Amomum villosum*, *Codonopsis pilosula*, *Pinellia ternata*, and *Astragalus membranaceus*) for the treatment of *Helicobacter pylori* -positive FD achieved an eradication rate of 87.93% ^[9]. Mechanistic studies have shown that Wenzhong Hewei Decoction can promote the repair and regeneration of the gastric mucosa, regulate gastrointestinal motility and gastric acid secretion, assist chronic gastritis patients in improving dyspepsia and enhancing appetite, restore gastric mucosal function and gastrointestinal balance. Additionally, it can improve gastric mucosal microcirculation to accelerate its repair, regulate gastrointestinal motility and gastric acid, mitigate gastritis damage, and improve digestion and appetite in patients with chronic gastritis ^[10].

2.2.3. Combination of herbal remedies and non-pharmacological interventions to enhance long-term management effects

The long-term management of FD requires a combination of lifestyle adjustments. In the integrated traditional Chinese and Western medicine model, herbal remedies can work synergistically with non-pharmacological approaches such as acupuncture and psychological interventions. For instance, in FD patients with comorbid anxiety and depression, combining “liver-soothing and depression-relieving herbs with psychological counseling” alongside acupuncture (targeting Neiguan, Zusanli, and Taichong acupoints) can improve both mood and gastrointestinal function through the dual pathways of “herbal regulation of the central nervous system and acupuncture stimulation of acupoint signals” ^[11]. Additionally, for elderly FD patients, herbal remedies (such as spleen-strengthening and stomach-nourishing formulas) combined with dietary guidance (e.g., eating smaller, more frequent meals and avoiding cold, raw, and greasy foods) can enhance gastrointestinal digestive function and reduce medication dependence.

3. Evidence-based medicine support for herbal remedies in integrated traditional Chinese and Western medicine treatment of FD

3.1. Evidence grading and core conclusions

According to the internationally recognized GRADE evidence grading system, the current evidence-based support

for herbal remedies in integrated traditional Chinese and Western medicine treatment of FD can be classified into high, moderate, and low levels, with significant differences in evidence strength across different syndrome types and application models.

3.1.1. High-level evidence

High-level evidence primarily focuses on the synergistic use of herbal remedies for liver-stomach disharmony syndrome and spleen-stomach deficiency-cold syndrome with PPIs or prokinetic drugs. Based on the results of multiple systematic reviews and meta-analyses, such combined treatment regimens significantly outperform monotherapy with Western medicine in terms of symptom relief rate, duration of therapeutic effect, and safety^[12,13].

The characteristics of this level of evidence include adequate sample sizes, well-designed studies (mostly multicenter, randomized controlled trials), consistent results, and low risk of bias, providing reliable evidence support for clinical application.

3.1.2. Moderate-level evidence

Moderate-level evidence primarily pertains to the synergistic use of herbal remedies in conjunction with *Helicobacter pylori* eradication therapy, as well as the combined application of herbal remedies for spleen-stomach damp-heat syndrome and food stagnation syndrome with Western medications. The core conclusion drawn from such evidence is that herbal remedies can significantly reduce the persistence rate of FD symptoms following *Helicobacter pylori* eradication while enhancing the tolerability of eradication therapy^[14].

However, due to relatively small sample sizes in some studies and geographical limitations (mostly single-region studies), the strength of this evidence is slightly lower than that of high-level evidence. For spleen-stomach damp-heat syndrome and food stagnation syndrome, owing to their relatively low clinical incidence, there are fewer relevant studies. Although existing research indicates that combined treatment approaches outperform Western medicine alone, more large-sample studies are needed to verify the stability and reliability of these results.

3.1.3. Low-level evidence

Low-level evidence primarily involves the synergistic use of herbal remedies with non-pharmacological interventions, as well as research on the mechanisms of action of herbal remedies. The limitations of such evidence are mainly reflected in the fact that most studies are single-center and small-sample designs, lacking placebo control or blinding, resulting in a high risk of bias. Mechanism studies are mostly *in vitro* or animal experiments, lacking human clinical trial data, making it difficult to directly translate into clinical recommendations^[15]. Although existing evidence suggests that herbal remedies can enhance the effects of non-pharmacological interventions, the reliability and repeatability of these conclusions still require further validation.

3.1.4. Factors influencing the quality of evidence-based evidence

Currently, the evidence-based evidence for the use of herbal remedies in integrated traditional Chinese and Western medicine treatment of FD exhibits “uneven overall quality”, primarily influenced by three factors: Firstly, there is a lack of uniformity in syndrome differentiation criteria and efficacy evaluation systems. Different studies have varying diagnostic criteria for FD syndromes in traditional Chinese medicine, symptom scoring thresholds, and lack standardized efficacy evaluation indicators, making it difficult to conduct cross-sectional comparisons and meta-analyses of research results. Secondly, there are flaws in research design. Some randomized controlled

trials (RCTs) do not employ strict random sequence generation or allocation concealment methods, lack placebo controls, and generally have short follow-up periods, making it difficult to comprehensively evaluate long-term efficacy and safety. Thirdly, there is a lack of quality control for herbal medicines. Variations in the origin, processing methods, dosage, and extraction techniques of the same herb across different studies lead to unstable content of active ingredients in herbal medicines, affecting the reproducibility and reliability of their therapeutic effects.

4. Conclusion and prospect

This review systematically reviews the current application status and evidence-based evidence of herbal medicines in the integrated traditional Chinese and Western medicine treatment of FD. The results indicate that classical formulas corresponding to liver-stomach disharmony syndrome and spleen-stomach deficiency-cold syndrome demonstrate advantages in “enhancing efficacy, reducing adverse reactions, and lowering recurrence rates” when combined with Western symptomatic medications or *Helicobacter pylori* eradication therapy, supported by high-level evidence-based evidence. However, current applications and research still face issues such as inconsistent syndrome differentiation criteria, flaws in research design, lack of quality control for herbal medicines, and lagging mechanism research. In the future, the development direction of herbal medicines in the integrated treatment of FD with traditional Chinese and Western medicine should focus on three aspects: First, clinical standardization, achieving “precise syndrome differentiation and standardized medication” through unified syndrome differentiation criteria and physician training; second, high-quality research, conducting multi-center large-sample RCTs and long-term safety studies to enhance international recognition of evidence; and third, in-depth mechanism exploration, utilizing multi-omics technologies to analyze the synergistic mechanisms of herbal medicines, promoting the transition from “empirical medicine” to “evidence-based medicine + precision medicine”. With the resolution of these issues, herbal medicines will play a greater role in the integrated treatment of FD with traditional Chinese and Western medicine, providing safer and more effective treatment options for patients while advancing the discipline of integrated traditional Chinese and Western medicine gastroenterology.

Disclosure statement

The author declares no conflict of interest.

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Mediating Effect of Medical Coping Styles in Patients with Chronic Pain between Pain Degree and Pain Catastrophe

Hui Qiang¹, Yan Hua^{2*}

¹Department of Nursing, School of Medicine, Shaanxi International Business College, Xianyang 712046, Shaanxi, China

²Department of Humanistic Nursing, Air Force Military Medical University, Xi'an 710032, Shaanxi, China

*Corresponding author: Yan Hua, 89439725@qq.com

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Abstract: *Objective:* To explore the relationship between pain degree and pain catastrophe and medical coping mode in patients with chronic pain. *Methods:* A visual analogue score scale, medical coping style questionnaire and pain catastrophe scale were used to survey 200 patients in the pain department. *Results:* The average scores of pain degree of patients with chronic pain were (5.97 ± 2.29), the average score of the total score of the Pain Catastrophe Scale was (21.21 ± 11.56), and the average scores of facing, avoidance and surrender in the Medical Response Style Questionnaire were (17.93 ± 3.4), (16.82 ± 2.4), and (8.87 ± 2.83), respectively. Pain degree was positively correlated with the yield dimension in pain catastrophe and medical coping ($p < 0.05$). The yield dimension of medical coping was positively correlated with pain catastrophe ($p < 0.05$). Medical coping methods played a partial mediating role between pain degree and pain catastrophe, and the mediating effect accounted for 21.59% of the total effect. *Conclusion:* The pain level of chronic pain patients can affect the level of pain catastrophe through medical coping, and clinical medical staff should guide patients to adopt positive coping methods to promote their healthy recovery.

Keywords: Chronic pain; Degree of pain; Medical responses; Catastrophic pain; Mediating effects

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1. Introduction

Pain, recognized as the fifth vital sign, not only leads to physical functional impairments in patients but also increases their psychological stress, resulting in a series of psychological issues such as anxiety and depression^[1]. Chronic pain, however, prolongs the negative effects of pain on patients, exacerbating and catastrophizing the physical and psychological problems caused by pain. According to relevant statistics, Chronic pain affects 20% of the global population, with such patients experiencing more severe physical and psychological issues compared to those with acute pain^[2,3]. Currently, clinical interventions such as physical therapy, pharmacological treatment,

and psychotherapy are employed to alleviate pain and reduce pain catastrophizing levels, yet their effectiveness remains limited. However, modifying patients' coping strategies for pain offers a new avenue for reducing pain catastrophizing. In terms of pain coping strategies, negative coping is more likely to exacerbate physical and mental health issues in patients compared to positive coping ^[4]. Poor coping strategies for chronic pain can lead to pain catastrophizing, yet domestic discussions on this issue remain scarce, and the argument that pain intensity can influence pain catastrophizing through medical coping styles is still unclear ^[5]. Based on this, this study focuses on the characteristics of clinical patients with chronic pain, clarifies the primary medical coping styles of current chronic pain patients, and their effects on the relationship between pain intensity and pain catastrophizing, in order to provide a theoretical basis for future clinical practice.

2. Objects and methods

2.1. Objects

A convenience sampling method was employed to collect data from patients visiting the Pain Department of a tertiary-grade A hospital in Xi'an from January 2023 to June 2023.

2.1.1. Inclusion criteria

Meeting the diagnostic criteria for chronic pain with a pain state persisting for over three months; aged 18 years or above; possessing certain cognitive reading and communication abilities; informed consent from both patients and their families.

2.1.2. Exclusion criteria

Critically ill patients; patients with mental disorders or other major life-threatening diseases; those who withdrew from the survey midway.

2.2. Sample size

According to Kendall's sample size estimation method, the sample size should be 5 to 10 times the number of variable items ^[6]. This study included 34 items in total (1 item from the Visual Analog Scale, 20 items from the Medical Coping Modes Questionnaire, and 13 items from the Pain Catastrophizing Scale, totaling 34 items). Taking 5 times the number of items and considering a 10% non-response rate, the minimum calculated sample size was 187 cases, with a final sample size of 200 cases included in this study. This study complies with the requirements of the Declaration of Helsinki.

2.3. Survey methods

All the investigators responsible for this survey underwent unified training before entering the departments to conduct the investigation. The survey was conducted in the form of anonymous face-to-face questionnaires to ensure that the respondents were informed and consented to participate voluntarily in this study. The first page of the questionnaire included an informed consent form, the purpose of the survey, and instructions. The respondents completed the survey under the guidance of the investigators. All questionnaires were distributed and collected on site. A total of 211 questionnaires were distributed, and 200 valid questionnaires were collected, resulting in a response rate of 94.7%.

2.4. Survey tools

- (1) A general information questionnaire was designed by the researchers themselves, covering age, gender, marital status, educational level, occupation, payment method, place of residence, cause of pain, and duration of pain.
- (2) The Visual Analog Scale (VAS) is the most commonly used single-dimensional pain intensity measurement and assessment tool, widely applied in clinical settings. The scale consists of 10 graduations divided into five levels: “0” indicates no pain, “1–3” indicates mild pain, “4–6” indicates moderate pain, “7–9” indicates severe pain, and “10” indicates excruciating pain. Patients select the appropriate graduation based on their specific feelings to indicate their current level of pain ^[7].
- (3) The Medical Coping Modes Questionnaire (MCMQ) was developed by Feifel and translated and adapted into Chinese by Shen Xiaohong and Jiang Qianjin ^[8]. It consists of three dimensions: confrontation (8 items, maximum score of 20), avoidance (7 items, maximum score of 25), and resignation (5 items, maximum score of 11), totaling 20 items. Each item is scored on a Likert 4-point scale. Higher scores indicate a greater tendency to use that coping style. The reliability coefficients for each dimension of the scale are 0.64, 0.85, and 0.67, respectively.
- (4) The Pain Catastrophizing Scale (PCS) was developed by psychologist Sullivan M ^[9]. It is concise and easy to administer, consisting of three dimensions: helplessness (H, 6 items), magnification (M, 3 items), and rumination (R, 4 items), totaling 13 items. Each dimension is scored on a Likert 5-point scale. The overall internal consistency of the scale is 0.94, and the reliability coefficients for each dimension are 0.82, 0.8, and 0.79, respectively.

2.5. Statistical analysis

The original data were entered by two individuals using EpiData 3.2. Statistical analysis was performed using SPSS 26.0. For categorical data, frequencies and percentages were used for representation, while for continuous data, the mean \pm standard deviation ($\bar{x} \pm s$) was utilized. Correlation analysis was conducted using Pearson correlation analysis for data conforming to a normal distribution. Stepwise linear regression was employed to detect the mediating effect of medical coping styles between pain intensity and pain catastrophizing. The structural equation model was established and the mediating effect was validated using AMOS 24.0 software. A statistically significant difference was considered when $p < 0.05$.

3. Results

3.1. General information

The specific content is shown in **Table 1**.

Table 1. General information of patients

Category	Number (n)	Percentage (%)
Age		
18—60	129	64.5
≥ 61	71	35.5
Gender		
Male	118	59.3

Table 1 (Continued)

Category	Number (n)	Percentage (%)
Female	81	40.7
Marital status		
Unmarried	19	9.5
Married	160	80.0
Divorced	3	1.5
Widowed	18	9.0
Education level		
Primary school or below	23	11.5
Junior high school	71	35.5
High school or technical secondary school	40	20.0
College	23	11.5
Bachelor's degree or above	43	21.5
Occupation		
Employee	15	7.5
Medical staff	20	10.0
Worker	19	9.5
Farmer	69	34.5
Self-Employed	19	9.5
Retired	35	17.5
Other	23	11.5
Payment method		
Public expense	12	6.0
Health insurance	133	66.8
Out-of-pocket	54	27.1
Residence		
Urban	89	44.5
County/Town	31	15.5
Rural	80	40.0
Cause of pain		
Bone/Joint/Spinal pain	121	61.5
Cancer pain	21	10.5
Neuropathic pain	10	5.0
Thrombotic pain	13	6.5
Liver cirrhosis pain	5	2.5
Other	28	14.0

Table 1 (Continued)

Category	Number (n)	Percentage (%)
Duration of pain		
< 1 year	49	24.5
1–5 years	126	63.0
6–10 years	19	9.5
> 10 years	6	3.0

3.2. Scores for pain, medical coping styles, and pain catastrophizing in this group of patients

The visual analog scale score for pain among the study subjects was (5.79 ± 2.29). Among them, the pain scores were as follows: 1–3 points (mild) in 27 patients (13.5%), 4–6 points (moderate) in 103 patients (51.5%), 7–9 points (severe) in 49 patients (24.5%), and 10 points (excruciating) in 21 patients (10.5%). The score for medical coping styles was (45.54 ± 5.77), with scores for each dimension as follows: confrontation (17.93 ± 3.4), avoidance (16.82 ± 2.4), and resignation (8.87 ± 2.83). The total score for pain catastrophizing was (21.21 ± 11.56), with scores for each dimension as follows: helplessness (8.86 ± 5.47), magnification (4.83 ± 3.10), and rumination (7.54 ± 3.97).

3.3. Correlation analysis of pain scores, medical coping styles, and pain catastrophizing in patients with chronic pain

Pairwise analysis of pain scores, medical coping styles, and pain catastrophizing revealed that pain intensity was significantly correlated with the confrontation and resignation dimensions of the Medical Coping Modes Questionnaire (MCMQ) and Pain Catastrophizing Scale (PCS) ($p < 0.05$), demonstrating a significant positive predictive effect. See **Table 2**.

Table 2. Correlation analysis of pain intensity, medical coping styles, and pain catastrophizing in patients with chronic pain (n = 200, r)

Category	Pain catastrophizing	Helplessness	Magnification	Rumination	Medical coping modes	Confrontation	Avoidance	Resignation
Pain catastrophizing	1	-	-	-	-	-	-	-
Helplessness	0.945 ^b	1	-	-	-	-	-	-
Magnification	0.908 ^b	0.804 ^b	1	-	-	-	-	-
Rumination	0.894 ^b	0.737 ^b	0.752 ^b	1	-	-	-	-
Medical coping modes	0.382 ^b	0.381 ^b	0.371 ^b	0.295 ^b	1	-	-	-
Confrontation	0.161 ^a	0.157 ^a	0.154 ^a	0.140 ^a	0.766 ^b	1	-	-
Avoidance	0.094	0.084	0.094	0.076	0.623 ^b	0.290 ^b	1	-
Resignation	0.506 ^b	0.516 ^b	0.493 ^b	0.369 ^b	0.589 ^b	0.115	0.073	1
Pain score	0.374 ^b	0.333 ^b	0.328 ^b	0.381 ^b	0.226 ^b	0.242 ^b	0.030	0.145 ^a

Note: ^a $p < 0.05$, ^b $p < 0.01$, “-” indicates repeated data.

3.4. Analysis of the mediating effect of medical coping styles on the relationship between pain scores and pain catastrophizing in patients with chronic pain

The dimensions of confrontation and surrender in the medical coping styles of patients with chronic pain were correlated with pain scores and pain catastrophizing, meeting the prerequisites for a mediating effect. The avoidance dimension in medical coping styles was not correlated with pain intensity or the dimensions of pain catastrophizing, and therefore was not included in the analysis of mediating effects. See **Table 3** for details.

Table 3. Analysis of the mediating effect of medical coping styles (confrontation, surrender) on the relationship between pain scores and pain catastrophizing in patients with chronic pain

Step	Dependent variable	Independent variable	β	SE	F	t	R ²	Adjusted R ²
Step 1	Pain catastrophizing	Pain score	0.37	2.134	32.133	5.67 ^b	0.140	0.135
Step 2	Confrontation	Pain score	0.24	0.102	12.333	3.51 ^a	0.059	0.054
	Resignation	Pain score	0.15	0.087	4.230	2.02 ^a	0.021	0.016
Step 3	Pain catastrophizing	Pain score	0.36	0.342	16.684	5.24 ^b	0.145	0.136
		Confrontation	0.07	0.231		1.10		
	Pain catastrophizing	Pain score	0.31	0.293	52.641	5.28 ^b	0.348	0.342
		Resignation	0.46	0.237		7.94 ^b		

Note: ^a $p < 0.05$, ^b $p < 0.001$.

3.5. Verification of the mediating effect of medical coping styles on the relationship between pain intensity and pain catastrophizing in patients with chronic pain

Using AMOS 24.0 software, a structural equation model was constructed with pain catastrophizing as the dependent variable, surrender in medical coping styles as the mediating variable, and pain intensity as the independent variable, as shown in **Figure 1**. The maximum likelihood method was used for model fitting, and the model was reasonably revised based on the model's modification indices. The revised model fitting results showed that the relative chi-square (CMIF/DF) = 0.639, goodness-of-fit index (GFI) = 0.996, comparative fit index (CFI) = 1.000, adjusted goodness-of-fit index (AGFI) = 0.981, incremental fit index (IFI) = 1.002, and root mean square error of approximation (RMSEA) = 0.000. All fitting indices were within acceptable ranges, indicating a good model fit. The mediating effect was tested using the Bootstrap method. The results revealed that the 95% confidence intervals for both the direct and indirect effects of pain intensity on pain catastrophizing did not include 0. This indicates that surrender plays a partially mediating role between pain intensity and pain catastrophizing, confirming the validity of the model. Consistent with the regression analysis results, the point estimate of the mediating effect was 0.016, accounting for 4% of the total effect, as shown in **Table 4**.

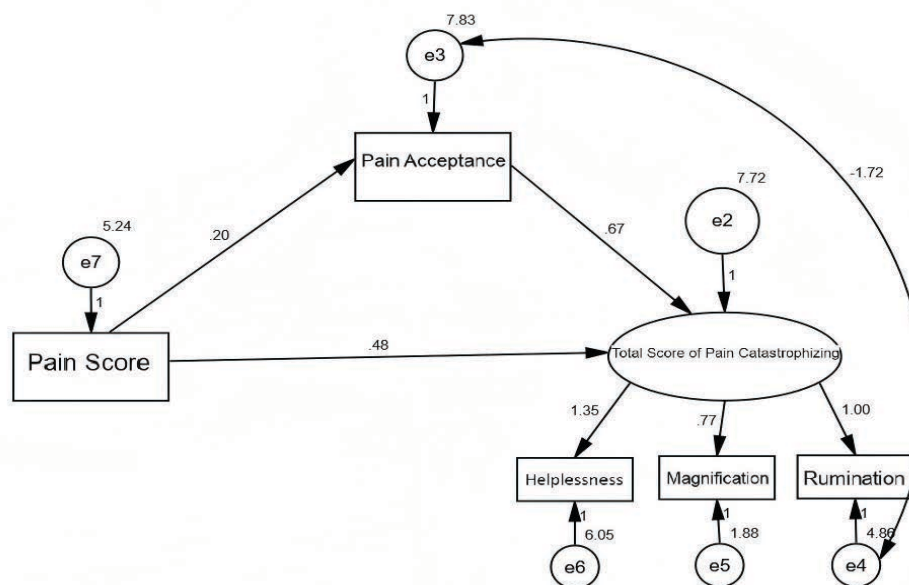


Figure 1. Structural equation model (standardized) of the mediating effect of medical coping styles on the relationship between pain intensity and pain catastrophizing in patients with chronic pain.

Table 4. Bootstrap analysis of path effects

Effect type	Effect value	Standard error	<i>p</i> -value	95% CI	Effect proportion
Direct effect	0.306	0.094	< 0.01	0.306–0.674	76.11%
Indirect effect	0.016	0.062	< 0.01	0.016–0.256	4%
Total effect	0.402	0.110	< 0.01	0.402–0.841	-

4. Discussion

4.1. Analysis of pain severity, medical coping styles, and pain catastrophizing in patients with chronic pain

The results of this study indicate that patients scored (5.79 ± 2.29) on the pain scale, indicating a relatively high level of pain. More than half of the patients experienced moderate to severe pain (76.0%), a finding similar to that of Ren Xiaoran's survey^[10]. This similarity may be related to the causes of pain, as most patients in this study suffered from bone, joint, and lumbar-shoulder-neck pain (61.5%). Such types of pain are significant contributors to “years lived with disability” (YLDs) globally^[11]. They are prone to recurrent episodes, can trigger neuropathic pain, produce radiating pain, and manifest as intense pain during flare-ups, causing indescribable suffering to patients and heightening their perception of pain^[3]. Furthermore, chronic pain has long-term adverse effects on patients' lifestyles, physical activities, and psychological well-being, reducing their quality of life, exacerbating the negative impacts of pain, and intensifying their original pain perception^[12]. Therefore, most patients with chronic shoulder and neck pain experience severe pain, warranting further exploration of comfortable nursing methods to mitigate the negative effects of pain on patients.

In this study, patients scored (17.93 ± 3.40) on the confrontation dimension of the Medical Coping Modes Questionnaire (MCMQ), (16.82 ± 2.40) on the avoidance dimension, and (8.87 ± 2.83) on the resignation

dimension. These results are similar to those of Li Hongmei's study on patients with cancer pain^[13]. The primary coping styles in this study were confrontation and resignation. The reason for this may be that 61.5% of the patients in this study suffered from shoulder, neck, lumbar, back, and joint pain. Although such pain has an acute onset and is intense, advances in medical technology have led to diverse and effective treatment methods for this type of chronic pain. Consequently, symptoms of chronic shoulder, neck, lumbar, back, and joint pain resolve quickly, with short acute pain periods. Therefore, patients have confidence in treatment and can actively confront acute pain episodes of their chronic pain conditions. During the course of disease treatment, patients are required to maintain strict bed rest and immobility, resulting in limitations to their daily lives and a sense of helplessness and resignation^[14]. Consequently, they are prone to feelings of resignation, and the accumulation of long-term negative emotions can lead to the development of negative psychological states such as depression and giving up in response to the disease. This suggests that healthcare professionals should pay closer attention to changes in the emotions and coping mechanisms of patients during the acute phase of chronic pain, strengthening both physical and psychological management for patients and providing timely assistance.

The results of this study indicate that the pain catastrophizing score for patients in this group was (21.21 \pm 11.56), which is similar to the findings of Xiang Wei's study on orthopedic pain patients and higher than the survey results of Liu Jia's study on patients after total knee arthroplasty^[15,16]. The reason for this discrepancy is that the types of pain included in this study were diverse, encompassing severe pain conditions such as cancer pain and trigeminal neuralgia, as well as recurrent pain in areas such as the lower back, neck, and joints. Severe pain is the primary cause of erroneous pain perception, leading to a high incidence of pain catastrophizing (52.3%)^[17]. Additionally, pain in the shoulders, neck, and lower back, although not as severe in nature, significantly impacts daily life and, in severe cases, can have long-term effects on physical function, reducing patients' quality of life and leading to excessive rumination and worry about pain.

4.2. Correlation analysis of pain intensity, medical coping styles, and pain catastrophizing

This study reveals that there is a correlation between the pain intensity of patients in this group, their medical coping styles, and pain catastrophizing. Pain intensity is positively correlated with pain catastrophizing ($r = 0.37$, $p < 0.01$), a finding similar to that of Morlion's study, indicating that the higher the pain intensity, the higher the level of pain catastrophizing^[18]. The more intense the pain, the greater the psychosocial negative impact on patients, leading to manifestations of pain catastrophizing. The results of this study also show a positive correlation between pain intensity and medical coping styles ($r = 0.23$, $p < 0.01$), consistent with the findings of Zhang Shan's study^[19]. The higher the pain intensity, the worse the patient's treatment compliance, the longer the treatment duration, and the more likely the patient is to adopt negative coping strategies. In this group of patients, medical coping styles were positively correlated with pain catastrophizing ($r = 0.38$, $p < 0.01$). This is because patients who adopt negative coping strategies when dealing with chronic pain are more prone to experiencing emotions such as irritability and helplessness, thereby increasing their levels of pain catastrophizing. Meanwhile, some foreign scholars have proposed the Fear-Avoidance Model, which suggests that when patients adopt negative coping strategies, it intensifies their experience of disease-related suffering, exacerbates their perception of pain, and subsequently leads to pain catastrophizing emotions^[20]. Therefore, by altering patients' negative attitudes towards pain, the impact of pain severity on emotional distress can be reduced^[21].

4.3. Medical coping styles partially mediate the relationship between pain severity and pain catastrophizing

The mediation effect results of this study revealed that pain severity has a positive predictive effect on pain catastrophizing. The level of pain severity can directly predict the degree of pain catastrophizing in patients. Medical coping styles partially mediate the relationship between pain severity and pain catastrophizing. Adopting correct coping strategies can alter catastrophic thinking. The reasons are as follows: Firstly, pain severity can directly influence pain catastrophizing. When pain persists or intensifies, patients with pain are prone to experiencing negative emotions such as anxiety and irritability, leading to an increase in pain catastrophizing levels ^[22]. Therefore, reducing the pain severity in patients with chronic pain can decrease their levels of pain catastrophizing. Previous studies have shown that methods such as systematic pain nursing management, three-step seven-method massage, and narrative medicine can reduce pain severity. Secondly, pain severity can also indirectly affect pain catastrophizing by influencing medical coping styles. When pain severity increases, patients are more likely to adopt negative coping strategies such as avoidance and submission, which increase the psychological burden of pain-related diseases, amplifying patients' feelings of helplessness and anxiety towards disease pain, thereby elevating pain catastrophizing levels ^[23]. Conversely, when pain severity is low, patients adopt positive coping strategies, leading to a decrease in pain catastrophizing levels. When pain cannot be alleviated, patients may resort to negative coping strategies and continuously focus on the pain ^[24]. Adopting negative strategies such as submission reflects the behavioral stress response of chronic pain patients to disease catastrophizing perception, while also indicating a certain degree of pain catastrophizing in patients.

A six-month longitudinal eye-tracking study revealed that shorter attention spans on pain were associated with more positive coping strategies ^[25]. Healthcare professionals should promptly address patients' negative emotional cognitions and take timely measures to help reduce their levels of pain catastrophizing, thereby improving their quality of life. This can be achieved by formulating reasonable and effective pain catastrophizing management strategies, employing cognitive-behavioral therapy to alter patients' negative perceptions of pain, fostering a correct, positive, and uplifting mindset, enhancing their sense of life's meaning, and reducing pain catastrophizing levels ^[26–28].

5. Limitations

This study utilized convenience sampling to select research subjects, resulting in a relatively small sample size and potential selection bias. Subsequent research will expand the scope of sample collection and adopt a multi-center approach for further validation. Additionally, this study solely examined the relationships between medical coping styles, pain intensity, and pain catastrophizing in patients experiencing pain, with limited exploration of other influencing factors. Future research will continue to delve deeper, conducting targeted intervention studies on specific diseases to provide more empirical data supporting the mediating effect of medical coping styles on the relationship between pain intensity and pain catastrophizing.

6. Conclusion

In conclusion, the pain intensity in chronic pain patients can influence their level of pain catastrophizing through medical coping styles. Therefore, healthcare professionals should guide patients to adopt more positive coping

strategies to promote recovery.

Disclosure statement

The authors declare no conflict of interest.

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