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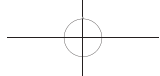
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Journal of Clinical and Nursing Research

Focus and Scope

Journal of Clinical and Nursing Research (JCNr) is an international, peer reviewed and open access journal that seeks to promote the development and exchange of knowledge which is directly relevant to all clinical and nursing research and practice. Articles which explore the meaning, prevention, treatment, outcome and impact of a high standard clinical and nursing practice and discipline are encouraged to be submitted as original article, review, case report, short communication and letters.

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Table of Contents

- 1 A Case Study on the Treatment of Obesity-type Polycystic Ovary Syndrome with Zhuang Medicine Mao Xia Yin**
Xiaolin Zhang, Huilu Cao, Zheng Huang, Guanfeng Lu, Gang Fang

- 8 Role of Ferroptosis in Cerebral Ischemia-Reperfusion Injury**
Jianmeng Lv, Tao Wang, Yajuan Pan, Juan Liu, Zheng Han, Xuan Wang

- 19 Efficacy and Safety of Miao Medicine Jinlong Zhi Xie Fang Enema in the Treatment of Ulcerative Colitis (Large Intestine Damp-Heat Syndrome): A Randomized Controlled Trial**
Chongwu Che, Yingxiang Yang, Liuying Cao, Qin Yang, Linmin Teng, Wang Long

- 28 Application of Responsibility-based Holistic Nursing in Elderly Patients with Severe Pneumonia**
Ying Cui

- 34 Research Status and Progress of Related Indicators for Early Diagnosis and Prognosis Evaluation of Autoimmune Encephalitis**
Dandan Shi

- 40 Analysis of the Effect of Comprehensive Nursing on the Psychological State of Patients with Pulmonary Micro-nodules**
Cuifang Liu

- 47 Application of the External Treatment Method of Traditional Chinese Medicine in the Elderly Diabetic High-Risk Foot Based on the Theory of “Preventive Treatment of Disease”**
Meilan Li, Tongping Gu, Jie Ji, Lifeng Ma

- 60 Efficacy Study of Molecular Diagnostic Techniques for Monitoring Tuberculosis Relapse**
Huai Huang

- 67 Influence of Personalized Nursing on Improving the Satisfaction of Emergency Pediatric Nursing**
Lihua Huang

- 74 Research Progress on Unplanned Readmission of Enterostomy Patients**
Jingjing Wang, Long Zhang
- 79 Role of Tisp40/Smad2 Protein in High Glucose-induced Renal Interstitial Fibrosis**
Yapeng Wang, Xueyi Wang, Ruixiao Wang
- 89 Research on Predicting the Nephrotoxicity Mechanism of Lianqiao-4 Based on Network Pharmacology and Molecular Docking**
Qingchun Bai, Gala Bai, Huan Wang
- 100 Study on the Influence of Nutrition Intervention on Children's Health during Follow-Up of High-Risk Infants**
Bei Li
- 105 Multidimensional Strategies to Prevent and Control Risk Factors in Patients with Nonvalvular Atrial Fibrillation: Mechanistic Explorations and Advances in Clinical Practice**
Li Yang , Dongming Xiang , Liling Zhong, Yuling Zou
- 114 A Comprehensive Review of the Phenomenon of Nipple Confusion and Coping Strategies**
Chong Yang, Jie Cui, Yongtao Kang, Longhai Song
- 121 The Prevalence and Influencing Factors of Posttraumatic Stress Disorder in Patients with Myocardial Infarction: A Systematic Review and Meta-analysis**
Simin Li, Xiaoyue Wang, Fengyin Zhang, Qinghua Wen, Juan Li
- 136 Scope of Nursing Practice as Perceived by Nurses Working in China: A Multicenter Cross-Sectional Survey**
Ningning Li, Ziwen Wang
- 145 Perioperative Nursing Gamification Course Design Based on Immersive Virtual Reality Technology Under the Concept of Medical and Educational Collaboration**
Xiwei Xiao, Yan Xiao
- 152 Research on the Impact of Conception Vessel Dredging Therapy Based on the Theory of Shifting Essence and Changing Qi in Inner Canon of Huangdi on Physical and Mental Health**
Yizhou Shen, Fengrun Liu
- 159 The Impact of Continuous Care on Independent Living Skills and Psychosocial Adaptation of Patients with Hypertensive Intracerebral Hemorrhage After Discharge**
Xiaomin Sun

- 166 Study on the Effect of Drug Therapy Combined with Psychological Intervention on Adolescent Patients with Depression**
Yue Wang
- 173 Effects of Standardized Bronchoscopic Interventional Therapy on Efficacy and Degree of Stenosis in Patients with Airway Stenosis**
Jiahe Wang, Wei Ji, Xuehui Mou, Hongjuan Lyu, Chen Chen
- 180 Evaluation of the Effectiveness and Satisfaction of Nurses' Full Humanistic Care in the Treatment and Nursing of Pediatric Nebulization**
Lijun He, Huiqing Wen, Ting He
- 187 Clinical Advances in Esophageal Anti-reflux Stents**
Yongqi Dang, Fende Liu, Aiai Yan, Caifeng Xu, Xu Yang, Yu Cai
- 194 Clinical Observation on the Efficacy of TCM Syndrome Differentiation in Treating Gouty Nephropathy**
Bin Wang, Shu Li
- 201 Clinical Study of Autologous Skull Transplantation for the Treatment of Skull Defects**
Haoran Zhang , Junfeng Zhang , Wanyin Ren, Yao Qian, Jian Xie
- 207 Application Analysis of Perioperative Comprehensive Nursing Management Intervention in Patients Undergoing Breast Surgery in Oncology Surgery**
Mengmeng Qi, Minxiang Wei
- 214 Analysis of the Therapeutic Effect of ZhenGan XiFeng Decoction in the Acute Phase of Hypertensive Intracerebral Hemorrhage**
Yanguo Hua, Yinfeng Zhang
- 221 Evaluating the Application of the PDCA Cycle Model in Nursing Management of the Hospital Disinfection Supply Room**
Bo Zhang
- 228 The Application Effect of Operating Room Nursing for Cerebral Hemangioma Combined with Preventive Measures for Moderate and Hypothermia**
Jiabin Zhou
- 234 Clinical Value of Quantitative Scoring Nursing Intervention for Adverse Reactions in PD-1 Monoclonal Antibody Treatment**
Na Jin, Liying Du, Qiaofeng Zhan, Fang Pang, Fanping Liu

- 245 Observation on the Effect of Internal Limiting Membrane Flipping and Covering Technique in the Treatment of High Myopic Macular Hole**
Zhiwei Li
- 252 Pharmacokinetics and Safety of Chiglitazar in Patients with Renal Impairment: A Multicenter, Open-label, Parallel-controlled Phase I Clinical Trial**
Jinjie Yuan, Jia Yu, Jiwen Sun, Huan Wang, Guoyuan Lu, Wengang Sha, Xiaodong Yang, Haixiang Cao, Yu Chen, Desi Pan, Xinhao Wang, Hua Zhang
- 264 Analysis of the Application Effect of Systematic Nursing Intervention in Patients with Knee Osteoarthritis**
Wei Zheng
- 271 Application of Lung Ultrasound Combined with Multi-organ Evaluation in Assessing the Risk of Weaning from Mechanical Ventilation in Severe Patients**
Xu Li, Yang Yuan
- 277 A Qualitative Study on the Influencing Factors of Training Transfer for Oral Specialist Nurses**
Jieling Zhan, Liying Sun, Liling Liu, Yan Zhang, Caiying Liang, Yarong Hou
- 284 Application of Transcranial Magnetic Stimulation Technology in the Management of Motor Symptoms of Parkinson's Disease**
Chengming Wang
- 291 The Effectiveness of Mirena Intrauterine Device in the Treatment of Adenomyosis**
Jianfen Bu, Fang Li, Liping Shen
- 297 Application of Bundle Nursing Strategy in the Maintenance of Difficult Blood Vessels for Long-term Hemodialysis Patients**
Yelin Wang, Liangmei Fei
- 304 Effect of Surgical Combination with Traditional Chinese Medicine Dialectical Therapy in Three Phases on Intertrochanteric Fracture of the Femur and Its Impact on Fracture Healing Time**
Wei Qiu, Yongqing Liu, Qizhan Duan, Jia Chai
- 311 Observation on the Clinical Efficacy of Moist Burn Ointment Combined with Rotating Moxibustion in the Treatment of Pressure Ulcers with Deficiency of Qi and Blood**
Song Li, Dingxing Zhou
- 319 Application and Challenges of Artificial Intelligence in the Care of Stroke Patients**
Shiyuan Feng, Shiyu Song, Tingting He

- 325 Study on the Application and Value of Multi-slice Spiral CT in Acute Appendicitis**
Zheng Zhang
- 332 Nursing Care after Cardiac Surgery for Termination of Pregnancy in Five Pregnant Women with Co-morbid Cardiac Disease**
Yaping Lu
- 338 Dental Caries Among Preschool Children and the Impact of Behavioral Intervention on Caries Rate**
Jianan Zhu
- 344 Effects of Nebulized α -Interferon on Immune Function in Elderly Patients with Respiratory Tract Infection**
Jianqiang Yang
- 350 Effects of Acupoint Catgut Embedding Combined with Auricular Point Pressing with Beans on Self-Efficacy of Symptom Management and Quality of Life of Patients with Nonalcoholic Steatohepatitis of Liver Depression and Spleen Deficiency Type**
Jiamin Feng, Zhentong Xia, Lifan Wu, Fangyao Zhao
- 359 Subchronic and Chronic Toxicity Tests of Fuyanxiao Capsules**
Lina Han, Xi Yan, Jian Pu, Qiling Dou, Yaqi Dou
- 371 Advances in Prevention and Treatment of Alzheimer's Disease among Community-Dwelling Elderly from the Perspective of Traditional Chinese Medicine (TCM)**
Peihua Zhuang, Dongxing Wang, Shuyu Zhao, Ting Yuan
- 378 Research on the Integration of Traditional Chinese Medicine Theory into Medical Students' Clinical Internship**
Yang Zhang, Yingxiang Yang, Yuyang Wang, Liuying Cao
- 387 A Bibliometric Analysis of Research Trends in Neck Pain from 2000 to 2025**
Shiliang Xi, Heqing Tang
- 397 Patient Journey Map In Chronic Disease Management: Theory, Practice And Future**
Juan Xu, Ran Li, Songnan Yao, Qianlin Sun, Haizhen Guo

A Case Study on the Treatment of Obesity-type Polycystic Ovary Syndrome with Zhuang Medicine Mao Xia Yin

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Abstract: As an important branch of traditional medicine, Zhuang Medicine is renowned for its unique prescriptions and techniques in clinical treatment, with significant therapeutic effects and widespread popularity. This article introduces Professor Fang Gang's experience in treating obesity-type polycystic ovary syndrome (PCOS) with modified Zhuang Medicine Mao Xia Yin. Professor Fang Gang proposes that the etiology and pathogenesis of obesity-type polycystic ovary syndrome (PCOS) primarily stem from spleen deficiency, which impairs the transport of water and dampness. This dysfunction leads to the accumulation of dampness that transforms into phlegm. Over time, the stagnation of phlegm and dampness generates internal heat, resulting in the formation of "dampness toxin," "phlegm toxin," and "heat toxin." These pathological toxins obstruct the circulation of Qi and blood, causing stasis and the emergence of "stasis toxin." The buildup of these toxins ultimately blocks the three channels and two pathways, disrupting the harmony among the three Qi of heaven, earth, and man. This disharmony culminates in impaired uterine gland function. Therefore, the treatment mainly focuses on tonifying deficiency, detoxifying, and regulating Qi.

Keywords: Zhuang Medicine Mao Xia Yin; Obesity-type polycystic ovary syndrome; Case study

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1. Introduction

Polycystic ovary syndrome (PCOS) is a common gynecological endocrine and metabolic disorder characterized by abnormally elevated androgen levels, ovulatory dysfunction, and menstrual irregularities. It is often accompanied by infertility, insulin resistance, and obesity etc., which has a great impact on female reproductive health and psychological status^[1]. Western medicine treatment primarily focuses on regulating menstrual cycle, reducing androgen levels, improving insulin resistance, and promoting ovulation. While these approaches yield

rapid effects, they are limited by significant side effects and high recurrence rates ^[2]. In recent years, traditional medicine and ethnic medicine have shown unique clinical advantages in the treatment of PCOS. Professor Fang Gang has been engaged in clinical research in obstetrics and gynecology for more than ten years, and has accumulated rich experience in the diagnosis and treatment of PCOS. His application of Zhuang Medicine Mao Xia Yin has achieved remarkable therapeutic efficacy in treating obesity-type PCOS. Through a typical case analysis, this article discusses the clinical diagnosis and treatment thoughts of PCOS and the clinical application value of Zhuang Medicine Mao Xia Yin.

2. Etiology and pathogenesis of PCOS in Zhuang Medicine

Although the term “polycystic ovary syndrome (PCOS)” is not found in the ancient books of Zhuang medicine, its clinical manifestation such as oligomenorrhea, decreased menstrual flow, and amenorrhea are consistent with the category of menstrual diseases such as Yuejingluan (menstrual disorder) and Jingse (amenorrhea) in Zhuang medicine ^[3]. Meanwhile, according to the ultrasonic characteristics of the polycystic changes of the ovary, PCOS can be classified into the category of Peixibing (Baezci) ^[4]. In Zhuang medicine, the uterus is referred to as Mihuachang, which belongs to the female reproductive system ^[5]. The physiological functions of the Mihuachang (uterus) depend on the synergistic interactions among Zang-Fu organs (Dong), Qi and blood (Xue), and muscle and bone (Duonuo), as well as unobstructed flow of the three pathways (including Gudao, grain pathway; Qidao, Qi pathway; and Shuidao, water pathway), and two vital networks (including Longlu, dragon network; and Huolu, fire network). Zhuang Medicine believes that toxins and deficiencies are the root cause of all diseases ^[6]. The core pathogenesis of PCOS is the exuberance of pathogenic toxins, deficiency of healthy Qi, obstruction of three pathways and two vital networks, as well as disharmony of Qi and blood. Congenital constitutional weakness or decline in Zang-Fu organ functions in women are prone to invasion of exogenous toxins or endogenous pathogenic toxins, leading to deficiency-excess syndrome, where healthy Qi is deficient and toxins are excessive. This triggers a struggle between healthy Qi and pathogenic factors, disrupting the interaction between Qi and blood, which manifests as an imbalance of Qi and blood, obstruction of three pathways and two vital networks, ultimately leading to dysfunction of the Mihuachang. Therefore, the treatment principles should focus on detoxification, tonifying deficiency, unblocking the three pathways and two vital networks, as well as harmonizing Qi and blood ^[7].

3. Diagnosis and treatment thoughts of PCOS

Western medicine primarily focuses on oral medications in treating PCOS. While these drugs act rapidly, they have obvious side effects and high recurrence rates. Zhuang medicine emphasizes regulation of holism to address the root causes of PCOS. Meanwhile, Zhuang medicine primarily utilizes natural herbs, demonstrates high safety and achieves comprehensive therapeutic effects by regulating endocrine function, improving metabolism, and promoting ovulation through multi-target mechanisms. For patients with insulin resistance, diabetes mellitus, or hyperandrogenism, integrated Zhuang and Western medicine can be adopted to give full play to the advantages of both ^[8].

Professor Fang Gang believes that the etiology and pathogenesis of PCOS is primarily deficiency-excess in complexity. The pathogenic excess belongs to Yang syndrome, e.g., dampness toxin, stasis toxin, phlegm

toxin, and heat toxin, while the healthy Qi deficiency belongs to Yin syndrome, characterized by insufficiency of healthy Qi. Meanwhile, females are susceptible to emotional disturbances. Emotional disharmony is also a significant contributing factor in disease onset^[9]. Therefore, the treatment of PCOS with Zhuang Medicine should focus on tonifying deficiency, removing toxin, and regulating Qi.

Wan's Gynecology: Regulation of Menstruation (Wan Shi Fu Ren Ke Tiao Jing) states, "In obese women with scanty menstruation, the condition is attributed to obstruction of the meridians by phlegm-dampness." Obesity-type PCOS is mostly due to constitutional Milong (spleen) deficiency, or improper diet, lack of exercise, or imbalance between work and rest, which damages the Milong, leading to Milong dysfunction, phlegm-dampness retention, stagnated phlegm-dampness transforming into heat, endogenous dampness-phlegm-heat toxin, and obstructed Xu (Qi) and Le (Blood) forming into stasis toxin. Accumulation of toxin pathogens obstruct the three pathways and two vital networks, leading to disharmony of triple qi (heaven-earth-human) and dysfunction of Mihuachang. The accumulation of phlegm-dampness toxins in the body may manifest as obesity. The congestion of phlegm-dampness-heat toxins in the body may manifest as acne. The obstruction of phlegm or stasis toxin in the ovary may manifest as polycystic ovarian changes.

Based on Zhuang medicine theory and the etiology-pathogenesis of obesity-type PCOS, Professor Fang Gang develops Zhuang Yi Mao Xia Yin through years of clinical practice." The formula is composed of Wu Zhi Mao Tao (*Ficus Hirta Root*), Ban Xia (*Pinelliae Rhizoma*), Xiang Fu (*Cyperus Rhizoma*), Cang Zhu (*Atractylodes Rhizoma*), Bai Shao (*Paeoniae Radix Alba*), Guang Shan Zha (*Crataegus pinnatifida*), Hu Lu Cha (Bottle Gourd Tea), Ji Xue Teng (*Spatholobus suberectus*), Long Xue Jie (*Dracaena*), and has actions of tonifying Milong (spleen) deficiency and regulating Xu (Qi), dispelling phlegm and removing dampness, dredging Longlu and Huolu, as well as regulating menstruation. Administration includes decocting in water, 1 dose daily, taken warmly after breakfast and dinner, discontinued during menstruation.

In this formula, Wu Zhi Mao Tao (*Ficus Hirta Root*) and Ban Xia (*Pinelliae Rhizoma*) tonify Milong (spleen) deficiency, remove dampness-phlegm toxins, tonify Xu (Qi), and dredge water pathway, serving as the main medicinal. Xiang Fu (*Cyperus Rhizoma*) regulates Xu (Qi), dredges Longlu, eliminates stagnation, regulates menstruation and stops pain. Guang Shan Zha (*Crataegus pinnatifida*) tonifies Milong and replenishes Dong (stomach), regulates Xu, transforms turbidity and reduce blood lipid and blood sugar, dredges Longlu, and regulates Gudao. Bai Shao (*Paeoniae Radix Alba*) nourishes Le (blood) and regulates menstruation, emolliates Midie (liver) and stops pain. Cang Zhu (*Atractylodes Rhizoma*) tonifies Milong, eliminates dampness toxin, and dredges water pathway. Ji Xue Teng (*Spatholobus suberectus*) tonifies Le (blood), eliminates dampness toxin, regulates Longlu and Huolu. Hu Lu Cha (Bottle Gourd Tea) dredges grain pathway and water pathway, eliminates dampness toxin, and reduces blood lipids. Long Xue Jie (*Dracaena*) dredges Longlu, regulates Qi pathway, tonifies Mixintou (heart) and nourishes Le (blood), eliminates stasis toxin and regulates menstruation, reduces blood lipid and blood sugar; all the above serving as the assistant medicinals. This formula simultaneously addresses both deficiency and excess through tonifying deficiency, removing toxin, and regulating Qi, to achieve the effect of tonifying Milong (spleen) and regulating Xu (Qi), dispelling phlegm and removing dampness, dredging two vital networks and regulating menstruation, thus ensuring a unobstructed flow of three pathways and two vital networks, as well as harmony of triple Qi (heaven-earth-human).

4. Case study

4.1. General Information

A 35-year-old female, Ms. Jiang, first presented to the clinic on November 29, 2023, with a chief complaint of amenorrhea lasting over two months.

4.2. Menstrual and obstetric history

- (1) Menarche: Age 13
- (2) Last Menstrual Period (LMP): September 18, 2023
- (3) Cycle Length: 30–60 days
- (4) Menstruation Duration: 6–7 days
- (5) Characteristics: Scanty dark-red menstrual flow with clots; accompanied by dysmenorrhea
- (6) Marital Status: Married, sexually active, history of contraceptive use

4.3. Presenting symptoms

At present, the patient presented with excessive phlegm in the throat, fatigue, normal appetite, poor sleep with dreaminess, normal urination, and initial dry stools followed by loose stools. The tongue was enlarged with teeth marks, light in color, with a white and greasy coating. The pulse was wiry and slippery. The patient also presented with scattered facial acne, obesity, recent emotional irritability, and high work-related stress.

4.4. Anthropometric data

- (1) Height: 159 cm
- (2) Weight: 63 kg
- (3) BMI: 24.92kg/m²

4.5. Auxiliary examination

- (1) HCG: Negative
- (2) Six test items of sex hormones: FSH: 12.16mIU/mL; LH: 57.61mIU/mL; E2: 352pg/mL; P: 1.00ng/mL; T: 3.11nmol/L; PRL: 10.48ng/mL.
- (3) Gynecological ultrasound: endometrial thickness 7 mm; polycystic changes in the bilateral ovaries.

4.6. Diagnoses

- (1) Zhuang medicine diagnosis: Yuejingluan (Yin syndrome complicated with Yang syndrome)
- (2) Chinese medicine diagnosis: Menstrual disorder (Spleen deficiency with phlegm-dampness syndrome)
- (3) Western medicine diagnosis: Polycystic ovary syndrome (PCOS)

4.7. Treatment

- (1) Modified Zhuang Medicine Mao Xia Yin measurements

The formula is composed of Wu Zhi Mao Tao (*Ficus hirta* Root), 40 g; Ban Xia (*Pinelliae Rhizoma*), 12 g; Xiang Fu (*Cyperus Rhizoma*), 12 g; Cang Zhu (*Atractylodes Rhizoma*), 9 g; Bai Shao (*Paeoniae Radix Alba*), 10 g; Guang Shan Zha (*Crataegus pinnatifida*), 10 g; Hu Lu Cha (*Bottle Gourd Tea*), 10 g; Ji Xue Teng (*Spatholobus suberectus*), 9 g; Long Xue Jie (*Dracaena Resin*), 3 g; Bai Zhi (*Angelica*

dahurica Root), 9 g; He Huan Hua (*Albizia Flower*), 12 g; Zhu Fu Shen (*Poria Root Bark*), 15 g; and Ye Jiao Teng (*Polygonum multiflorum Stem*), 25 g.

(2) Administration

One dose/day, decocted in water and taken warm after breakfast and supper for 7 days.

(3) Additional therapy

Progesterone capsules during the luteal phase.

(4) Lifestyle advice

Weight loss, blood sugar control, emotional regulation, and sufficient rest.

4.8. Follow-up visitations

(1) Second visit (December 11, 2023)

Day 1 of menstruation. Sleep quality has improved compared to the previous visit. Scattered facial acne remained. The tongue was enlarged with teeth marks, light in color with white and greasy coating. The pulse was wiry and slippery. Treatment: The initial prescription was continued for 14 doses, taken after menstruation ends, but it is combined with Diane-35 treatment. The patient is instructed to control blood sugar and lose weight, regulate emotions, and ensure adequate rest.

(2) Third visit (December 31, 2023)

Weight decreased by 2 kg. The last menstrual period was on December 11, 2023. Slightly heavier flow with dark-red clots and mild dysmenorrhea. Normal appetite and sleep, normal urination and bowel movements. Facial acne has decreased. The tongue was enlarged with teeth marks, light in color, with a white coating. The pulse was wiry. The diagnosis remained unchanged. Treatment: The previous prescription was adjusted by changing the dosage of Bai Shao to 15g, Ji Xue Teng to 12g, and removing He Huan Hua, Zhu Fu Shen, and Ye Jiao Teng, 14 doses. The method of administration remained the same as before and combined with Diane-35 treatment. The patient is instructed to control blood sugar and lose weight, regulate emotions, and ensure adequate rest.

(3) Fourth visit (February 1, 2024)

Weight decreased by 2.5 kg. The last menstrual period was January 6, 2024. Normal volume, red color, no significant blood clots, no dysmenorrhea. Normal appetite and sleep, normal urination and bowel movements. No noticeable facial acne. The tongue was light in color with teeth marks and thin white coating. The pulse was wiry. The diagnosis and treatment remained unchanged. The patient is instructed to control blood sugar and lose weight, regulate emotions, and ensure adequate rest.

(4) Fifth visit (February 29, 2024)

Weight decreased by 1 kg, with the current weight being 57.5 kg and the BMI is 22.74. The last menstrual period was on February 28, 2024. Normal volume, red color, no blood clots, no dysmenorrhea. Normal appetite and sleep, normal urination and bowel movements. No noticeable facial acne. The tongue was light in color with teeth marks and thin white coating. The pulse was wiry. The diagnosis remained unchanged. The results of the six test items of sex hormones were: FSH: 5.50 mIU/mL, LH: 6.35 mIU/mL, E2: 21 pg/mL, P: 0.50 ng/mL, T: 1.08 nmol/L, PRL: 10.26 ng/mL. Treatment: The 3-month menstrual cycle therapy was completed, and Diane-35 was discontinued. The previous Zhuang medicine prescription was continued for 14 doses to consolidate the treatment. The method of administration remained the same as before.

At the six-month follow-up visit, the patient reported regular menstrual cycles with normal flow volume, color, and quality, no dysmenorrhea, and no significant changes in body weight.

5. Analysis of case study

This case involves a patient with obesity-type PCOS, which was diagnosed as Yuejingluan-Yin syndrome (Milong deficiency) complicated with Yang syndrome (dampness toxin, phlegm toxin, heat toxin, stasis toxin). At the initial visit, the patient presented with amenorrhea for over 2 months. Zhuang Medicine Mao Xia Yin was prescribed to tonify Milong (spleen) and regulate Xu (Qi), dispel phlegm and remove dampness, dredge the two vital networks (Longlu and Huolu), nourish Le (blood) and regulate menstruation, to stimulate menstrual flow. For facial acne, poor sleep, and excessive dreaming, Bai Zhi was added to reduce acne; He Huan Hua was added to relieve depression and calm the mind; Zhu Fu Shen was added to settle the heart and calm the mind, replenish Qi and invigorate spleen, as well as promote urination; Ye Jiao Teng was added to nourish the heart and calm the mind. It was combined with progesterone capsules treatment during the latter half menstrual cycle to induce menstrual flow and regulate endocrine function.

At the second visit, the menstruation arrived, sleep quality improved, yet acne persisted. Tongue and pulse patterns were the same as before, indicating incomplete resolution of phlegm and dampness. Thus, the original Zhuang medicine prescription was maintained. Elevated LH/FSH ratio and hyperandrogenism were noted. Diane-35 therapy was combined to regulate the hormones. At the third visit, based on the patient's symptoms, signs, and tongue/pulse patterns, phlegm and dampness were gradually resolved, Qi and blood were improved. The dosage of Bai Shao and Ji Xue Teng were increased to nourish blood and regulate menstruation, activate blood and resolve stasis, and stop pain. After the sleep was normal, He Huan Hua, Zhu Fu Ling, and Ye Jiao Teng were removed to simplify the formula to focus on the therapeutic efficacy. The Western medicine prescription remained unchanged. At the fourth visit, the body weight was reduced, and the symptoms were improved, indicating further resolution of phlegm-dampness and progressive harmonization of Qi and blood. The third-visit Zhuang medicine and Western medicine prescriptions were continued. At the fifth visit, the patient exhibited resolved phlegm-dampness and restored Qi-blood harmony based on symptoms, signs, and tongue and pulse patterns.

The six test results of the tested sex hormones showed LH/FSH ratio normalized, androgen levels decreased, endocrine balance achieved, BMI reduced to normal limits, with significant efficacy. At six-month follow-up visit, the patient reported regular menstrual cycles with normal volume, color, and quality, absence of dysmenorrhea, stable body weight, and significant improvement in quality of life. This suggested that Zhuang Medicine Mao Xia Yin combined with Diane-35 can effectively improve the clinical symptoms and demonstrates favorable long-term efficacy in patients with obesity-type PCOS. In addition, lifestyle optimization plays an indispensable role in disease management and cannot be overlooked.

6. Conclusion

The Zhuang Medicine Mao Xia Yin, developed by Professor Fang Gang through years of clinical practice, is an empirical formula rooted in the basic theory of Zhuang Medicine for treating obesity-type PCOS. Professor Fang believes that the common pathogenesis of obesity-type PCOS is primarily Yin syndrome (Milongxu,

spleen deficiency) complicated with Yang syndrome (dampness toxin, phlegm toxin, heat toxin, and stasis toxin). The clinical presentation typically includes menstrual disorders, obesity, and excessive leukorrhea etc. The treatment should focus on invigorating Milong (spleen) and removing dampness toxin, regulating Xu (Qi) and resolving phlegm toxin, activating Le (blood) and resolving stasis toxin, tonifying deficiency, and regulating menstruation. The formula is modified based on individual symptoms, signs, and fertility needs. Emphasis is placed on the holism concept, integrating the characteristics of the menstrual cycle, emotional regulation, and lifestyle modifications to fully leverage the unique therapeutic advantages of Zhuang medicine. This case study provides new thoughts and approaches for the treatment of obesity-type PCOS.

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Disclosure statement

The authors declare no conflict of interest.

References

- [1] Xie X, Kong B, Duan T, 2018, Obstetrics and Gynecology. People's Medical Publishing House, 2018: 348–351.
- [2] Jia R, Liu Y, 2020, Research Progress on Polycystic Ovary Syndrome in Traditional Chinese and Western Medicine. World Chinese Medicine, 15(12): 1827–1831+1835.
- [3] Qin J, 2006, Zhuang Medicine Gynecology. Guangxi Nationalities Publishing House, China.
- [4] Lin C, 2014, Zhuang Medicine Acupuncture. Guangxi Science and Technology Publishing House, 2014: 236–237.
- [5] Pang Y, Lin C, Huang D, 2006, Introduction to Zhuang Medicine Pharmacy. Guangxi Nationalities Publishing House, 2006: 44–45.
- [6] Pang Y, 2017, Overview of Zhuang Medicine Culture. Guangxi Science and Technology Publishing House, 2017: 15–17.
- [7] Huang L, 2019, Clinical Observation of Zhuang Medicine Acupuncture in the Treatment of Polycystic Ovary Syndrome. Guangxi University of Chinese Medicine, 2019: 22–23.
- [8] Li Z, Chen H, Hu S, et al., 2021, Professor Sun Bing's Experience in Treating Infertility Caused by Polycystic Ovary Syndrome and a Case Study. Journal of Jining Medical University, 44(4): 261–264.
- [9] Xu F, Qin X, Shi C, et al., 2023, A Case Study on the Treatment of Chronic Pelvic Pain of Pelvic Inflammatory Disease Sequelae with Zhuang Medicine Pi Chou Fang Teng Yin. Primary Healthcare and Traditional Chinese Medicine, 2(2): 19–23.

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Role of Ferroptosis in Cerebral Ischemia-Reperfusion Injury

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Abstract: Ferroptosis is a novel form of non-apoptotic cell death that has been widely studied in recent years and is involved in a variety of pathophysiological processes. The core treatment goal of ischemic stroke is to restore blood flow as early as possible, while the pathological mechanism of reperfusion injury after restoring blood flow is complex, involving oxidative stress, calcium overload, and inflammatory response. In recent years, more and more studies have found that ferroptosis mediation is involved in the occurrence and development of cerebral ischemia-reperfusion injury. This paper elaborates on the concept, mechanisms, and regulation of ferroptosis, detailing its role in cerebral ischemia-reperfusion injury and potential inhibition strategies. The aim is to deepen the understanding of ferroptosis in this pathological process and provide insights for possible targeted therapies.

Keywords: Ferroptosis; Ischemic stroke; Reperfusion injury; Targeted therapy

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1. Introduction

Stroke is one of the leading global causes of death and disability, ranking as the second leading cause of mortality and the primary cause of adult disability worldwide. With its elevated disability, recurrence, and fatality rates, this condition presents a major public health risk and stands as one of the most pressing disease burdens globally. Timely and effective restoration of cerebral blood flow is critical for patient survival and is typically achieved through thrombolysis or thrombectomy. However, numerous studies have demonstrated that reperfusion itself can exacerbate tissue damage, leading to further deterioration of the patient's condition and, in severe cases, death. This pathological process is known as cerebral ischemia-reperfusion injury (CIRI)^[1, 2]. Therefore, it is necessary to seek treatments to reduce CIRI. CIRI involves complex pathophysiological processes, and its mechanism is extremely complex, which is related to multiple links such as inflammatory response and oxidative stress, as well as various modes of cell death such as apoptosis, pyroptosis, and programmed necrosis^[3].

Among them, ferroptosis is closely related to CIRI and has emerged as a potential therapeutic target in

acute ischemic stroke ^[4-6]. Iron death, unlike apoptosis, necrosis, and autophagy, is a form of iron-dependent cell death characterized by excessive accumulation of lipid peroxides leading to oxidative damage of the cell membrane and ultimately causing cell death ^[7]. Ferroptosis is closely related to many diseases, such as tumors, neurodegenerative diseases, renal impairment, and ischemia-reperfusion injury ^[8]. Ferroptosis has emerged as a novel mode of cell death implicated in cerebral ischemia–reperfusion injury (CIRI). Fang *et al.* reported iron accumulation in the injured brain regions of rats subjected to ischemia–reperfusion, while Tuo *et al.* observed significant iron deposition in the brain tissue of rats with unilateral transient middle cerebral artery occlusion (MCAO) ^[9, 10]. Notably, treatment with the ferroptosis inhibitor ferrostatin-1 was shown to reduce cerebral infarct volume and improve behavioral outcomes in MCAO models. It has been revealed that cerebral ischemia–reperfusion induces ferroptosis in neurons, while inhibition of ferroptosis attenuates CIRI ^[11, 12]. These studies all suggest that ferroptosis is strongly associated with brain injury.

Studies have shown that targeted therapies can inhibit ferroptosis through several mechanisms, including reducing iron overload, decreasing reactive oxygen species (ROS) production, suppressing lipid peroxidation, and activating endogenous defense signaling pathways. These interventions have demonstrated potential in mitigating cerebral ischemia–reperfusion injury (CIRI). Ferroptosis is expected to be an important potential target for CIRI intervention. In this paper, the pathological mechanism of ferroptosis in CIRI and the progress of targeted therapy for ferroptosis are discussed to provide new ideas for the mechanism study and clinical prevention and treatment of CIRI.

2. Overview of iron deaths

2.1. Concept of iron death

Iron is an indispensable trace element in the human body. Low or high iron content and abnormal distribution in the body will affect the physiological function of the body. Ferroptosis is a novel form of programmed cell death first identified and named by Dixon *et al.* ^[13]. It is characterized by intracellular iron accumulation, which activates lipid peroxidation, leading to cell membrane rupture. This process also affects the mitochondria, resulting in mitochondrial atrophy, increased density of the mitochondrial bilayer membrane, reduction or loss of cristae, and ultimately, cell death.

Iron death is an iron-dependent mode of programmed cell death, which is different from apoptosis, necroptosis, and autophagy. The main hallmarks of ferroptosis are: iron accumulation and unrestricted “phospholipid peroxidation” in the cell membrane. Peroxidation products destroy the integrity of the membrane and thus induce cell death. It is a series of processes leading to cell death by iron metabolism disorders and massive accumulation of lipid peroxidation products. Ferroptosis is an iron-dependent non-apoptotic cell necrosis due to excessive accumulation of ferric iron, glutathione depletion, and lipid peroxidation ^[14].

Ferroptosis differs from other types of cell death because it does not trigger DNA fragmentation or follow typical apoptotic or necrotic pathways. Instead, it is defined by iron-dependent lipid peroxidation and dysregulated iron metabolism, resulting in cellular membrane damage and eventual cell rupture. Under certain pathological factors or drug induction, intracellular iron uptake increases, iron-dependent Fenton reaction intensifies, cellular antioxidant capacity decreases, fatal peroxide accumulation is produced, and ultimately, cell death occurs.

2.2. Rationale for iron death

The mechanism of ferroptosis involves multiple intracellular processes, mainly including iron metabolism disorders, lipid peroxide accumulation, imbalance of amino acid antioxidant system, and cell membrane damage. Ferroptosis is based on abnormal accumulation of intracellular free iron. When iron metabolism is imbalanced (e.g., increased iron intake, decreased storage, or blocked efflux), free iron accumulates in excess intracellularly, leading to iron death, mainly through the following mechanisms:

(1) Accumulation of iron ions

Iron ions enter the cell through transporters (e.g., transferrin receptor, TFR1) and are stored by iron storage proteins (e.g., ferritin) or excreted through iron-releasing proteins (e.g., ferroportin). In iron death, an imbalance in iron metabolism leads to excessive intracellular iron concentrations.

(2) Lipid peroxidation

Iron ions are involved in the generation of reactive oxygen species (ROS), especially free radicals such as hydrogen peroxide (H₂O₂), which react with polyunsaturated fatty acids on the cell membrane to form lipid peroxidation products, such as 4-hydroxydialyl peroxide (4-HNE). These peroxides can damage cell membranes and cause cell rupture. Therefore, metabolic processes such as iron absorption, transport, storage, utilization, and excretion are closely related to the occurrence of iron death.

3. The relationship between ferroptosis and cerebral ischemia-reperfusion injury

Restoration of blood flow is the most critical aspect of stroke treatment; however, paradoxically, reperfusion following ischemia can exacerbate brain tissue damage. Ischemia represents the initial phase of reperfusion injury. During the hypoxic stage, anaerobic metabolism becomes predominant, resulting in the accumulation of lactic acid, reduced synthesis and increased consumption of adenosine triphosphate (ATP), and subsequent cellular energy failure. These metabolic disturbances lead to calcium ion (Ca²⁺) overload, mitochondrial dysfunction, and activation of inflammatory responses, collectively contributing to further neuronal injury.

In the refilling stage, the rapid recovery of blood flow supplied oxygen gas to the oxygen-deficient group, and also promoted the production of reactive oxygen species (ROS) at the same time. Reactive oxygen species (ROS) can damage various intracellular biomolecules, impair cellular functions, and induce inflammatory responses. In addition, ROS contribute to the formation of thrombi, thereby exacerbating cellular injury. In them, ROS pass through and interact with cell membrane lipids, causing lipid peroxidation, which damages cell membrane structure and leads to dysfunction, a process closely related to iron death ^[15]. Studies have shown that after cerebral ischemia, the blood-brain barrier (BBB) is disrupted and the permeability of cerebral microvascular endothelial cells increases, which in turn promotes the massive entry of iron from the blood into the brain parenchyma, resulting in iron overload ^[16].

In addition, under pathological conditions of ischemia and hypoxia, the acidic environment in brain tissue can reduce the binding capacity of iron and TF, and a large amount of free iron ions are released. Free iron ions released promote iron uptake by neurons, resulting in abnormally high intracellular iron content ^[17]. Intracellular iron ionomers are heterogeneously accumulated, and ROS are generated by passing through the Fenton reaction or the Haber-Weiss reaction, which in turn oxidizes polyunsaturated fatty acids in lipids, causing the accumulation of polyunsaturated fatty acid peroxides, resulting in cell membrane destruction and mitochondrial damage ^[18, 19].

The above process is central to the development of ferroptosis and is associated with oxidative stress response in IRI. The intracellular antioxidant system can reverse lipid peroxidation and prevent the accumulation of lipid peroxides, thereby inhibiting ferroptosis. Consequently, the mechanism of ferroptosis in cerebral ischemia-reperfusion injury involves three key processes: iron metabolism, lipid peroxidation, and antioxidant defense. The following are the specific mechanisms of iron death:

3.1. Iron metabolism disorders and cerebral ischemia-reperfusion injury

Iron death is based on disturbances in iron metabolism, particularly accumulation of intracellular free iron. Iron can enter cells via the iron transporter receptor (TFR), be stored in ferritin, or be expelled from cells via iron expulsion protein (FPN). When there is a disruption in iron regulation, excess iron builds up within cells, increasing its reactivity with oxygen and leading to the production of free radicals.

Iron is an essential trace element in the human body. Circulating Fe^{3+} binds to transferrin and is transported into cells via the transferrin receptor (TFR). Once inside the cell, Fe^{3+} is reduced and released into the labile iron pool (LIP) within the cytosol. Excess iron is stored in ferritin, where it remains in a bound and non-toxic form ^[20]. The labile iron pool within cells primarily consists of free Fe^{2+} , which is highly reactive and unstable. Through the Fenton reaction, Fe^{2+} catalyzes the production of hydroxyl radicals that readily react with polyunsaturated fatty acids in cellular and plasma membranes, leading to the generation of large amounts of lipid reactive oxygen species (ROS) and ultimately resulting in cell death. Membrane ferroportin 1 (FPN1) is currently the only known iron export protein responsible for transporting Fe^{2+} outside the cell ^[21].

Promoting intracellular iron import and breakdown of iron derivatives and inhibiting iron export can cause Fe^{2+} overload in labile iron pools. Accumulated Fe^{2+} generates ROS by reacting with H_2O_2 or O_2 , causing lipid peroxidation damage and cellular iron death. Iron deposition has previously been reported to occur in the thalamus and basal ganglia of patients with cerebral ischemia, and subsequent studies have found that iron, transferrin, and transferrin receptor levels in the brain are increased to varying degrees after ischemia ^[22–24]. These findings suggest that neuronal cells increase their own iron intake by up-regulating the expression of transferrin and TFR during ischemic brain injury, which leads to an increase in free Fe^{2+} content in the cells, which is clinically characterized by iron deposition in ischemic injured areas of the brain. Neuronal cells showed a decrease in iron excretion in addition to increased iron intake during reperfusion in ischemic stroke.

Tuo *et al.* found that cerebral ischemia-reperfusion injury significantly suppresses tau protein expression, which has been previously reported to play a key role in iron efflux in neural cells. Tau protein mediates the interaction between the membrane iron exporter ferroportin (FPN) and amyloid precursor protein (APP), thereby facilitating normal iron excretion ^[25, 26]. Ischemic brain injury also affects the efflux capacity of the membrane iron transporter (FPN) after tau protein is inhibited. Increased intracellular free Fe^{2+} content activates the ferroptosis pathway due to increased iron intake and decreased iron excretion. On the one hand, excessive Fe^{2+} strengthens the Fenton reaction and produces a hydroxyl group from the base; the synthesis of another square Fe^{2+} reference with lipoxygenase catalyzes the production of lipid peroxides ^[27].

Iron death is dependent on iron, and proteins involved in the maintenance of iron homeostasis play an important role in the regulation of iron death. Dysregulation of these proteins results in elevated intracellular iron concentrations, promoting the accumulation of lipid peroxides through two primary mechanisms. First, the iron-dependent Fenton reaction facilitates the generation of reactive oxygen species (ROS), whereby redox-active ferrous iron (Fe^{2+}) catalyzes the conversion of hydrogen peroxide into highly reactive hydroxyl radicals

and hydroxide ions. These ROS then directly promote the formation of phospholipid hydroperoxides (PLOOH). Additionally, iron overload activates iron-dependent enzymes, such as iron-containing lipoxygenases (LOX) and cytochrome P450 oxidoreductase. These enzymes, particularly LOX, drive the production of phospholipid hydroperoxides, thereby promoting the increased occurrence of iron death, reduced iron storage, and limited paste outflow. This results in intracellular iron accumulation, further increasing iron-related reactive oxygen species and lipid peroxide, which leads to iron death.

3.2. Lipid peroxidation and cerebral ischemia-reperfusion injury

Lipid peroxidation is the core process of iron death, while polyunsaturated fatty acids (PUFAs) are the main substrates of peroxidation, especially arachidonic acid (AA) and epinephrine. Iron ions promote lipid peroxidation and form lipid peroxide by generating free radicals. Oxidized lipids can disrupt the structure of the cell membrane, impairing its integrity and leading to dysregulation of cellular function, ultimately resulting in cell death. Several studies have now shown that PUFAs, such as arachidonic acid and adrenic acid, are specific substrates for PLOOH synthesis and play an important role in the development of iron death, and thus, the increase of these PUFAs increases the risk of iron death. The destruction of cell membranes by lipid peroxidation products is an important marker of iron death. Peroxidized lipid products can lead to structural and functional dysfunction of the cell membrane, forming membrane pores, resulting in the leakage of cellular contents, which in turn triggers cell rupture and death. During iron death, unsaturated fatty acid phospholipids are oxidized to lipid peroxides by reactive oxygen species (ROS) and lipoxygenase^[28]. Lipoxygenase is not the sole catalytic enzyme for lipid peroxidation, and studies have shown that reduced nicotinamide adenine dinucleotide phosphate oxidase and cytochrome P450 oxidoreductase also play key roles in lipid peroxidation during iron death^[29, 30].

Gubern *et al.* investigated the association between ACSL4 and brain ischemic injury and found that brain ischemic injury was able to induce miR-347 upregulation which in turn suppressed ACSL4 expression^[31]. Increased expression of 12/15 lipoxygenase (12/15 - LOX) has been found in mouse models of ischemic stroke, and these studies point to 12/15-LOX mediated increased lipid peroxide levels and associated with neuronal cell damage^[32, 33]. It has been suggested that the level of 12/15-LOX is regulated by glutathione in ischemic stroke, and that decreased glutathione in ischemic brain tissue contributes to the activation of 12/15-LOX^[34]. Both 12/15-LOX and ACSL4 are increased in ischemic stroke, so inhibiting ferroptosis by regulating lipoxygenase and ACSL4 has the potential to be a new target for the treatment of ischemic stroke.

3.3. Imbalance of antioxidant system and cerebral ischemia-reperfusion injury

Under normal conditions, cells possess a well-coordinated antioxidant system that plays a crucial protective role by effectively scavenging excessive reactive oxygen species (ROS) and preventing the onset of lipid peroxidation. The main antioxidant enzymes include glutathione peroxidase (GPX4), superoxide dismutase (SOD) and catalase (CAT), which are selenium-containing enzymes expressed in mammalian cells and play a central role in resistance to iron death. Glutathione (GSH), as an important non-enzymatic antioxidant, can react with peroxides to form non-toxic products, thereby alleviating the effects of oxidative stress.

GPX4 catalyzes the conversion of reduced glutathione (GSH) into oxidized glutathione (GSSG), which reduces phospholipid hydroperoxides (PL-OOH) to phospholipid alcohols (PL-OH), thereby protecting membrane lipids from oxidative damage. For GPX4 to effectively inhibit ferroptosis, proper functioning of the

GSH synthesis pathway is essential. Glutathione (GSH), as a small antioxidant molecule, changes from reduced to oxidized form under the action of glutathione peroxidase 4 (GPX4), while converting lipid peroxides to the corresponding alcohols. Inhibition of GSH synthesis and reduction of GPX4 activity promotes the accumulation of lipid peroxides, which leads to ferroptosis in cells ^[35]. It has been suggested that enhancing the function of the antioxidant system may be an effective strategy to suppress iron death, which provides a new direction for the treatment of related diseases ^[36, 37].

In addition, panthenol (CoQH2)/ferroptosis-suppressor-protein 1 (FSP1) system and tetrahydrobiopterin (BH4)/GTP cyclohydrolase 1 (GCH1) system are two novel and independent ferroptosis antioxidant systems independent of GSH/GPX4. The FSP1/CoQ10 pathway acts as an independent system, and the FSP1/CoQ10 pathway cooperates with the GSH/GPX4 pathway to inhibit iron death. However, the coenzyme Q10/iron death inhibitory protein 1 (FSP1) system plays an antioxidant role through coenzyme Q10 and is able to capture lipid peroxyl radicals and prevent excessive oxidation of membrane lipids. FSP1 converts ubiquinone (CoQ) to the lipophilic radical trapping agent CoQH2, preventing the peroxidation of unsaturated fatty acids in lipid bilayers ^[38]. As a result, cells will become more susceptible to ferroptosis when this system fails.

The GCH1/BH4 pathway represents an independent ferroptosis suppression system. As a potent membrane-associated radical-trapping antioxidant, BH4 selectively shields phospholipids containing diunsaturated fatty acyl chains, functioning either alone or synergistically with vitamin E. Additionally, BH4 indirectly suppresses lipid autoxidation by contributing to CoQ10 biosynthesis. GCH1 protein is involved in the regulation of ferroptosis by synthesizing BH4 to prevent the autoxidation of the acyl residues of polyunsaturated fatty acids ^[39]. However, ferroptosis occurs when the antioxidant defense system of the cell fails, resulting in the inability of lipid peroxidation products to be removed, thereby driving the progression of ferroptosis.

4. Potential therapeutic targets for iron death

Iron death is a ROS-dependent form of cell death driven by iron-mediated Fenton reactions, which generate reactive oxygen species that oxidize polyunsaturated fatty acid-containing phospholipids, ultimately inducing lipid peroxidation. Cellular defense against this process primarily involves two key antioxidant systems that catalyze lipid peroxide reduction. The occurrence of ferroptosis is regulated by several key molecules, and the following are some important regulators:

- (1) GPX4 (glutathione peroxidase 4): GPX4 is an important antioxidant enzyme capable of inhibiting lipid peroxidation. Functional restriction of GPX4 promotes the development of iron death, and therefore, GPX4 is an important suppressor of iron death.
- (2) System Xc- (Cysteine/Glutamate exchange system): System Xc- is a transporter responsible for intracellular and extracellular cysteine and glutamate exchange. Cysteine is a precursor for glutathione synthesis, whereas glutathione has ROS scavenging effects. When the function of System Xc- is impaired, glutathione synthesis is inhibited and ferroptosis occurs.
- (3) FSP1 (Ferroptosis Suppressor Protein 1): FSP1 is a suppressor of iron death, which inhibits ferroptosis by reducing the occurrence of oxidative stress.

Iron metabolism, lipid metabolism and redox pathways regulate ferroptosis together, so currently therapeutic drugs mainly affect bioactive molecules of ferroptosis by targeting the core molecules of these three pathways, and small molecule inhibitors or inducers against ferroptosis have been widely used in preclinical

practice, and become new therapeutic hotspots by regulating iron death.

4.1. Iron chelators

Iron is a crucial factor in the induction of lipid peroxidation and iron death. Common iron chelators, such as deferoxamine (DFO), the potent antioxidants deferoxamine mesylate (DFOM), and 2,2-bipyridyl (2,2-BP), can inhibit ferroptosis by chelating intracellular non-heme iron, reducing free iron ion levels ^[40]. In a rat model, DFO treatment reduced brain injury following transient focal ischemia and improved neurological recovery ^[41].

It has been documented that iron chelators such as 2,2-dipyridyl and deferoxamine can inhibit injury in a rat model of ischemic brain injury ^[42, 43]. These studies further suggest that free iron and its related ferroptosis pathways play an important role in the regulation of neuronal cell injury, while iron chelators may inhibit the opening of iron damage-related signaling pathways by directly binding extracellular free iron. However, in terms of intervention of iron efflux, Ding *et al.* inhibited the increase of ferritin and the decrease of FPN protein in neural cells by down-regulating Hephcidin using small interfering RNA in a rat cerebral ischemia-reperfusion model ^[44]. This therapeutic approach mitigates the declining iron export capacity in neuronal cells and identifies novel therapeutic targets for cerebral ischemia-reperfusion injury intervention.

4.2. Antioxidants

Because both 12/15-LOX and ACSL4 expression are increased in ischemic stroke, ferroptosis can be inhibited and cell damage can be alleviated by regulating lipoxygenase and ACSL4. In a mouse model of transient global ischemia, treatment with the selective 5-LOX inhibitor zileuton significantly reduced levels of inflammatory cytokines and chemokines and ameliorated brain injury ^[45].

Lip-1 and Fer-1 have been identified as classical ferroptosis inhibitors used in vitro and in vivo. These two compounds are also categorized as radical-trapping antioxidants (RTAs). Xu *et al.* demonstrated that Fer-1 could upregulate GPX4 and reduce ROS levels by inhibiting the cyclooxygenase-2/prostaglandin E2 (COX-2/PGE2) signaling pathway, thereby suppressing ferroptosis in CIRI and improving neurological outcomes ^[46]. Baicalein, a polyphenolic compound, was shown to inhibit both iron accumulation and lipid peroxidation, thus alleviating brain injury following ischemia in mice ^[47].

In 2007, Lapchak *et al.* found that baicalein was able to inhibit 15-LOX, thereby reducing brain cell injury ^[48]. These findings not only facilitate the development of novel ferroptosis-inhibiting therapeutics, but also offer innovative approaches and promising treatment strategies for cerebral ischemia-reperfusion injury (CIRI). Intervention of lipid peroxidation through 12/15-LOX and upstream regulators such as ACSL4 represents a promising strategy to suppress ferroptosis and warrants further in-depth investigation.. The pharmacokinetic study of these inhibitors in vivo may become a future research hotspot.

4.3. Intervention of an antioxidant system

System Xc- and GPX4 play a key role in iron death, while regulatory intervention for system Xc- and GPX4 can play an important role in ischemic brain injury. GPX4 acts as an important endogenous antioxidant, and its up-regulation can inhibit iron death, thereby protecting neurons in the brain from injury. It has been demonstrated that the trace element selenium (Se), as an important component of GPX4, can promote GPX4 expression, and then inhibit the occurrence of ferroptosis ^[49]. In addition, carvacrol upregulated GPX4 in the ferroptosis pathway, thereby reducing lipid peroxide damage ^[50]. It has been demonstrated that compound

Naotaifang extract can increase the expression of GPX4 and SLC7A11, thereby inhibiting ferroptosis in nerve cells ^[51].

5. Prospects

The high morbidity, disability, and mortality of ischemic stroke still cause great pressure on families and society, and it has become urgent to explore the therapeutic target of ischemia-reperfusion injury. Iron death, as a novel programmed cell death mode, is involved in the pathophysiological process of ischemia-reperfusion injury in a variety of organs and has been confirmed by many scholars to play a key role in the process of ischemia-reperfusion injury. Although ferroptosis in cerebral ischemia-reperfusion injury is a hot research field, there are still many urgent problems to be solved. First, the pathological mechanisms by which ferroptosis is involved in and aggravates CIRI are complex and diverse, and the specific mechanisms need to be studied in depth. Secondly, the pathological progression of cerebral ischemia-reperfusion injury (CIRI) involves multiple cell death modalities, including ferroptosis, apoptosis, necrosis, and pyroptosis, which interact through various signaling pathways. In addition, the specific molecular targets of ferroptosis inhibitors in the context of CIRI remain unclear, raising important questions regarding how ferroptosis can be selectively modulated in this condition. Therefore, elucidating the specific regulatory mechanism of ferroptosis in CIRI and how to effectively regulate ferroptosis and clarify the target of ferroptosis inhibitors will provide new research ideas and treatment strategies for the treatment of cerebral ischemia-reperfusion injury.

6. Conclusion

Ferroptosis plays a critical role in cerebral ischemia-reperfusion injury (CIRI), yet its precise mechanisms and interactions with other cell death pathways remain unclear. Further research is needed to elucidate the specific regulatory mechanisms of ferroptosis in CIRI and identify targeted inhibitors, which could provide novel therapeutic strategies for mitigating ischemic stroke damage. Addressing these challenges will advance the development of effective treatments for CIRI.

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References

- [1] Barthels D, Das H, 2020, Current Advances in Ischemic Stroke Research and Therapies. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, 1866(4): 165260.
- [2] Rabinstein AA, 2020, Update on Treatment of Acute Ischemic Stroke. *Continuum: Lifelong Learning in Neurology*, 26(2): 268–286.
- [3] Li ZZ, Zhang DC, 2020, Research Progress on the Mechanisms Related to Cerebral Ischemia-Reperfusion Injury. *Journal of Hebei North University (Medical Edition)*, 10(6): 60–63.
- [4] Yan HF, Zou T, Tuo QZ, et al., 2021, Ferroptosis: Mechanisms and Links With Diseases. *Signal Transduction and Targeted Therapy*, 6(1): 49.

- [5] Wu MY, Yang GT, Liao WT, et al., 2018, Current Mechanistic Concepts in Ischemia and Reperfusion Injury. *Cellular Physiology and Biochemistry*, 46(4): 1650–1667.
- [6] Shi XH, Mang J, Xu ZX, 2022, Research Progress on Cell Death Patterns in Cerebral Ischemia-Reperfusion Injury. *Journal of Jilin University (Medicine Edition)*, 48(6): 1635–1643.
- [7] Galluzzi L, Vitale I, Aaronson SA, et al., 2018, Molecular Mechanisms of Cell Death: Recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death & Differentiation*, 25(3): 486–541.
- [8] Zhang LY, Li FR, Wang C, et al., 2019, Emerging Roles of p53 in Ferroptosis and Its Potential Application. *Chinese Journal of Pathophysiology*, 35(12): 2299–2304.
- [9] Fang KM, Cheng FC, Huang YL, et al., 2013, Trace Element, Antioxidant Activity, and Lipid Peroxidation Levels in Brain Cortex of Gerbils After Cerebral Ischemic Injury. *Biological Trace Element Research*, 152: 66–74.
- [10] Tuo Q, Lei P, Jackman K, et al., 2017, Tau-Mediated Iron Export Prevents Ferroptotic Damage After Ischemic Stroke. *Molecular Psychiatry*, 22(11): 1520–1530.
- [11] She X, Lan B, Tian H, et al., 2020, Cross Talk Between Ferroptosis and Cerebral Ischemia. *Frontiers in Neuroscience*, 14: 776.
- [12] Zille M, Karuppagounder SS, Chen Y, et al., 2017, Neuronal Death After Hemorrhagic Stroke In Vitro and In Vivo Shares Features of Ferroptosis and Necroptosis. *Stroke*, 48(4): 1033–1043.
- [13] Dixon SJ, Lemberg KM, Lamprecht MR, et al., 2012, Ferroptosis: An Iron-Dependent Form of Nonapoptotic Cell Death. *Cell*, 149(5): 1060–1072.
- [14] Bertrand RL, 2017, Iron Accumulation, Glutathione Depletion, and Lipid Peroxidation Must Occur Simultaneously During Ferroptosis and Are Mutually Amplifying Events. *Medical Hypotheses*, 101: 69–74.
- [15] Xu Y, Li K, Zhao Y, et al., 2023, Role of Ferroptosis in Stroke. *Cellular and Molecular Neurobiology*, 43(1): 205–222.
- [16] Degregorio-Rocasolano N, Martí-Sistac O, Gasull T, 2019, Deciphering the Iron Side of Stroke: Neurodegeneration at the Crossroads Between Iron Dyshomeostasis, Excitotoxicity, and Ferroptosis. *Frontiers in Neuroscience*, 13: 85.
- [17] Wang Y, Wu S, Li Q, et al., 2023, Pharmacological Inhibition of Ferroptosis as a Therapeutic Target for Neurodegenerative Diseases and Strokes. *Advanced Science*, 10(24): 2300325.
- [18] Liu B, Qian DH, 2023, Research and Progress on the Role of Ferroptosis in Pancreatic Cancer. *China Journal of General Surgery*, 32(3): 434–440.
- [19] Rochette L, Dogon G, Rigal E, et al., 2022, Lipid Peroxidation and Iron Metabolism: Two Corner Stones in the Homeostasis Control of Ferroptosis. *International Journal of Molecular Sciences*, 24(1): 449.
- [20] Vogt AS, Arsiwala T, Mohsen M, et al., 2021, On Iron Metabolism and Its Regulation. *International Journal of Molecular Sciences*, 22(9): 4591.
- [21] Dutt S, Hamza I, Bartnikas TB, 2022, Molecular Mechanisms of Iron and Heme Metabolism. *Annual Review of Nutrition*, 42(1): 311–335.
- [22] Baenziger O, Martin E, Steinlin M, et al., 1993, Early Pattern Recognition in Severe Perinatal Asphyxia: A Prospective MRI Study. *Neuroradiology*, 35: 437–442.
- [23] Park UJ, Lee YA, Won SM, et al., 2011, Blood-Derived Iron Mediates Free Radical Production and Neuronal Death in the Hippocampal CA1 Area Following Transient Forebrain Ischemia in Rat. *Acta Neuropathologica*, 121: 459–473.
- [24] Degregorio-Rocasolano N, Martí Sistac O, Gasull T, 2019, Deciphering the Iron Side of Stroke: Neurodegeneration at the Crossroads Between Iron Dyshomeostasis, Excitotoxicity, and Ferroptosis. *Frontiers in Neuroscience*, 13: 85.
- [25] Tuo Q, Lei P, Jackman K, et al., 2017, Tau-Mediated Iron Export Prevents Ferroptotic Damage After Ischemic Stroke. *Molecular Psychiatry*, 22(11): 1520–1530.

- [26] Lei P, Ayton S, Finkelstein DI, et al., 2012, Tau Deficiency Induces Parkinsonism With Dementia by Impairing APP-Mediated Iron Export. *Nature Medicine*, 18(2): 291–295.
- [27] Tuo Q, Lei P, Jackman K, et al., 2017, Tau-Mediated Iron Export Prevents Ferroptotic Damage After Ischemic Stroke. *Molecular Psychiatry*, 22(11): 1520–1530.
- [28] Zhang HX, Zhang S, 2024, Research Progress on PTPN13 Regulation of Lipid Metabolism and Ferroptosis in Tumor Cells. *China Journal of General Surgery*, 33(1): 131–137.
- [29] Yang WH, Huang Z, Wu J, et al., 2020, A TAZ-ANGPTL4-NOX2 Axis Regulates Ferroptotic Cell Death and Chemoresistance in Epithelial Ovarian Cancer. *Molecular Cancer Research*, 18(1): 79–90.
- [30] Zou Y, Li H, Graham ET, et al., 2020, Cytochrome P450 Oxidoreductase Contributes to Phospholipid Peroxidation in Ferroptosis. *Nature Chemical Biology*, 16(3): 302–309.
- [31] Gubern C, Camos S, Ballesteros I, et al., 2013, miRNA Expression Is Modulated Over Time After Focal Ischaemia: Up-Regulation of miR-347 Promotes Neuronal Apoptosis. *The FEBS Journal*, 280(23): 6233–6246.
- [32] Iaccarino G, Ciccarelli M, Sorriento D, et al., 2005, Ischemic Neoangiogenesis Enhanced by β 2-Adrenergic Receptor Overexpression: A Novel Role for the Endothelial Adrenergic System. *Circulation Research*, 97(11): 1182–1189.
- [33] Jung JE, Karatas H, Liu Y, et al., 2015, STAT-Dependent Upregulation of 12/15-Lipoxygenase Contributes to Neuronal Injury After Stroke. *Journal of Cerebral Blood Flow & Metabolism*, 35(12): 2043–2051.
- [34] Zheng Y, Liu Y, Karatas H, et al., 2019, Contributions of 12/15-Lipoxygenase to Bleeding in the Brain Following Ischemic Stroke. *Advances in Experimental Medicine and Biology*, 1161: 125–131.
- [35] Ursini F, Maiorino M, 2020, Lipid Peroxidation and Ferroptosis: The Role of GSH and GPx4. *Free Radical Biology and Medicine*, 152: 175–185.
- [36] Zhang L, Luo YL, Xiang Y, et al., 2024, Ferroptosis Inhibitors: Past, Present and Future. *Frontiers in Pharmacology*, 15: 1407335.
- [37] Zhu L, Zhu D, Ran J, et al., 2024, Autophagy Aggravates Multi-Walled Carbon Nanotube-Induced Ferroptosis by Suppressing PGC-1 α Dependent-Mitochondrial Biogenesis in Lung Epithelial Cells. *Chemico-Biological Interactions*, 400: 111158.
- [38] Doll S, Freitas FP, Shah R, et al., 2019, FSP1 Is a Glutathione-Independent Ferroptosis Suppressor. *Nature*, 575(7784): 693–698.
- [39] Kraft VA, Bezjian CT, Pfeiffer S, et al., 2019, GTP Cyclohydrolase 1/Tetrahydrobiopterin Counteract Ferroptosis Through Lipid Remodeling. *ACS Central Science*, 6(1): 41–53.
- [40] Zhang Y, Lu X, Tai B, et al., 2021, Ferroptosis and Its Multifaceted Roles in Cerebral Stroke. *Frontiers in Cellular Neuroscience*, 15: 615372.
- [41] Liu H, An N, Wang L, et al., 2023, Protective Effect of Xingnaojing Injection on Ferroptosis After Cerebral Ischemia Injury in MCAO Rats and SH-SY5Y Cells. *Journal of Ethnopharmacology*, 301: 115836.
- [42] Van Hoecke M, Prigent-Tessier A, Bertrand N, et al., 2005, Apoptotic Cell Death Progression After Photothrombotic Focal Cerebral Ischaemia: Effects of the Lipophilic Iron Chelator 2, 2'-Dipyridyl. *European Journal of Neuroscience*, 22(5): 1045–1056.
- [43] Hanson LR, Roeytenberg A, Martinez PM, et al., 2009, Intranasal Deferoxamine Provides Increased Brain Exposure and Significant Protection in Rat Ischemic Stroke. *The Journal of Pharmacology and Experimental Therapeutics*, 330(3): 679–686.
- [44] Ding H, Yan CZ, Shi H, et al., 2011, Hepsidin Is Involved in Iron Regulation in the Ischemic Brain. *PLoS One*, 6(9): e25324.

- [45] Tu XK, Zhang HB, Shi SS, et al., 2016, 5-LOX Inhibitor Zileuton Reduces Inflammatory Reaction and Ischemic Brain Damage Through the Activation of PI3K/Akt Signaling Pathway. *Neurochemical Research*, 41: 2779–2787.
- [46] Xu Y, Liu Y, Li K, et al., 2022, COX-2/PGE2 Pathway Inhibits the Ferroptosis Induced by Cerebral Ischemia Reperfusion. *Molecular Neurobiology*, 59(3): 1619–1631.
- [47] Sun SJ, Tu H, Tang LJ, et al., 2020, Research Progress on Ferroptosis Inducers and Inhibitors. *Chinese Journal of Pharmacology and Toxicology*, 34(8): 623–633.
- [48] Lapchak P, Maher P, Schubert D, et al., 2007, Baicalein, an Antioxidant 12/15-Lipoxygenase Inhibitor Improves Clinical Rating Scores Following Multiple Infarct Embolic Strokes. *Neuroscience*, 150(3): 585–591.
- [49] Guan X, Li X, Yang X, et al., 2019, The Neuroprotective Effects of Carvacrol on Ischemia/Reperfusion-Induced Hippocampal Neuronal Impairment by Ferroptosis Mitigation. *Life Sciences*, 235: 116795.
- [50] Ingold I, Berndt C, Schmitt S, et al., 2018, Selenium Utilization by GPX4 Is Required to Prevent Hydroperoxide-Induced Ferroptosis. *Cell*, 172(3): 409–422.
- [51] Lan B, Ge JW, Cheng SW, et al., 2020, Extract of Naotaifang, a Compound Chinese Herbal Medicine, Protects Neuron Ferroptosis Induced by Acute Cerebral Ischemia in Rats. *Journal of Integrative Medicine*, 18(4): 344–350.

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Efficacy and Safety of Miao Medicine Jinlong Zhi Xie Fang Enema in the Treatment of Ulcerative Colitis (Large Intestine Damp-Heat Syndrome): A Randomized Controlled Trial

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Abstract: Ulcerative colitis (UC) is a chronic inflammatory bowel disease that significantly affects the quality of life of patients. Traditional treatments often have limitations, and alternative therapies are being explored. Miao Medicine, particularly Jinlong Zhi Xie Fang Enema, is a traditional herbal remedy used to treat UC symptoms, especially in patients with Large Intestine Damp-Heat Syndrome. However, clinical evidence supporting its efficacy is limited.

Keywords: Ulcerative colitis; Jinlong Zhi Xie Fang; Miao Medicine; Intestinal mucosal barrier; Randomized controlled trial; Herbal medicine

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1. Introduction

1.1. Overview of ulcerative colitis (UC)

Ulcerative colitis (UC) is a chronic, inflammatory bowel disease (IBD) primarily affecting the large intestine and rectum. It is characterized by the presence of continuous mucosal inflammation, which often leads to the formation of ulcers, bleeding, and pus in the colon. Patients commonly present with symptoms such as persistent diarrhea, abdominal pain, bloody stools, urgency, and fatigue, all of which significantly impair the quality of life.

The incidence of UC has been steadily rising globally, with Western countries historically reporting the highest prevalence rates. In the United States and Europe, UC affects approximately 1–2 million individuals,

and the disease typically presents between the ages of 15 and 30 years. While the prevalence of UC in China is lower compared to Western nations, it has been increasing in recent years, reflecting broader changes in dietary habits, lifestyle, and environmental factors ^[1–5].

Pathophysiologically, UC is believed to arise from an aberrant immune response, where the body's immune system attacks its own gastrointestinal tract. This immune dysregulation, combined with genetic predisposition and environmental factors, leads to chronic inflammation and tissue damage in the colon. As the disease progresses, patients often experience flare-ups, during which symptoms worsen, followed by periods of remission. However, without effective management, repeated flare-ups can result in irreversible damage to the intestinal lining, leading to complications such as bowel perforation, toxic megacolon, and an increased risk of colorectal cancer.

1.2. Current treatment landscape

Current treatment strategies for UC primarily involve pharmacological interventions aimed at reducing inflammation and controlling symptoms. The first-line treatment for mild to moderate UC includes 5-aminosalicylic acid (5-ASA) drugs such as Mesalazine, which work by inhibiting the production of inflammatory mediators in the colon. For more severe cases, corticosteroids are often prescribed to rapidly control inflammation. Immunosuppressive agents, including thiopurines and methotrexate, are used for patients who do not respond to steroids or for those requiring long-term maintenance therapy.

Despite the availability of these treatments, many patients with UC experience limited efficacy, frequent relapses, or significant side effects, leading to a need for alternative therapies. In addition, a portion of patients fail to achieve full remission or experience intolerance to conventional medications, underscoring the importance of exploring novel approaches to UC management ^[4–7].

1.3. Role of traditional Chinese medicine (TCM) in treating UC

Traditional Chinese medicine (TCM) is an ancient healing system that has been practiced for over 2,000 years. TCM is based on the concept of balancing the body's vital energy, known as “Qi,” and maintaining harmony between Yin and Yang, which are two complementary forces that govern physiological processes. The TCM approach to disease treatment emphasizes holistic care, viewing the body as an interconnected system rather than focusing solely on isolated symptoms.

In TCM, disease is often seen as a result of an imbalance in the body's energy flow, which can be influenced by factors such as diet, lifestyle, environment, and emotional well-being. One of the key principles in TCM is the concept of “damp-heat,” a pathological condition that arises when excess moisture and heat accumulate in the body, obstructing the normal flow of Qi. This imbalance is often linked to conditions such as digestive disturbances, skin diseases, and inflammatory disorders, including ulcerative colitis ^[8–12].

The treatment of UC in TCM involves addressing the underlying Damp-Heat syndrome by clearing excess heat, resolving dampness, and restoring the balance of Qi. TCM uses a variety of modalities to achieve this, including herbal medicine, acupuncture, dietary adjustments, and lifestyle modifications. Herbal treatments are particularly important in TCM, and they are carefully selected to target specific imbalances in the body. Herbs that have cooling, detoxifying, and anti-inflammatory properties are commonly used to treat conditions like UC, to reduce intestinal inflammation, promote mucosal healing, and improve gastrointestinal function ^[13–17].

In recent years, there has been growing interest in integrating TCM into the treatment of UC, especially in

cases where conventional treatments are insufficient or lead to undesirable side effects. Studies have shown that TCM therapies can help reduce the frequency and severity of UC flare-ups, improve clinical symptoms such as diarrhea and abdominal pain, and enhance overall gut health. Miao Medicine, a branch of TCM originating from the Miao ethnic group in China, is gaining attention for its unique and potent herbal formulas that are particularly effective in treating digestive disorders like UC ^[18–20].

1.4. Miao medicine and Jinlong Zhi Xie Fang

Miao medicine is a traditional healing system practiced by the Miao ethnic group in southwest China. The system includes a wide variety of herbal remedies, many of which are used to treat gastrointestinal diseases. Jinlong Zhi Xie Fang is a traditional Miao herbal formula specifically designed for treating UC and other gastrointestinal disorders characterized by damp-heat. The formula is composed of several herbs, each chosen for its ability to clear heat, dispel dampness, and strengthen the gastrointestinal system.

The key components of Jinlong Zhi Xie Fang include herbs such as Si Leng Cao (*Houttuynia cordata*), Shi Hun Cao (Chronic Wound Herb), Suan Cai (Sour Cabbage), Bai Tou Guo (*Cresson*), and Long Ya Cao (Dragon Grass). These herbs are known for their synergistic effects in reducing inflammation, detoxifying the body, and improving intestinal motility. According to traditional Miao medicine, this formula is particularly effective in treating conditions where the digestive system is disrupted by excess dampness and heat, which corresponds to the Damp-Heat syndrome in TCM.

1.5. Research gap and study objective

While conventional treatments for UC, such as 5-aminosalicylic acid (5-ASA), corticosteroids, and biologics, are commonly used in clinical practice, these therapies often have limited effectiveness and are associated with significant side effects. Additionally, some patients with UC experience a recurrence of symptoms despite adherence to these treatments, highlighting the need for alternative therapies that are both effective and have a more favorable safety profile.

Despite the growing body of research supporting the use of TCM in managing gastrointestinal disorders, there is limited clinical evidence on the efficacy and safety of Miao Medicine and Jinlong Zhi Xie Fang specifically for UC. While TCM principles suggest that herbal formulas like Jinlong Zhi Xie Fang can effectively address the root causes of UC, there remains a need for rigorous clinical trials to evaluate their therapeutic potential in a modern, evidence-based context.

1.6. Potential impact

This research could potentially offer new insights into the role of traditional herbal formulas in the management of UC, and it may pave the way for more personalized and holistic approaches to treatment. If Jinlong Zhi Xie Fang proves to be effective, it could offer an important alternative to conventional therapies, especially for patients seeking more natural treatments with fewer side effects. Furthermore, this study could contribute to the modernization and global recognition of Miao Medicine, supporting its role in treating chronic inflammatory diseases like UC.

2. Methods

2.1. Study design

This study is a single-center, prospective, randomized controlled trial (RCT) designed to evaluate the clinical efficacy, safety, and impact on intestinal mucosal barrier function of Miao medicine and Jinlong Zhi Xie Fang enema in patients with ulcerative colitis (UC), specifically those diagnosed with large intestine damp-heat syndrome. The trial adheres to ethical guidelines and is approved by the ethics committee of the relevant institution.

A total of 40 patients diagnosed with moderate to severe UC will be enrolled and randomly assigned to two groups: the treatment group (n = 20) will receive Jinlong Zhi Xie Fang enema, while the control group (n = 20) will receive oral Mesalazine (a standard treatment for UC). All participants will provide informed consent before participating in the trial, ensuring voluntary participation and confidentiality of personal data.

The study will be conducted over a 4-week treatment period, with follow-up assessments conducted at baseline, mid-treatment (2 weeks), and post-treatment (4 weeks). The primary objective is to assess the improvement in clinical symptoms, including diarrhea, abdominal pain, and stool blood. The secondary objective focuses on evaluating the repair of the intestinal mucosal barrier function through endoscopic examination and histopathological analysis.

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Adult patients (aged 18–65 years) who meet the clinical criteria for UC according to the established guidelines (Mayo Clinic criteria or similar diagnostic criteria).
- (2) Patients diagnosed with UC during the active phase, with a disease duration of 4 to 6 weeks.
- (3) Patients diagnosed with large intestine damp-heat syndrome according to traditional Chinese medicine (TCM) diagnostic criteria.
- (4) Patients who have experienced persistent or recurrent symptoms despite previous treatment with conventional therapies.
- (5) Willingness to comply with the study protocol and provide informed consent.

2.2.2. Exclusion criteria

- (1) Patients with severe complications of UC, such as bowel perforation, toxic megacolon, or severe hemorrhagic colitis.
- (2) Patients with other significant comorbidities, including severe liver, kidney, cardiovascular, or respiratory diseases.
- (3) Pregnant or breastfeeding women.
- (4) Patients with contraindications to Mesalazine or Miao medicine Jinlong Zhi Xie Fang.
- (5) Patients participating in other clinical trials or receiving other investigational treatments during the study period.
- (6) Patients with poor compliance or inability to follow the study protocol.

2.3. Randomization and blinding

Eligible patients will be randomly assigned to either the treatment group (Jinlong Zhi Xie Fang enema) or the

control group (Mesalazine oral treatment) using a computer-generated randomization table. The randomization will be performed by an independent statistician to minimize any potential bias.

Blinding will be maintained throughout the study: both patients and researchers assessing clinical outcomes will be blinded to the treatment group assignments. This double-blind design ensures the objectivity of the assessment process and minimizes bias in the evaluation of outcomes.

2.4. Treatment protocol

2.4.1. Treatment group

Patients in the treatment group will receive Jinlong Zhi Xie Fang enema. The formula will be prepared by boiling a combination of herbs traditionally used in Miao medicine, including Si Leng Cao (*Houttuynia cordata*), Shi Hun Cao (Chronic Wound Herb), Suan Cai (Sour Cabbage), Bai Tou Guo (*Cresson*), and Long Ya Cao (Dragon Grass). The herbal decoction will be concentrated and administered as an enema. Each patient will receive a 200 mL enema once daily, to be administered in the evening before bedtime. The treatment will continue for 4 weeks.

2.4.2. Control group

Patients in the control group will receive Mesalazine, a 5-aminosalicylic acid (5-ASA) drug, which is commonly used for UC treatment. The dose will be 0.5 g of Mesalazine, administered three times daily, for a total of 4 weeks. Mesalazine will be taken orally in the form of enteric-coated tablets or granules as per the manufacturer's instructions.

Both groups will be instructed to avoid other medications commonly used for UC during the study period (e.g., corticosteroids, immunosuppressants), and any patients using such medications will be excluded from the study. Additionally, all participants will be advised to avoid eating spicy or irritating foods and will be instructed to follow a mild, easily digestible diet during the treatment period.

2.5. Outcome measures

2.5.1. Primary outcome

Clinical symptom improvement, including diarrhea (daily stool frequency and consistency), abdominal pain (VAS score 0–10), and stool blood (graded scale). Symptoms will be evaluated at baseline, 2 weeks, and 4 weeks.

2.5.2. Secondary outcomes

- (1) Mucosal barrier function: Colonoscopy and biopsy at baseline and 4 weeks, assessed by Mayo score and histological grading.
- (2) Safety: Adverse events recorded and classified by severity and relevance; liver and kidney function monitored through blood tests; other side effects like gastrointestinal discomfort or allergic reactions tracked.

2.6. Statistical analysis

Data will be analyzed using SPSS software (version 20.0, IBM Corporation). The primary outcome measures (symptom improvement) will be analyzed using paired t-tests to compare changes from baseline to post-

treatment within each group, and independent t-tests will be used to compare between the two groups at each time point.

For non-normally distributed data, the Mann-Whitney U test will be applied. Categorical data, such as the presence of adverse events, will be analyzed using the Chi-square test. A *P*-value of < 0.05 will be considered statistically significant.

2.7. Ethical considerations

This study will be conducted in full compliance with the principles outlined in the Declaration of Helsinki. Informed consent will be obtained from all participants, and the confidentiality of all personal information will be maintained. Any adverse events or concerns regarding patient safety will be immediately reported to the ethics committee for review.

3. Results

3.1. Patient demographics and baseline characteristics

Forty UC patients were randomized into treatment (Jinlong Zhi Xie Fang enema) and control (Mesalazine) groups, with comparable age, gender, disease duration (~5 weeks), and baseline severity (Mayo scores ~8.1 vs. 8.4).

3.2. Clinical symptom improvement

After 4 weeks, both groups improved, but the treatment group showed greater reductions in diarrhea (4.3→2.1 vs. 4.1→3.4 times/day), abdominal pain (VAS 6.5→2.2 vs. 6.2→2.9), and stool blood presence (75% to mild vs. 50% mild-moderate).

3.3. Intestinal mucosal barrier repair

Endoscopic Mayo scores and histopathology showed better mucosal healing in the treatment group (Mayo 2.5→1.2 vs. 2.6→1.8; histological damage 2.6→1.1 vs. 2.5→1.7).

3.4. Safety and adverse events

Both treatments were safe. Mild abdominal discomfort (15%) occurred in the treatment group, while the control group reported higher rates of GI discomfort (25%). No major liver or kidney issues were observed.

3.5. Statistical analysis

SPSS analysis confirmed significantly better clinical and mucosal outcomes in the treatment group (*P* < 0.05).

3.6. Summary of results

The Jinlong Zhi Xie Fang enema group showed superior symptom relief, mucosal repair, and a favorable safety profile compared to oral Mesalazine.

4. Discussion

4.1. Interpretation of findings

This study demonstrates that Jinlong Zhi Xie Fang enema is significantly more effective than Mesalazine in improving symptoms and promoting mucosal healing in UC patients with large intestine damp-heat syndrome. The enema's targeted action on mucosal areas, based on Miao medicine principles, enhances therapeutic efficacy while minimizing systemic side effects. Endoscopic and histopathological improvements further support its role in mucosal repair, aligning with previous findings on TCM-based treatments for UC.

4.2. Comparison with conventional treatments

Compared to Mesalazine, Jinlong Zhi Xie Fang enema showed superior symptom relief, mucosal healing, and a better safety profile, with fewer gastrointestinal and liver-related side effects. Its localized delivery ensures higher concentrations at inflammation sites, providing an advantage over systemic therapies like Mesalazine.

4.3. Mechanisms of action

Jinlong Zhi Xie Fang's key herbs, such as *Houttuynia cordata* and Sour Cabbage, exert anti-inflammatory, detoxifying, and mucosal healing effects. They reduce pro-inflammatory cytokines, clear damp-heat, and support gut barrier integrity, collectively addressing UC pathology and symptoms.

4.4. Clinical implications

Jinlong Zhi Xie Fang enema offers a promising alternative or adjunct for UC management, particularly for patients intolerant to standard treatments. Its holistic, localized approach and favorable safety profile make it a valuable addition to clinical practice.

4.5. Limitations and future research directions

The study's single-center design and short duration limit generalizability. Future multi-center, long-term studies are needed to validate findings and explore molecular mechanisms to support standardization of the formulation.

5. Conclusion

5.1. Summary of key findings

This study showed that Jinlong Zhi Xie Fang Enema was significantly more effective than Mesalazine in improving UC symptoms and promoting mucosal healing in patients with large intestine damp-heat syndrome. The enema group had greater reductions in diarrhea, abdominal pain, and stool blood, along with better endoscopic and histological mucosal repair. Jinlong Zhi Xie Fang also demonstrated a favorable safety profile, with fewer side effects compared to Mesalazine.

5.2. Clinical implications

Given the need for effective and safe UC therapies, Jinlong Zhi Xie Fang Enema offers a promising alternative, particularly for patients unresponsive or intolerant to conventional treatments. Its localized action allows targeted symptom relief and mucosal repair with minimal systemic side effects, making it a strong candidate for

long-term UC management.

5.3. Study limitations and future research

Limitations include the single-center design, small sample size, and short 4-week duration. Future larger, multi-center studies with long-term follow-up are needed to confirm efficacy, assess relapse prevention, and elucidate the immune-modulating mechanisms of Jinlong Zhi Xie Fang.

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Disclosure statement

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References

- [1] He Y, Wang J, Zheng C, 2025, Research Progress on Traditional Chinese Medicine Treatment of Ulcerative Colitis. *Guangming Traditional Chinese Medicine*, 40(1): 195–198. DOI: 10.3969/j.issn.1003-8914.2025.01.056
- [2] Bu Z, Liu F, Hou W, et al., 2025, Multi-Center Cross-Sectional Study on the Acceptability of Ulcerative Colitis Patients to Traditional Chinese Medicine Therapy Such as Traditional Chinese Patent Medicines and Simple Preparations. *China Pharmacovigilance*, 22(2): 183–187, 220–221. DOI:10.19803/j.1672-8629.20240212.
- [3] Ma Y, Wang H, Ding L, et al., 2025, Research Progress on Traditional Chinese Medicine for Repairing Intestinal Mucosal Barrier and Treating Ulcerative Colitis. *Chinese Journal of Ethnic and Folk Medicine*, 34(3): 71–75. DOI: 10.3969/j.issn.1007-8517.2025.03. zgmzmjyzz202503014
- [4] Li X, Li J, Cao Z, et al., 2024, Research Progress on Iron Death, Ulcerative Colitis and Traditional Chinese Medicine Treatment. *World Science and Technology – Modernization of Traditional Chinese Medicine*, 26(4): 861–867. DOI: 10.11842/wst.20230405003
- [5] Wen N, Huang C, Hu Y, 2025, Exploring the Relationship Between Ulcerative Colitis and Gut Microbiota, as Well as the Cold and Hot Properties of Fecal Microbiota Based on Traditional Chinese Medicine. *Chinese Medicine Review*, 31(1): 153–168. DOI: 10.13862/j.cn43-1446/r.2025.01.027
- [6] Liu L, Zhao M, He J, et al., 2024, Exploring the Traditional Chinese Medicine Syndrome Characteristics and Differentiation Rules of Ulcerative Colitis Based on Hidden Structure Model. *Chinese Medicine Guide*, 30(5): 140–160. DOI: 10.13862/j.cn43-1446/r.2024.05.027
- [7] Mo J, Huang Y, Tu B, et al., 2024, Research Hotspots and Future Prospects of Traditional Chinese Medicine in the Treatment of Ulcerative Colitis: Visualization Analysis Based on CiteSpace. *Western Traditional Chinese Medicine*, 37(12): 65–70. DOI: 10.12174/j.issn. 2096-9600.2024.12.16
- [8] Zhu X, Deng X, Dou D, et al., 2024, Traditional Chinese Medicine Diagnosis and Treatment of Ulcerative Colitis Based on Intestinal Ultrasound. *Beijing Journal of Traditional Chinese Medicine*, 43(11): 1323–1326. DOI: 10.16025/6.1674-1307.2024.11.021
- [9] Wang J, Qi H, Guo J, 2024, Research Progress on Traditional Chinese Medicine Treatment of Ulcerative Colitis. *Journal*

- of Practical Chinese Medicine, 38(2): 106–109. DOI: 10.13729/j.issn.1671-7813. Z20230049
- [10] Sun Z, Yang L, Tang Y, 2024, Exploring the Medication Rules of Traditional Chinese Medicine for Treating Damp Heat Ulcerative Colitis Based on Data Mining. *Guangming Traditional Chinese Medicine*, 39(22): 4451–4455. DOI: 10.3969/j.issn.1003-8914.2024.22.001
- [11] Jin H, Feng W, 2024, Observation on the Therapeutic Effect of Acupuncture and Moxibustion in Treating Chronic Ulcerative Colitis. *Inner Mongolia Journal of Traditional Chinese Medicine*, 43(2): 98–100.
- [12] Wang D, Tan W, Jin L, et al., 2024, Observation on the Clinical Efficacy of Mangzhen Combined with Traditional Chinese Medicine Syndrome Differentiation Intervention for Ulcerative Colitis of Liver Stagnation and Spleen Deficiency Type. *Grassroots Traditional Chinese Medicine*, 3(5): 29–33. DOI: 10.20065/j.cnki.btcn.20240094
- [13] Yang H, Li Y, Tian X, et al., 2025, Research Progress on Signaling Pathways in the Treatment of Ulcerative Colitis with Traditional Chinese Medicine. *Chinese New Drugs and Clinical Pharmacology*, 36(2): 299–306. DOI: 10.19378/j.issn.1003-9783.2025.017
- [14] Shu Y, Yu D, Rong Y, et al., 2024, Research Progress on the Mechanism of Traditional Chinese Medicine Improving Ulcerative Colitis Based on the PI3K/AKT Signaling Pathway. *Chinese Journal of Traditional Chinese Medicine Information*, 31(2): 191–196. DOI: 10.19879/j.cnki. 1005-5304.20230282
- [15] Chen H, Yang Z, 2024, Visual Analysis of Knowledge Graph on Traditional Chinese Medicine Treatment of Ulcerative Colitis. *Clinical Research of Traditional Chinese Medicine*, 16(7): 123–131. DOI: 10.3969/j.issn.1674-7860.2024.07.023
- [16] Qin J, Zhang X, Zhu Z, et al., 2024, Review of Traditional Chinese Medicine Syndrome Elements and Differentiation of Ulcerative Colitis. *Journal of Shaanxi University of Traditional Chinese Medicine*, 47(4): 7–11. DOI: 10.13424/j.cnki. jsctcm. 2022.4.002
- [17] Li X, Zhang T, Wen J, et al., 2024, Research Progress on the Regulation of Endoplasmic Reticulum Stress in the Treatment of Ulcerative Colitis by Traditional Chinese Medicine. *Shanxi Traditional Chinese Medicine*, 40(1): 64–66, 70. DOI: 10.20002/j.issn.1000-7156.204.025
- [18] Xu Y, Wang J, Lei G, et al., 2024, Interpretation of Professor Shen Shuwen's Experience in Distinguishing and Treating Ulcerative Colitis, a Renowned Traditional Chinese Medicine Practitioner. *Journal of Shaanxi University of Traditional Chinese Medicine*, 47(4): 12–17. DOI: 10.13424/j.cnki. jsctcm. 2022.4.003
- [19] Wu H, Chen L, Yang W, et al., 2023, Research on the Mechanism of Traditional Chinese Medicine in Treating Ulcerative Colitis and Its Lung Injury. *Chinese Journal of Basic Chinese Medicine*, 29(2): 339–344.
- [20] Zhang Y, Liu X, 2024, The Pathogenesis of Ulcerative Colitis and the Progress of Traditional Chinese Medicine Intervention. *Journal of Practical Chinese Medicine*, 38(6): 136–138. DOI: 0.13729/j.issn.1671-7813. Z20231053

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Application of Responsibility-based Holistic Nursing in Elderly Patients with Severe Pneumonia

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Abstract: *Objective:* To explore the clinical effects of applying responsibility-based holistic nursing in elderly patients with severe pneumonia. *Methods:* Ninety-six elderly patients with severe pneumonia admitted to a hospital from January 2023 to December 2024 were selected and divided into an observation group (52 cases) and a control group (44 cases) based on a random number table method. The observation group received responsibility-based holistic nursing, while the control group received basic nursing. The clinical effects (time to normalize body temperature, disappearance of cough, disappearance of dyspnea symptoms, disappearance of lung rales, changes in oxygenation index) and nursing satisfaction were observed in both groups. *Results:* The observation group showed superior results compared to the control group in terms of time to normalize body temperature, disappearance of cough, disappearance of dyspnea symptoms, disappearance of lung rales, and changes in oxygenation index, with statistically significant differences ($P < 0.05$). The satisfaction rate with nursing services in the observation group (92.31%) was significantly higher than that in the control group (86.36%) ($P < 0.05$). *Conclusion:* Implementing responsibility-based holistic nursing in elderly patients with severe pneumonia can improve their oxygenation function, enhance quality of life, and increase nursing satisfaction.

Keywords: Responsibility-based holistic nursing; Elderly; Severe pneumonia

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1. Introduction

Elderly patients with severe pneumonia often face critical conditions, multiple complications, and significant treatment challenges. Inappropriate management can easily lead to various complications and even death^[1]. Therefore, it is essential to implement scientific nursing interventions for these patients. Responsibility-based holistic nursing combines the advantages of traditional nursing with modern nursing concepts, enriched with humanistic care and holistic nursing connotations, to better meet patients' needs, improve their quality of life, and promote recovery^[2]. This study selected 96 elderly patients with severe pneumonia admitted to a hospital

from January 2023 to December 2024 for investigation. The results showed that the clinical efficacy and nursing satisfaction of elderly patients with severe pneumonia who received responsibility-based holistic nursing were significantly better than those of the control group, with statistically significant differences. This indicates that responsibility-based holistic nursing positively impacts the treatment effectiveness and nursing satisfaction of elderly patients with severe pneumonia, effectively improving nursing quality. The detailed report is as follows.

2. Materials and methods

2.1. General information

A total of 96 elderly patients with severe pneumonia admitted to a hospital from January 2023 to December 2024 were selected and divided into an observation group (52 cases) and a control group (44 cases) based on a random number table method. There were no statistically significant differences in age, gender, or disease severity between the two groups ($P > 0.05$), making them comparable (see **Table 1**).

Inclusion criteria: Elderly patients aged ≥ 65 years; meeting the diagnostic criteria for severe pneumonia in the “Guidelines for the Diagnosis and Treatment of Community-Acquired Pneumonia in Chinese Adults (2023 Edition)” and confirmed by chest CT/X-ray and laboratory tests (such as PCT, CRP, blood routine); needing to satisfy at least one of the following: oxygenation index ($\text{PaO}_2/\text{FiO}_2$) $\leq 250\text{mmHg}$, requiring mechanical ventilation or high-flow nasal cannula (HFNC), complicated with sepsis or multiple organ dysfunction (SOFA score ≥ 2); patients or their families signed informed consent and could cooperate with nursing interventions and follow-up.

Exclusion criteria: Advanced malignant tumors (expected survival < 3 months); severe cardiac insufficiency (NYHA class IV) or end-stage liver and kidney failure; active tuberculosis, pulmonary embolism, or interstitial lung disease; those who withdrew from treatment or were automatically discharged within 24 hours of admission; those already participating in other interventional clinical studies; those with Alzheimer’s disease or mental illness unable to cooperate with nursing assessments.

Table 1. General information

Group	Control group ($n=44$)	Observation group ($n=52$)	t/χ^2	P
Age (years)	65.32 ± 6.78	66.15 ± 7.23	0.582	> 0.05
Gender (Male/Female)	24(54.55)/20(45.45)	28(53.85)/24(46.15)	0.011	> 0.05
Duration of illness (months)	3.25 ± 1.42	3.18 ± 1.37	0.251	> 0.05

2.2. Nursing methods

2.2.1. Observation group patients

- (1) Inform patients of their condition and treatment plan promptly after admission.
- (2) Conduct lung auscultation and observe the patient’s respiratory status.
- (3) Closely monitor the patient’s vital signs, including heart rate (HR), respiratory rate (RR), blood pressure (BP), blood oxygen saturation (SpO_2), and body temperature (T).
- (4) Communicate effectively with the patient’s family members, encourage patients to actively cooperate with treatment, and alleviate their psychological stress^[3]
- (5) Implement responsibility-based holistic nursing while providing routine basic nursing to the patients.
- (6) Strengthen the nursing of underlying diseases, such as providing nebulization and oxygen inhalation for

cardiopulmonary insufficiency, and enhancing nutritional support.

- (7) Pay attention to the patient's eating situation, perform oral care to prevent food from entering the trachea and inducing aspiration pneumonia.
- (8) Administer medication strictly according to doctor's orders and closely observe side effects.
- (9) Inform patients of discharge instructions.

2.2.2. Control group patients

- (1) Provide routine basic nursing, including promptly notifying doctors of changes in the patient's condition and assisting in treatment.
- (2) Adjust the dietary structure according to the patient's physical condition to ensure balanced nutrition.
- (3) Maintain fresh indoor air to avoid cross-infection^[4].
- (4) Ensure adequate rest time for patients.

2.3. Observation indicators

Compare the clinical effects (time to normalize body temperature, disappearance of cough, disappearance of dyspnea symptoms, disappearance of lung rales, changes in oxygenation index) and nursing satisfaction between the two groups.

- (1) Body temperature: refers to the average body temperature drop of no more than 0.36°C per hour for normal people at a room temperature of 24°C, while the average body temperature of pneumonia patients is lower than this value.
- (2) Cough: refers to the process of discharging sputum and purulent secretions from the trachea or bronchi through breathing, clinically used to judge the severity of the disease based on cough and sputum symptoms^[5].
- (3) Time to relief of dyspnea symptoms: refers to the time when patients show improvement and gradual disappearance of symptoms after reasonable treatment^[6].
- (4) Lung rales: refer to a sound produced by the accumulation of air in the alveoli, generally related to lung texture disorders^[7]; observe whether there is a trend of increase or decrease.
- (5) Oxygenation index: the percentage of the maximum exhalation peak flow after inhaling pure oxygen relative to the predicted value, which is an important indicator to measure the degree of hypoxia in the body^[8], reflecting the oxygen demand status of body tissues and organs.
- (6) Nursing satisfaction: measured using a self-made anonymous survey questionnaire, categorized into very satisfied, satisfied, and dissatisfied. Satisfaction rate = (very satisfied + satisfied) ÷ total number of cases × 100%.

2.4. Statistical processing

Statistical analysis was performed using SPSS 27.0 software. Measurement data were expressed as mean ± standard deviation (±s), and comparisons between groups were made using the t-test. Count data were expressed as rates (%), and comparisons between groups were made using the chi-square test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of clinical effects between the two groups

The observation group showed better results in terms of time to normalize body temperature, disappearance of cough, disappearance of dyspnea symptoms, disappearance of lung rales, and changes in oxygenation index compared to the control group. The differences were statistically significant ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of clinical effects between the two groups [$\pm s$]

Group	Temperature returns to normal time (d)	Cough disappearance time (d)	Dyspnea symptom disappearance time (d)	Lung rales disappearance time (d)	Oxygenation index (mmHg)
Control group ($n=44$)	3.25 ± 0.68	5.42 ± 1.23	4.36 ± 1.05	6.15 ± 1.32	285.34 ± 32.15
Observation group ($n=52$)	2.13 ± 0.54	3.87 ± 0.96	3.02 ± 0.88	4.28 ± 1.07	342.67 ± 28.74
t	8.765	6.892	6.543	7.421	8.934
P	0.000	0.000	0.000	0.000	0.000

3.2. Comparison of nursing satisfaction between the two groups

The satisfaction rate of nursing services among patients in the observation group (92.31%) was significantly higher than that in the control group (86.36%) ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of nursing satisfaction between the two groups [$n(\%)$]

Group	Very satisfied	Satisfied	Dissatisfied	Satisfaction rate
Control group ($n = 44$)	18(40.91)	20(45.45)	6(13.64)	38(86.36)
Observation group ($n = 52$)	30(57.69)	18(34.62)	4(7.69)	48(92.31)
χ^2				6.472
P				0.034

4. Discussion

Severe pneumonia is a common disease among elderly patients, especially prone to complications on the basis of respiratory system dysfunction and decreased immune system. Due to its critical condition, long treatment duration, and being prone to complications, coupled with the degradation of cognitive and behavioral abilities common in elderly patients, as well as their sensitivity to pain and hospital environments, it can easily lead to physical and psychological impairments, increasing the difficulty of nursing work. Therefore, actively implementing responsibility-based holistic nursing can improve patients' various indicators and enhance their quality of life. The responsibility-based holistic nursing adopts a responsibility nursing model, emphasizing patient-centeredness, proactive observation of the patient's condition, and providing effective assistance based on the patient's actual situation, thereby reflecting a good relationship between nurses and patients, and alleviating negative emotions such as fear, anxiety, and tension.

Simultaneously, promoting patient participation in treatment decisions through group discussions and other methods helps establish a healthy and positive attitude towards life, thereby improving treatment outcomes.

Elderly patients with severe pneumonia face critical conditions, and without effective treatment and care, they can develop multiple complications, leading to poor patient outcomes. Elderly patients often experience varying degrees of cognitive decline and psychosocial issues, which, to some extent, also increase the difficulty of nursing work. Responsibility-based holistic nursing, on the other hand, is a novel nursing model that focuses on the “person” as the center, prioritizing patients’ life needs, social functions, and living abilities. By providing high-quality personalized care, it meets patients’ physiological, psychological, and other needs^[9]. The holistic concept of responsibility-based nursing emphasizes a people-oriented approach, focuses on individual differences among patients, and adopts a combination of comprehensive evaluation and classified management. Based on the specific conditions of patients, reasonable nursing measures are developed to maximize patients’ potential^[10].

This study shows that the observation group had better results than the control group in terms of time to normalize body temperature, disappearance of cough, disappearance of dyspnea symptoms, disappearance of lung rales, and changes in oxygenation index, with statistically significant differences ($P < 0.05$). Additionally, the satisfaction rate of nursing services among patients in the observation group (92.31%) was significantly higher than that in the control group (86.36%) ($P < 0.05$). Evidently, implementing responsibility-based holistic nursing for elderly patients with severe pneumonia can improve their clinical symptoms, enhance quality of life, help alleviate patient suffering, reduce hospital stay, and is worthy of promotion and application. Given that pneumonia often occurs in the elderly and is frequently associated with multiple medical comorbidities, leading to poor nutritional status, low resistance, and susceptibility to various infections, resulting in complex conditions, long treatment durations, and prone to complications.

The advantage of responsibility-based holistic nursing lies in strengthening communication between nursing staff and patients, gaining patients’ trust, thereby enhancing nurses’ work enthusiasm, strengthening nurse-patient relationships, timely grasping patients’ psychological changes, meeting their spiritual needs, and facilitating patients’ recovery. Establishing an equal relationship between nurses and patients, working closely together, and making joint efforts to overcome the disease can yield maximum benefits. Considering that most elderly patients with severe pneumonia suffer from malnutrition, low immune system, and difficulty in discharging viscous respiratory secretions, coupled with comorbidities such as hypertension, diabetes, and coronary heart disease, if not effectively controlled, they can easily trigger or exacerbate other systemic pathologies. Hence, corresponding measures should be taken to ensure patients’ physical recovery.

Under the responsibility-based holistic nursing model, medical staff fully consider patients’ physiological and psychological needs, adopt responsibility-based nursing, and develop detailed nursing plans, clarifying each nurse’s responsibilities, implementing hierarchical management, and fully leveraging team members’ enthusiasm and creativity. Simultaneously, they focus on continuous quality improvement in nursing. In nursing work, the head nurse regularly convenes meetings to guide the entire nursing team to learn new nursing knowledge and techniques, continuously improving nursing professionalism; the nursing department organizes 1–2 training sessions monthly to enhance overall nursing standards; the department organizes weekly morning shift changes to summarize nursing work for the week, analyze existing problems, propose solutions, discuss and resolve difficult issues, standardize various operational procedures, and ensure nursing safety; clinical departments hold 1–2 academic lectures monthly to introduce the latest nursing developments domestically and internationally, enabling all nurses to gain experience through learning and improve through practice, comprehensively enhancing the professional skills and service capabilities of the entire nursing team.

5. Conclusion

In summary, implementing responsibility-based holistic nursing for elderly patients with severe pneumonia can improve their clinical symptoms, enhance their oxygenation function, enhance quality of life, and increase nursing satisfaction. However, due to factors such as economic conditions, human resource allocation, and hospital culture, the promotion of responsibility-based holistic nursing in China is still not ideal. How to better integrate responsibility-based holistic nursing into the modern nursing system is an urgent problem to be solved. Therefore, relevant departments should attach importance to the promotion of responsibility-based nursing to meet the growing needs of patients and provide them with high-quality medical services.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Sun J, 2022, The Value of Holistic Nursing Responsibility System in the Care of Elderly Patients With Severe Pneumonia. *Medical Diet Therapy and Health*, 20(11): 96–98, 106.
- [2] Shen T, 2021, Application of the Holistic Nursing Responsibility System in the Care of Elderly Patients With Severe Pneumonia. *Mother and Baby World*, 2021(10): 227.
- [3] Wu Y, 2020, Application of the Holistic Nursing Responsibility System in the Care of Elderly Patients With Severe Pneumonia. *Health Must-Read*, 2020(2): 124.
- [4] Li X, 2024, The Impact of Hierarchical Holistic Nursing Responsibility System Combined With Standardized Nursing on Patients With Severe Pneumonia and Heart Failure. *China Standardization*, 2024(24): 326–328, 336.
- [5] Wu H, 2022, Observation on the Application Effect of the Holistic Nursing Responsibility System in the Care of Elderly Patients With Severe Pneumonia. *Marriage, Childbearing, and Health*, 28(24): 73–75.
- [6] Lei T, 2022, Observation on the Clinical Effect of Applying the Holistic Nursing Responsibility System to Elderly Patients With Severe Pneumonia. *Capital Food and Medicine*, 29(10): 101–103.
- [7] Liu W, 2021, Observation and Analysis of the Implementation of the Holistic Nursing Responsibility System Intervention to Improve Nursing Effects in Elderly Patients With Severe Pneumonia. *Smart Healthcare*, 7(30): 189–191.
- [8] Ye Y, Chen D, Li W, et al., 2021, Clinical Value Analysis of Holistic Nursing Interventions for Elderly Patients With Severe Pneumonia. *Health Care Guide*, 2021(4): 211.
- [9] Zhao C, Yang H, Qin G, et al., 2019, Analysis of the Nursing Effect of the Holistic Nursing Responsibility System on Lung Function and Blood Gas Indicators in Patients With Severe Pneumonia. *International Journal of Nursing*, 38(20): 3384–3387.
- [10] Liu J, 2020, The Application Value of Holistic Nursing Responsibility System Based on Nursing Procedures in ICU Patients With Ventilator-Associated Pneumonia. *Henan Medical Research*, 29(9): 1712–1714.

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Research Status and Progress of Related Indicators for Early Diagnosis and Prognosis Evaluation of Autoimmune Encephalitis

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Abstract: Addressing the challenges of difficult early diagnosis and the incomplete prognosis evaluation system for Autoimmune Encephalitis (AE), this study comprehensively reviews the relevant indicators for early diagnosis and prognosis evaluation of AE. The analysis reveals that multiple indicators currently exhibit unique value in the diagnosis and treatment of AE, but each has its limitations. This article aims to systematically review these indicators and clarify their current application in clinical practice, to help improve the accuracy of early diagnosis and prognosis evaluation of AE, and provide a theoretical basis for clinicians to develop more effective treatment strategies.

Keywords: Autoimmune Encephalitis; Early diagnosis; Prognosis evaluation; Biomarker

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1. Introduction

Within the scope of neurological diseases, Autoimmune Encephalitis (AE) is experiencing a significant increase in incidence and has become a focus of clinical and scientific research. The clinical manifestations of AE are extremely complex, including severe abnormalities in mental behavior. Patients may experience unexplained mania, depression, or hallucinations. Cognitive function can also be severely impaired, with significant decreases in memory and attention. Frequent epileptic seizures are also one of the common symptoms. These manifestations are highly similar to a variety of neurological diseases, posing significant challenges for early and accurate diagnosis. Relevant clinical data shows that more than half of AE patients are misdiagnosed during their first visit, resulting in the loss of valuable treatment opportunities. If AE is not intervened in a timely and effective manner early on, patients may face severe neurological sequelae, such as permanent cognitive dysfunction and limb movement disorders, which seriously affect daily life and social integration, and increase the burden of family care and economic pressure. Some critically ill patients may even lose their lives due to rapid deterioration

of the disease. Currently, there is a lack of specific and sensitive indicators for the early diagnosis of AE, and the prognosis evaluation system also needs to be improved. Therefore, in-depth research on relevant indicators for early diagnosis and prognosis evaluation of AE, and the construction of a more precise and efficient diagnosis and treatment system are crucial to improving patients' clinical outcomes and reducing the disease burden. This is an important topic that urgently needs to be broken through in the current field of neuromedicine.

2. Pathogenesis of AE

2.1. Abnormal immune system

The core function of the human immune system is to recognize and eliminate foreign pathogens while maintaining immune tolerance to its own tissues ^[1]. In patients with AE, this balance is disrupted, leading to abnormal activation of the immune system ^[2]. Generally speaking, T and B lymphocytes work together to fight foreign antigens. However, in AE, the antigen-presenting cells mistakenly present their own neuronal antigens to T lymphocytes, leading to the activation of T lymphocytes and triggering an immune response. Activated T lymphocytes further stimulate B lymphocytes, promoting their differentiation into plasma cells and secreting a large number of antibodies targeting their own neurons. Additionally, regulatory T cell dysfunction fails to effectively inhibit overactive immune responses, leading to continuous immune attacks and ultimately causing brain tissue damage. For example, in anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, the immune system produces specific antibodies against the NMDAR on the surface of neurons, triggering a series of immune responses and disrupting normal neuronal function.

2.2. Role of the blood-brain barrier

The blood-brain barrier, formed by brain capillary endothelial cells, basement membrane, pericytes, and astrocytes, plays a crucial role in maintaining the stability of the central nervous system. Generally, the blood-brain barrier can effectively prevent the invasion of pathogens, toxins, and macromolecules. However, in the pathogenesis of AE, various factors can increase the permeability of the blood-brain barrier. Studies have found that under viral infection or inflammatory stimulation, the expression of adhesion molecules on cerebrovascular endothelial cells can absorb and cross the blood-brain barrier. Additionally, inflammatory mediators (such as TNF- α and IL-6) can damage the blood-brain barrier, leading to barrier impairment and increased permeability. When the permeability of the blood-brain barrier increases, autoantibodies and immune cells in the circulatory system can invade brain tissue, bind to surface antigen molecules on neurons, launch an "immune attack," trigger an inflammatory response, and ultimately induce AE.

2.3. Pathogenic mechanism of autoantibodies

The autoantibodies produced in AE patients can damage neurons through various mechanisms. Taking anti-NMDAR antibodies as an example, after binding to the GluN1 subunit of NMDAR, these antibodies reduce the receptors on the neuronal surface through endocytosis, leading to decreased neuronal reactivity to glutamate and affecting neurotransmitter transmission and neuronal excitability. Furthermore, antibody binding can also activate the complement system, forming membrane attack complexes that directly disrupt the integrity of neuronal cell membranes and trigger apoptosis. Anti-leucine-rich glioma-inactivated protein 1 (LGI1) antibodies, on the other hand, bind to LGI1 protein, interfering with its interaction with ADAM22 and ADAM23, and affecting potassium

channel function. This leads to abnormal neuronal excitability, which in turn causes typical symptoms such as faciobrachial dystonic seizures. Different types of autoantibodies damage neuronal function through their unique targets and mechanisms, ultimately resulting in the diverse clinical manifestations of AE.

3. AE early diagnosis indicators

3.1. Cerebrospinal fluid immunoglobulins

The detection of cerebrospinal fluid (CSF) immunoglobulin levels is significant in the early diagnosis of AE. Under normal circumstances, the immunoglobulin content in CSF is relatively low and mainly consists of IgG. In AE patients, due to the activation of the immune response within the central nervous system, the immunoglobulin level in CSF often rises significantly. This has been confirmed by studies such as that conducted by Hu *et al.* ^[3]. In particular, the appearance of oligoclonal bands (OCBs) has high suggestive value for the diagnosis of AE. OCBs are immunoglobulin bands that appear in the CSF but are not detected in the serum, indicating localized immunoglobulin synthesis within the central nervous system. Additionally, an elevated IgG index in the CSF (reflecting the proportion of IgG synthesis in the CSF relative to the serum) is also commonly seen in AE patients ^[4].

3.2. Features of head MRI - FLAIR

Fluid-attenuated inversion recovery (FLAIR) sequences in head magnetic resonance imaging (MRI) play a crucial role in the early diagnosis of AE. AE patients often show characteristic changes on FLAIR sequences, with the most common being high signals in the limbic system areas such as the medial temporal lobe (especially the hippocampus), insula, and cingulate gyrus ^[5]. For example, in anti-LGI1 encephalitis, approximately 80% of patients may exhibit bilateral medial temporal lobe high signals on FLAIR, and some patients may be accompanied by hippocampal atrophy. Although the overall MRI positivity rate in anti-NMDAR encephalitis is relatively low (approximately 20%–40%), some patients may still show nonspecific high signals in the cortex or subcortex on FLAIR sequences. Additionally, some AE patients may exhibit abnormal signals in other brain regions, such as the frontal and parietal lobes. It should be noted that MRI-FLAIR findings are not specific to AE, as similar imaging manifestations may also occur in certain viral encephalitis, cerebral infarction, and other diseases. Therefore, MRI-FLAIR results need to be comprehensively analyzed in combination with the patient's clinical symptoms, cerebrospinal fluid examination, and antibody detection to improve the accuracy of early AE diagnosis.

3.3. The weight of video electroencephalogram

Video electroencephalogram (VEEG) can continuously record patients' brain electrical activity and synchronously monitor their clinical manifestations, providing unique advantages in the early diagnosis of AE. VEEG in AE patients often shows an increase in focal or diffuse slow waves, and some patients may exhibit epileptiform discharges, including spike waves, sharp waves, and spike-and-wave complexes. Additionally, VEEG can be used to monitor changes in AE patients' condition and evaluate treatment effectiveness. For example, as treatment progresses, the patient's brain electrical activity gradually returns to normal, and epileptiform discharges decrease or disappear, indicating improvement in the condition ^[6]. However, the interpretation of VEEG results has a certain degree of subjectivity, and some AE patients may not show significant abnormalities in brain electrical activity

early in the disease. Therefore, analysis by experienced electroencephalogram physicians and comprehensive judgment based on other examination results are necessary.

4. AE prognostic indicators

4.1. Antibody titer

The antibody titer in serum has a certain reference value for the prognosis evaluation of AE. Generally speaking, the higher the antibody titer in serum, the more severe the patient's disease and the worse the prognosis ^[7, 8]. Taking anti-NMDA encephalitis as an example, before receiving treatment, patients with higher antibody titers in their serum have a higher frequency of acute seizures, longer durations of coma, and a higher risk of developing neurological sequelae. Therefore, monitoring changes in antibody titers in serum during treatment can evaluate the efficacy of the treatment. If the antibody titer in the serum gradually decreases after immunotherapy, it indicates that the treatment is effective and the patient has a better prognosis. Conversely, it suggests that the patient's condition is not well-controlled and prone to recurrence.

4.2. Neutrophil-to-lymphocyte ratio in peripheral blood

The neutrophil-to-lymphocyte ratio (NLR) in peripheral blood is an important parameter that can reflect inflammation and immune homeostasis in the body. AE patients often have significantly elevated NLR levels. This was confirmed by the research of Miao *et al.*, who compared the peripheral blood cell counts of AE patients and healthy patients and found that the NLR has certain significance for the prognosis of AE ^[9].

Studies have shown that an increase in NLR is associated with disease severity and poor prognosis. An elevated NLR indicates the presence of excessive inflammatory responses and immune dysfunction in the body, which may exacerbate damage to brain tissue and have a negative impact on the patient's prognosis. For example, a study on AE patients showed that the NLR of patients with poor prognosis was significantly higher than that of patients with better prognosis. Additionally, NLR can be used to monitor patients' inflammatory responses during treatment. If the NLR gradually decreases to normal levels during treatment, it indicates that inflammation has been effectively controlled, and the patient's prognosis will be better. However, NLR is affected by many factors such as infection and stress, so other interfering factors need to be considered when using NLR to evaluate patients' prognosis ^[10].

4.3. High-density lipoprotein cholesterol

High-density lipoprotein cholesterol (HDL-C) has a potential protective role in the prognosis of AE. HDL-C not only participates in reverse cholesterol transport but also has various functions such as anti-oxidation, anti-inflammation, and anti-thrombosis. Studies have found that decreased serum HDL-C levels in AE patients are associated with disease severity and poor prognosis. Lower HDL-C levels may weaken its neuroprotective effects, making neurons more susceptible to immune attacks and inflammatory damage ^[11]. Clinical studies have also shown that AE patients whose HDL-C levels rebound after treatment have better neurological recovery and prognosis. Therefore, HDL-C is expected to become an important indicator for evaluating the prognosis of AE and guiding treatment.

4.4. B Lymphocyte-related cytokines

B lymphocytes play a critical role in the pathogenesis of AE, and various cytokines secreted by them have an

impact on disease prognosis. Interleukin-6 (IL-6) is an important proinflammatory cytokine, and its levels are often significantly elevated in the serum and cerebrospinal fluid of AE patients. High levels of IL-6 can promote the activation and proliferation of B lymphocytes, enhance immune responses, lead to increased inflammatory damage to brain tissue, and affect prognosis. Conversely, interleukin-10 (IL-10) is a cytokine with anti-inflammatory effects that can inhibit the activation of B lymphocytes and the secretion of proinflammatory cytokines. Studies have shown that AE patients have relatively low levels of IL-10, and the lower the IL-10 level, the more severe the patient's condition and the worse the prognosis. By regulating the levels of B lymphocyte-related cytokines, it is possible to improve the immune status of AE patients, thereby affecting disease prognosis.

5. Conclusion

In summary, the early diagnosis and prognosis evaluation of autoimmune encephalitis involve multiple indicators. In terms of pathogenesis, immune system abnormalities, blood-brain barrier disruption, and autoantibody pathogenesis are key links. Early diagnostic indicators such as cerebrospinal fluid immunoglobulin, head MRI-FLAIR features, and video electroencephalogram have their respective advantages but also have certain limitations, requiring comprehensive application to improve diagnostic accuracy. Prognostic indicators include antibody titer, neutrophil-to-lymphocyte ratio in peripheral blood, high-density lipoprotein cholesterol, B lymphocyte-related cytokines, and neurobiological factors of nerve injury. These indicators reflect the severity of the patient's condition, immune status, and nerve damage from different perspectives and are important for evaluating prognosis. However, the early diagnosis and prognosis evaluation of AE still face many challenges, such as insufficient specificity of some indicators and differences in research results. In the future, further research is needed on the pathogenesis of AE, exploring more sensitive and specific biomarkers, optimizing existing detection methods, and establishing a comprehensive multi-indicator diagnosis and prognosis evaluation system to improve the diagnosis and treatment level of AE and improve patients' clinical outcomes.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Li W, Wen S, Chen J, et al., 2025, Relationship Between Serum Immunoglobulin Levels and Disease Prognosis in Children With Autoimmune Encephalitis. *Journal of Clinical and Experimental Medicine*, 24(01): 54–58.
- [2] Ma H, Xu J, Hao F, et al., 2023, Clinical Characteristics and Treatment Analysis of Autoimmune Encephalitis. *Chinese Journal of Practical Nervous Diseases*, 26(05): 566–571.
- [3] Hu X, Li J, Xu W, et al., 2024, Clinical Diagnostic Value of Cerebrospinal Fluid Immunoglobulins, Peripheral Blood Inflammatory Cell Indicators, and Cellular Immune Indicators in Children With Autoimmune Encephalitis. *China Modern Medicine*, 31(23): 105–108.
- [4] Wang D, Zheng G, Shao C, et al., 2023, The Value of Cerebrospinal Fluid Indicators in the Differential Diagnosis of Autoimmune Encephalitis and Viral Encephalitis. *Labeled Immunoassays and Clinical Medicine*, 30(02): 186–190, 222.
- [5] Cao D, Zhang L, Guo X, et al., 2017, Analysis of Clinical Manifestations and MRI Features of Autoimmune Encephalitis. *Chinese Journal of Neurology and Psychiatry*, 43(06): 341–345.

- [6] Wu G, Wang C, Huang N, et al., 2024, Discussion on the Correlation and Weight of Diagnostic Elements of Autoimmune Encephalitis. *Journal of Stroke and Nervous Diseases*, 41(03): 264–269.
- [7] Kuang Z, Liu B, Yang H, et al., 2020, Clinical Analysis and Dynamic Observation of Serum Antibodies in Anti-N-Methyl-D-Aspartate Receptor Encephalitis. *Chinese Journal of Neuroimmunology and Neurology*, 27(04): 270–275.
- [8] Gresa-Arribas N, Titulaer M, Torrents A, et al., 2014, Antibody Titres at Diagnosis and During Follow-Up of Anti-NMDA Receptor Encephalitis: A Retrospective Study. *Lancet Neurol*, 13(2): 167–177.
- [9] Miao C, Zhu Y, Liu P, 2023, Clinical Significance of the Neutrophil-to-Lymphocyte Ratio in Peripheral Blood of Patients With Autoimmune Encephalitis. *Modern Medicine and Health*, 39(12): 2049–2053.
- [10] Zhang Q, Shi Y, Yuan Y, 2024, Current Status of Cognitive Impairment in Patients With Autoimmune Encephalitis and Its Relationship With Poor Prognosis. *Chinese Journal of Practical Nervous Diseases*, 27(10): 1189–1194.
- [11] Liu Y, Ma L, Ma X, et al., 2022, Simple and Effective Serum Biomarkers With Potential for Predicting Status Epilepticus in Anti-N-Methyl-D-Aspartate Receptor Encephalitis. *BMC Neurol*, 22(1): 27.

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Analysis of the Effect of Comprehensive Nursing on the Psychological State of Patients with Pulmonary Micro-nodules

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Abstract: *Objective:* To explore the effect of comprehensive nursing on relieving psychological pressure in patients with pulmonary micro-nodules. *Methods:* One hundred and twenty patients with pulmonary micro-nodules who received diagnosis and treatment in our hospital from January 2024 to December 2024 were randomly divided into control and observation groups. The control group received routine nursing, while the observation group received comprehensive nursing. The Self-Rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) were used to evaluate the patients' psychological states before and after nursing. Patient satisfaction with nursing was analyzed using a nursing satisfaction survey scale. *Results:* After nursing, the SAS and SDS scores of the observation group were significantly lower than those of the control group ($P < 0.05$). The nursing satisfaction rates of the observation and control groups were 98.33% and 83.33%, respectively, with statistically significant differences ($P < 0.05$). *Conclusion:* Comprehensive nursing intervention for patients with pulmonary micro-nodules can effectively relieve their psychological pressure and improve nursing satisfaction, demonstrating clinical value.

Keywords: Pulmonary micro-nodules; Comprehensive nursing; SAS; SDS; Nursing satisfaction

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1. Introduction

Pulmonary micro-nodules generally refer to nodules with a diameter of < 1 cm, which are a common clinical lung disease with various inducing factors^[1-3]. With the popularization of low-dose lung cancer screening, more and more pulmonary micro-nodules are being detected. Pulmonary micro-nodules carry a certain risk of malignancy, and some patients may experience clinical symptoms such as elevated body temperature, cough, night sweats, and loss of appetite, which can stimulate patients psychologically and physiologically and reduce their quality of life. Therefore, this disease requires high attention.

Numerous clinical studies have shown that scientific and effective nursing intervention combined with

clinical treatment for patients with pulmonary micro-nodules can relieve their psychological pressure, improve treatment compliance, and assist in enhancing clinical efficacy ^[4]. However, conventional nursing intervention has significant limitations and cannot meet the clinical treatment needs of patients. Comprehensive nursing intervention is a clinically classic nursing measure that emphasizes providing patients with various nursing services, such as psychological, lifestyle, and health education to meet clinical treatment needs and thereby assist in improving clinical efficacy ^[5]. Based on the above, this study focused on analyzing the effect of comprehensive nursing on relieving psychological pressure in patients with pulmonary micro-nodules, aiming to provide a reference for subsequent clinical nursing.

2. Materials and methods

2.1. Basic data source

The sample consists of 120 patients with pulmonary micro-nodules, recorded from January 2024 to December 2024. They were randomly divided into a control group and an observation group, with 60 patients in each group. Among them, 75 patients presented with varying degrees of cough, chest tightness, chest pain, etc., while the other 45 patients were asymptomatic and were discovered through health screenings. The control group consisted of 39 males and 21 females, aged between 45 and 75 (mean age: 60.25 ± 6.23 years). The observation group consisted of 41 males and 19 females, aged between 44 and 76 (mean age: 60.96 ± 6.25 years). A comparison of the basic information between the two groups showed $P > 0.05$, indicating that the results are comparable.

Inclusion criteria: Patients who underwent CT scanning and were found to have round or quasi-circular nodules in their lungs, with nodule diameters less than 0.5 cm; patients with good compliance, normal understanding ability, and agreement to participate in this study.

Exclusion criteria: Patients with cognitive dysfunction or mental illness; patients with atelectasis, obstructive pneumonia, pleural effusion, or other pathological conditions.

2.2. Methods

2.2.1. Nursing in the control group patients

This group received routine nursing intervention, including medication nursing based on the patient's treatment plan, distributing health education brochures, patiently explaining factors related to the occurrence of the disease, treatment measures, precautions, and general treatment effects, to enhance patients' treatment information. Additionally, disease monitoring was strengthened, and any abnormalities were promptly reported to the doctor for treatment.

2.2.2. Nursing in the observation group

Patients in this group received comprehensive nursing intervention, which included the following aspects:

(1) Psychological nursing

After detecting pulmonary micro-nodules, patients may experience anxiety, nervousness, and other negative emotions, mainly due to concerns about the deterioration of the nodules. At this time, nurses need to actively communicate with patients, patiently explain the universality of this situation, popularize relevant medical knowledge about pulmonary micro-nodules, and correct patients' cognitive biases. Some patients may become emotionally excited or use excessive language after learning about their disease

condition. In such cases, nursing staff should maintain sufficient patience, provide explanations, help patients calm down, and encourage them to undergo treatment in their best state. Additionally, nurses need to communicate with patients' families and urge them to provide emotional support to the patients ^[6]. Playing soft music can also help divert their attention and relieve emotional stress.

(2) Diet nursing

After the onset of the disease, some patients may experience loss of appetite, which can affect the body's nutrition in the long run. Therefore, it is essential to emphasize dietary nursing for patients with pulmonary micro-nodules. Patients are advised to consume a diet rich in calories, protein, and vitamins, with a reasonable combination of foods, and to eat more fresh fruits and vegetables to enhance their body's resistance. During the treatment phase of the disease, patients should try to reduce their intake of fatty meat, dairy products, and spicy foods.

(3) Lifestyle nursing

For patients with a history of smoking, they are advised to quit smoking to avoid increasing the pressure on lung organs. They should avoid going to places with severe dust and pollen pollution, and if they do, they should wear a mask.

(4) Exercise nursing

Nurses guide patients in performing appropriate exercises based on their recovery status, thus promoting disease rehabilitation. Exercise programs can include Tai Chi, dancing, walking, jogging, etc., while actively participating in social activities to gain more support.

(5) Medication nursing

Patients are advised to strictly follow medical advice regarding medication. During medication, patients should be provided with detailed instructions on drug usage, possible adverse reactions, and response measures to reduce their resistance and fully enhance their medication compliance.

(6) Environmental nursing

During hospitalization, due to the large volume of hospital traffic and various microorganisms in the air, it is not conducive to disease recovery. Therefore, it is necessary to strengthen the environmental nursing of the ward, maintaining a quiet and clean environment while controlling the appropriate temperature and humidity.

2.3. Observation indicators

2.3.1. Psychological state evaluation

The SAS and SDS scales were used to evaluate patients' anxiety and depression before and after nursing. The total scores of both scales are 100 points. For the SAS scale, a critical value of 50 points indicates the presence of anxiety, and a higher score indicates more pronounced anxiety. For the SDS scale, a critical value of 53 points indicates the presence of depression, and a higher score indicates more pronounced depression.

2.3.2. Nursing satisfaction

A self-made nursing satisfaction survey scale was used to analyze patients' satisfaction with different nursing services, evaluating aspects such as nurses' language, tone, service content, and skills. The scale was divided into three levels: satisfied, basically satisfied, and unsatisfied. The sum of the satisfaction rate and the basic satisfaction rate represents the total satisfaction rate.

2.4. Statistical analysis

Statistical software SPSS 24.0 was used to analyze the differences between data. Chi-square and t-tests were used for counting and measurement data, respectively, with a significance level of $\alpha = 0.05$.

3. Results

3.1. Comparison of psychological states

Before nursing intervention, the scores of the SAS and SDS scales were similar between the two groups. After nursing intervention, the scores of the observation group were lower than those of the control group, with statistically significant differences ($P < 0.05$). The results are shown in **Table 1**.

Table 1. Comparison of SAS and SDS scale scores before and after nursing intervention between the two groups [(±s) points]

Group	SAS		SDS	
	Before nursing	After nursing	Before nursing	After nursing
Observation group (n = 60)	45.12 ± 2.32	30.05 ± 2.12	40.01 ± 3.58	29.56 ± 2.82
Control group (n = 60)	44.53 ± 3.96	34.46 ± 1.95	40.25 ± 3.25	33.03 ± 4.14
t Value	1.812	3.630	0.718	2.295
P Value	0.239	0.001	0.416	0.001

3.2. Comparison of nursing satisfaction

Under different nursing service conditions, the total nursing satisfaction rates of the observation group and the control group were 98.33% and 83.33%, respectively, with statistically significant differences ($P < 0.05$). The results are shown in **Table 2**.

Table 2. Comparison of nursing satisfaction between the two groups [n(%)]

Group	Number of cases	Satisfied	Basically satisfied	Dissatisfied	Overall satisfaction rate
Observation group	60	41(68.33)	18(30.00)	1(1.67)	59(98.33)
Control group	60	30(50.00)	20(33.33)	10(16.67)	50(83.33)
χ^2 value					4.915
P value					0.024

4. Discussion

In clinical diseases, the lungs are organs prone to diagnosing space-occupying lesions. Especially with the rapid development of diagnostic technology today, spiral CT and other methods can be used for qualitative analysis of patients' conditions. Pulmonary micro-nodules are non-infectious, and in clinical induction mechanisms, benign tumors, malignant tumors, fungal infections, tuberculosis, and pulmonary vascular abnormalities are all associated factors. Some patients may have no obvious symptoms after the onset of the disease, and continuous disease progression can delay the best treatment opportunity, thereby threatening the patient's life safety^[7, 8].

Currently, clinical treatment for small pulmonary nodules generally involves selecting scientific and reasonable treatment plans based on the patient's condition, including:

- (1) Surgical treatment: For lung nodules exceeding 3cm or with possible malignant lesions, surgical resection of the lung lobe to remove the lesion is required.
- (2) Follow-up observation: For micro-nodules, a follow-up observation mode can be adopted, generally recommending imaging examination every 3 to 6 months to determine whether the nodules have increased.
- (3) Interventional therapy: Tools such as bronchoscopy and fiberoptic bronchoscopy are used to take tissue samples from lung nodules for analysis of their benignity or malignancy, thereby determining subsequent treatment plans.

However, patients may exhibit varying degrees of anxiety and nervousness when diagnosed with small pulmonary nodules, which is related to their understanding of the disease and excessive worry about factors of deterioration. At this time, corresponding nursing interventions are needed to alleviate their psychological pressure and improve treatment cooperation.

Traditional nursing involves simple nursing care according to medical advice and treatment procedures, with relatively singular nursing content and obvious limitations, which can no longer meet the treatment needs of modern patients. With the development of nursing concepts, more new nursing models have begun to be used in clinical practice, among which comprehensive nursing is a classic one. It requires providing patients with comprehensive nursing intervention, improving their comfort, and meeting treatment needs, thereby enhancing the overall quality of nursing.

In this study, patients in the control group received routine nursing, while patients in the observation group received a comprehensive nursing model. In comprehensive nursing intervention, psychological nursing helps patients alleviate psychological pressure, build confidence in treatment, and improve their compliance with subsequent treatment and nursing. Dietary nursing improves the internal environment of the body and provides more nutrition. Lifestyle nursing assists patients in correcting unhealthy habits and reducing adverse factors that affect lung health. Appropriate exercise helps patients improve their body's resistance and lung function. Medication nursing enhances patients' compliance with medication and reduces adverse events caused by improper medication. Environmental nursing reduces surrounding factors that harm the lungs.

After the above comprehensive nursing interventions, the scores of the SAS and SDS scales in the observation group were lower than those in the control group. The reason for this is that under comprehensive nursing intervention, patients can correctly understand the disease, achieve benign communication with nurses, and experience relief from psychological pressure under high-level nursing services. The total nursing satisfaction rates of the observation group and the control group were 98.33% and 83.33%, respectively. The reason for this is that during the comprehensive nursing process, nurses appropriately meet patients' treatment needs, resulting in higher satisfaction. The results obtained in this study are basically consistent with previous reports^[9, 10].

In recent years, the incidence of pulmonary nodules has significantly increased due to severe environmental pollution and the increasing number of unhealthy lifestyle habits. If timely intervention is not provided for this disease, it can lead to fibrosis of lung tissue, damage to alveolar walls and interstitium, and severe impairment of patients' lung organs^[11, 12]. Generally speaking, pulmonary micro-nodules are not easy to deteriorate, but timely intervention is still needed to avoid disease progression. Good nursing intervention is an important method to help improve clinical efficacy and patients' mental state. Therefore, attention should be paid to nursing during the

treatment process. In this study, after providing comprehensive nursing intervention to patients in the observation group, their psychological pressure was significantly alleviated, and they were highly satisfied with this nursing model. Therefore, it is believed that comprehensive nursing intervention for patients with pulmonary micro-nodules can effectively relieve their psychological pressure and improve nursing satisfaction, which has clinical value.

5. Conclusion

The implementation of a holistic nursing intervention for patients diagnosed with pulmonary micro-nodules has been shown to significantly alleviate psychological distress, including anxiety and depression, while substantially improving patient satisfaction with care. By integrating personalized psychological support, detailed health education, and regular follow-up monitoring, this approach not only addresses the emotional and cognitive needs of patients but also fosters better adherence to medical advice and treatment plans. Furthermore, such interventions contribute to early detection of potential complications, thereby optimizing clinical outcomes. Given its multifaceted benefits, comprehensive nursing care demonstrates considerable clinical value in the management of pulmonary micro-nodules, enhancing both patient well-being and healthcare efficiency.

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Disclosure statement

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References

- [1] Chen M, Wang J, Fan Q, 2019, Investigating the Effectiveness of Preoperative CT Sclerosing Technique Detection and Tumor Occurrence in Patients With Small Pulmonary Nodules Using Thoracoscopy. *Chinese Journal of Cancer Prevention and Treatment*, 26(S1): 47, 49.
- [2] Oudkerk M, Liu S, Heuvelmans M, et al., 2021, Lung Cancer LDCT Screening and Mortality Reduction – Evidence, Pitfalls, and Future Perspectives. *Nat Rev Clin Oncol*, 18: 135–151.
- [3] Li N, Sun N, Li X, et al., 2024, Characteristics and Influencing Factors of Pulmonary Nodules in Healthy Individuals Undergoing Physical Examination. *Journal of Clinical Pulmonary Medicine*, 29(4): 546–550.
- [4] Yin Y, Gao Y, Yang X, et al., 2024, Application of Family Participatory Nursing Model Under the Concept of Rapid Rehabilitation in the Perioperative Nursing of Patients With Pulmonary Nodules. *Journal of Practical Clinical Medicine*, 28(11): 129–133.
- [5] Yu Q, 2018, Study on the Application of Comprehensive Nursing Intervention in Patients With Pulmonary Nodules. *Aerospace Medicine*, 29(10): 1284–1286.
- [6] Li Y, Zhang J, Yin C, Li H, 2021, Application of Family Synchronous Cognitive Intervention in Patients With Small Pulmonary Nodules. *Chinese Modern Medicine*, 28(29): 221–224.
- [7] Chen Y, 2021, Application of Rapid Rehabilitation Nursing in Patients After Thoracoscopic Pulmonary Nodule

- Resection. Heilongjiang Journal of Traditional Chinese Medicine, 50(2): 189–190.
- [8] Weng Y, Chen J, Jiang J, 2020, The Effect of Nursing Intervention Based on the Concept of Rapid Rehabilitation Surgery on the Stress Response and Rehabilitation of Patients Undergoing Thoracoscopic Pulmonary Nodule Resection. China Medical Herald, 2020(3): 177–180.
- [9] Fan Z, Zhang S, Zhang Y, et al., 2021, The Impact of Comprehensive Nursing on the Psychological State of Patients With Micro-Pulmonary Nodules. China Healthcare Nutrition, 31(6): 91.
- [10] Zhang Y, 2024, Analysis of the Influence of Comprehensive Nursing Intervention on the Emotional State and Follow-Up Compliance of Patients With Small Pulmonary Nodules. Chinese Scientific Journal Database (Citation Version) Medicine and Health, 2024(12): 185–188.
- [11] Xiao M, Tu R, 2022, The Effect of Multi-Mode Respiratory Function Training Combined With Health Education on Improving Lung Function in Patients With Pulmonary Nodules. Jilin Medical Journal, 43(10): 2843–2846.
- [12] Xiao M, Tu R, 2022, The Effect of Multi-Mode Respiratory Function Training Combined With Health Education on Improving Lung Function in Patients With Pulmonary Nodules. Jilin Medical Journal, 43(10): 2843–2846.

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Application of the External Treatment Method of Traditional Chinese Medicine in the Elderly Diabetic High-Risk Foot Based on the Theory of “Preventive Treatment of Disease”

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Abstract: Diabetic foot (DF) has emerged as one of the most common chronic consequences of diabetes mellitus, characterized by prolonged disease duration, high treatment costs, a poor prognosis, and a high disability rate. Diabetic high-risk foot is the early stage of diabetic foot, the “disease prevention” of “treating no disease”, which provides a critical window for clinical prevention and treatment. Traditional Chinese medicine (TCM) has emphasized the importance of preventive health care since ancient times. External therapies such as acupuncture, massage, acupoint injection, foot bath fumigation, and moxibustion have the advantages of simplicity, low cost, precise efficacy, and fewer side effects in preventing and treating diabetic high-risk foot. The multidisciplinary synergistic model formed by TCM complementary therapies and modern medical treatments, such as nutritional, peripheral nerve, and blood glucose regulation, provides new ideas for establishing standardized prevention and treatment protocols. In this paper, studies related to TCM-related complementary therapies for diabetic high-risk feet are systematically reviewed. Current advances in external application in TCM were described to better understand its effectiveness and safety in elderly patients.

Keywords: Diabetic high-risk foot; External Chinese medicine treatment method; Treatment of undiagnosed disorder; Review

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1. Introduction

According to the International Diabetes Federation (IDF)'s most recent estimations in 2021, diabetes mellitus is highly common among people over the age of 65 ^[1]. China, the United States, and India have the most diabetic patients over 65, with prevalence rates ranging from 14.9% to 25.0%. The prevalence of diabetes in China is

10.6% in people aged 20–79 years, with a prevalence of 141 million people, making it the country with the largest number of diabetic patients in the world ^[2].

The incidence of diabetic foot (DF) increases with the duration of diabetes mellitus. It is assumed that between 19%–34% of the estimated 537 million people with diabetes worldwide will develop diabetic foot ulcers (DFUs) in their lifetime, with the prevalence of diabetic foot as high as 8.1% among people with diabetes over the age of 50 years, with a two-year mortality rate of 51% and a limb amputation rate of more than 50% ^[3]. Neurologic function testing on diabetes patients found that around 60% to 90% of diabetic individuals have varied degrees of neuropathy, with 30% to 40% of these people exhibiting no subjective symptoms, and the nerve damage is often permanent and irreversible ^[4, 5]. Older patients with diabetic foot have a longer duration of disease, more comorbidities, and a higher risk of amputation. Therefore, early prevention and treatment of the diabetic foot is important to promote and maintain the health status of diabetic patients, especially elderly diabetic patients. Studies have shown that effective preventive measures for high-risk diabetic feet and mitigation of adverse effects can reduce the rate of diabetic foot amputation by 49% to 85%, showing that prevention is better than cure ^[6].

Diabetic high-risk foot is an early stage of the diabetic foot and is defined as the presence of risk factors for foot ulceration without the development of a foot ulcer. A multicenter cross-sectional study in the UK that included 6,487 patients with diabetes showed an overall detection rate of 28.5% for diabetic high-risk feet ^[7]. The prevalence correlated with the duration of diabetes, which reached 44% of diabetic patients aged 70 to 79 years. Diabetes mellitus type 2 (T2DM) in the elderly is a special population group with declining cognitive function, coexistence of multiple diseases, multiple medications, and complex medication regimens, which pose a major challenge to its management. Currently, there are diverse traditional Chinese medicine (TCM) management programs for type 2 diabetes mellitus in China and it is important to rationally integrate TCM and Western medicine resources to provide personalized management services to patients. Traditional Chinese medicine external treatment is the external use of Chinese herbal medicines through the action of the physical way, through the human skin, mucous membranes, and acupuncture points to absorb the drug into the body. This article provides an overview of the importance of prevention of high-risk diabetic foot, the current status and problems of early prevention, and the interventional measures of external treatment with TCM for early prevention, to provide reference for clinical care and research.

2. Chinese and Western medical understanding of the diabetic high-risk foot

In 2015, the International Working Group on Diabetic Foot (IWGDF) clearly defined diabetic high-risk foot as “diabetic patients without active ulcers, but with peripheral neuropathy, with or without foot deformity or lower extremity vascular lesions, or a history of foot ulcers, or a history of amputation of the lower extremity or foot.” ^[8]. According to the Wagner Diabetic Foot Classification Criteria, there are grades 0 to 5. Wagner grade 0 is defined as DF with risk factors for foot ulceration but without ulceration, also known as diabetic high-risk foot.

The TCM guidelines and expert consensus define diabetic high-risk foot as “gangrene (diabetic foot disease - diabetic arterial occlusive disease of the limb) without ulceration.” ^[9]. The onset of the disease is characterized by poor Qi and blood. The veins and channels are not smooth, causing meridian obstruction, and gradually affect the skin, muscles, veins, nerves, and bone lesions. Serious cases can involve the five viscera and six bowels. In the advanced stages, disorders of Qi and blood impair circulation further. The balance of Qi and blood, as well as Yin and Yang, is disrupted, leading to the accumulation of phlegm, dampness, and toxic stagnation. The veins and

collaterals become thin and blocked, depriving the skin, tendons, and muscles of nourishment. This pathological progression ultimately contributes to the development of diabetic foot.

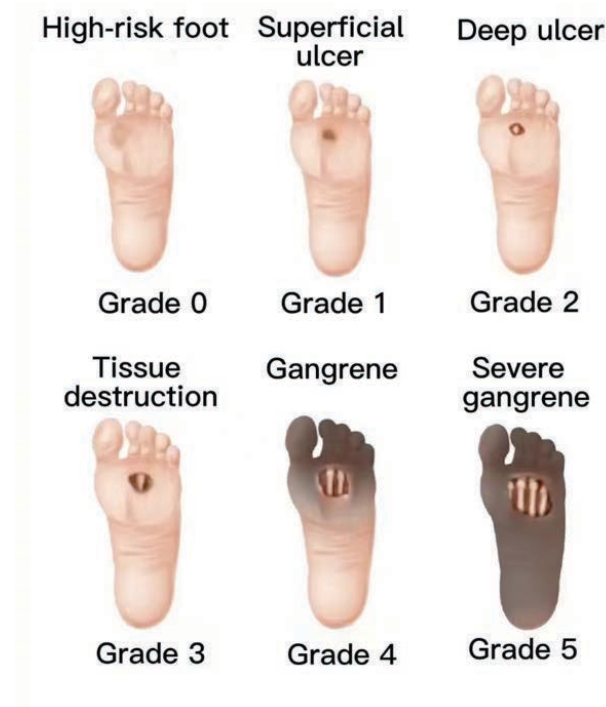


Figure 1. Wagner classification

3. The impact of elderly diabetic high-risk foot on the quality of life

Diabetic high-risk foot includes peripheral neuropathy and peripheral arterial lesions, with a variety of clinical symptoms, including sensory abnormalities, loss of sensation, itchy skin, dry skin, asymptomatic hypoglycemia, and postural hypotension. Among them, sensory nerve abnormalities are more common, presenting with numbness and pain. Damage to the motor nerves, common peroneal, and tibial nerves, can leave the patient with limb weakness and an inability to perform normal daily activities. So much so that the muscles of the lower limbs atrophy over time and the toes flex and deform, triggering changes in plantar pressure. In addition, diabetic high-risk feet are associated with gait, posture, and balance abnormalities. The results of a study by Fan *et al.* showed that the fall rate among hospitalized diabetic patients in China reached 21.58%, while another study on elderly diabetic patients found that the fall rate among elderly diabetic patients was 24.75%^[10, 11].

Persistent progression of the high-risk foot can lead to ulceration of the patient's foot, which, without good healing management, can lead to avascular necrosis and muscle gangrene. In severe cases, amputation is even required, increasing the disability and mortality rates of elderly T2DM patients. In a community-based study that included 15,692 diabetic patients, symptoms of painful neuropathy were seen in 32.7% of patients aged 35–54 years, and in 35.7% of patients aged 55 years or older^[12]. Data show that the global prevalence of diabetic foot ulcers is 6.3% (95% CI: 5.4%–7.3%), with an annual incidence of 1%–4%, of which the incidence in China is 4.1% (95% CI: 3.1%–5.2%)^[13, 14]. Related studies have shown that diabetic patients have a lifetime probability of developing diabetic foot ulcers ranging from 19% to 34%, with a recurrence rate of 40% in the first year and 60% within three years for those who are cured^[12, 15].

Elderly patients with high-risk diabetic foot often exhibit reduced self-management capabilities, with inconsistent adherence to insulin administration and medication regimens. Inadequate knowledge of diabetic foot prevention and poor foot care behavior. Cognitive ability declines with age. Older people with diabetes have reduced independence and lower adherence to medical care^[16]. The elderly have insufficient knowledge of diabetic foot prevention and poor foot nursing behavior^[17, 18]. In terms of foot care knowledge, diabetic patients have the worst knowledge of daily foot care and foot pain problem management. Negative emotions generated by changes in disease and insufficient family support tend to make patients lose confidence in treatment, which in turn hinders patients' healthcare behaviors. Persistent pain reduces treatment adherence, and depression occurs in 38.98% of patients^[19, 21].

The average length of hospitalization for patients with diabetic foot in China is 15.59 days, and the average total cost of hospitalization is 28825.79 yuan^[20, 22]. According to statistics, the global medical cost of diabetes in 2017 was as high as \$727 billion, of which \$110 billion was spent in China^[23]. The treatment of diabetic foot takes up 12%–15% of diabetes healthcare costs in developed countries and up to 40% in developing countries^[24]. The direct cost of diabetes care in the US was \$237 billion in 2022, a third of which was spent on lower limb complications. Healthcare spending on DF care in the UK is even higher than for breast, prostate, and lung cancer combined^[25]. Several studies have shown that the mean six-minute walk distance in patients with Diabetic peripheral neuropathy (DPN) is significantly lower than in healthy controls, with a general reduction of 20–35%^[26, 27]. In patients with diabetic peripheral neuropathy, high mean peak pressure (MPP) and pressure–time integral (PTI) are common in forefoot segments, indicating overloading of high-risk segments of the plantar foot^[28]. Diabetic foot is characterized by a high disability rate, high mortality rate, and high treatment cost, which seriously affects the quality of patients' survival and brings a heavy economic burden to patients, their families, and society.

4. Feasibility of Chinese medicine's idea of “treating the future disease” in the prevention and treatment of high-risk diabetic foot

For diabetic high-risk foot, Western medicine mainly uses pharmacological intervention for peripheral neuropathy and vascular lesions, with glycemic control, nerve nourishment, and pain management as the main principles of treatment. Western therapies for DF include foot care and infection management, blood sugar control, such as taking metformin, improving blood supply, and the common use of methylcobalamin to provide nutrients to nerve cells. However, treatment outcomes have been lacklustre. Only 24% or 30% of diabetic foot ulcers (DFUs) heal within 12 or 20 weeks, respectively, and patients are susceptible to serious complications, including wounds, osteomyelitis, cellulitis, and amputation^[29]. Up to 40% of DFUs may require amputation, and following a major amputation, 50% of patients require another major amputation within two years. The relative mortality rate after amputation is about 50%, second only to lung cancer (86%) and higher than colorectal (39%) or breast cancer (23%)^[30].

Western drug therapy alone only relieves and controls existing clinical symptoms in patients with diabetic high-risk feet. Chinese medicine can alleviate the adverse effects of diabetic high-risk foot as an adjunctive treatment. The IWGDF emphasizes that interventions for DFUs based on a multidisciplinary team approach with systematic and comprehensive education and preventive measures can significantly improve the prognosis and reduce the rate of amputation by 49%–85%. External treatment of diabetic foot in TCM is a major feature of TCM therapy. The Chinese Diabetic Foot Prevention and Control Guidelines (2019) state that prevention is better than

cure for diabetic foot, and that the occurrence of diabetic foot can be reduced by strengthening the management of high-risk diabetic foot to detect, diagnose, and treat high-risk foot at an early stage^[31]. Diabetic foot is difficult to treat and prevention is better than cure. The Clinical Practice Guidelines for the Prevention and Management of the Diabetic Foot state that the five cornerstones of preventing the diabetic foot are identification of the diabetic foot at risk, regular screening of the diabetic foot at risk, education of the patient, their family and healthcare professionals, appropriate footwear for daily use, and treatment of the risk factors for ulceration.

The theory of “treating the disease before it occurs” has three levels of significance: (1) prevention of disease before it occurs, which requires improvement of living habits and strengthening the body; (2) preventing the change of the disease after it occurs, which suggests early diagnosis and treatment; and (3) prevention of recurrence of the disease, which means that active measures can be taken to promote the recovery of the organism after the disease, and to prevent the disease from recurring and reduce the after-effects. As far as diabetic foot is concerned, early treatment can prevent the disease from changing from light to heavy and from surface to inside. Therefore, early treatment of diabetic foot is very important. Especially when the diabetic foot grade 0 timely control the development of the disease, delay or even block its development from grade 0 to grade 1 will greatly reduce the disability and mortality rate of patients. Multiple guidelines recommend continuous, vigilant, and regular foot examinations for early detection and prevention of diabetic foot ulcers, integrating the concept of “treating the future illness” with clinical nursing to improve the prognosis of patients will be the focus of future research.

The unique advantages of external treatment of Chinese medicine for the prevention and treatment of chronic diseases in the elderly are becoming more and more prominent: (1) it is simple to administer and does not need to be taken internally; (2) it is applied directly to the lesion and the effect of the medicine is concentrated. The reason is that through the skin and mucous membrane penetration, the drug is absorbed into the body through the skin and mucous membrane, which avoids the first-pass effect of the drug and strengthens the targeting effect of the drug and does not need to be taken internally, avoiding direct damage to the organs and improving the efficiency of utilization; and the second is to stimulate the whole body reaction through the meridians of the acupoints. Clinicians mostly use Ashi acupoints to take points through the channels and collaterals to find the right points, through the body surface acupuncture points to stimulate the meridian conduction. The body has a drug absorption system to help distribute the essence and harmonize the Qi and blood to reach the internal organs, to achieve the effect of disease prevention and treatment. The external treatment methods of Chinese medicine applied to elderly diabetic high-risk feet are traditional Chinese medicine foot bath fumigation, acupoint paste, acupoint injection, moxibustion, acupoint massage, etc., which can effectively improve the local blood circulation and nerve conduction function^[38, 42, 47, 50].

5. Application of external treatment of Chinese medicine in the prevention and treatment of diabetic high-risk foot

With the application of Chinese medicine in the care of diabetes mellitus patients, Chinese medicine nursing is more standardized and scientific, and the guidance of clinical patient care is more practical and effective. TCM nursing is guided by evidence-based thinking and supported by TCM nursing techniques, which can effectively improve the prognosis of patients by dredging the meridians and activating the lateral branches to help the normal function of Qi and blood.

5.1. Chinese medicine fumigation

Chinese medicine fumigation is a therapeutic method that uses medicines decocted in a broth and fumigated or drenched on the skin or affected area while it is warm. Generally, the medicinal soup is first smoked with steam and then washed when the medicine cools down. With the help of drug action and heat effect, this therapy acts on the body through the skin and mucous membranes, which can stimulate vasodilatation of the extremities, promote local blood and lymphatic reflux, and play the role of activating blood circulation, relieving pain, dispersing cold, and replenishing Qi. Zhong *et al.* randomly divided 102 patients with diabetic high-risk foot into control group (51 cases) and treatment group (51 cases), the control group was given basic drug hypoglycemic treatment, and the treatment group was given Baiyu Lingxian fumigation, which resulted in better improvement of the clinical symptoms, faster nerve conduction, and better repair of the damaged nerves of the patients^[32]. Wang *et al.* tested the treatment of diabetic high-risk foot patients with *Paeonia lactiflora* and licorice soup plus flavor combined with traditional Chinese medicine fumigation for a period of 3 months^[33]. The results showed that compared with the control group (54 cases) treated with oral methylcobalamin tablets, the observation group showed better improvement in symptoms and signs, and more significant improvement in nerve and blood flow.

Despite its efficacy, TCM fumigation, as a method of treating high-risk diabetic foot in the elderly, has some drawbacks, especially when used on the elderly, with the temperature control being a significant problem. The temperature of fumigation is difficult to grasp for the elderly. Due to ageing, the elderly population has reduced body's perceptual ability and reaction speed, as well as reduced sensitivity to temperature changes^[34]. When performing TCM fumigation, if the water temperature is too high, diabetic patients with abnormal sensory nerves and decreased temperature awareness may not be able to detect it in time, thus leading to skin burns. Elderly patients with diabetic foot skin are inherently more fragile. Once scalded, not only will there be difficulty in healing, but will also be prone to infection, further aggravating the condition. Secondly, elderly diabetic foot patients are often accompanied by vascular and neuropathy. These lesions affect the patient's foot blood circulation and nerve function. An over 10-minute foot soak will cause a decrease in sympathetic excitability and an increase in vagal tone, resulting in an increase in heart rate and a decrease in blood pressure^[35]. When Chinese medicine fumigation is carried out, all the blood is quickly concentrated in the lower limbs, causing a transient insufficient blood supply to the brain and the heart. This will lead to dizziness, panic, and chest tightness, and even induce cardiovascular and cerebrovascular diseases. Preventive measures can be taken in the form of smart temperature-controlled foot bath tubs and controlled foot soaking time.

5.2. Acupuncture point patching

Acupoint therapy is based on the meridian theory. The corresponding disease-related acupoints were selected, and the precise treatment of the appropriate drugs are turned into a fine powder. The powder is then turned into a paste using water or vegetable oil. Alternatively, solidifying agents such as petroleum jelly, yellow vinegar, rice, or jujube paste may be used to prepare ointments, pills, or therapeutic cakes^[36]. The paste, used to treat the disease of a non-invasive pain acupoint therapy, is directly applied to the acupoints and the affected area (Ashi point). The medicine, with the help of herbal action and meridian stimulation, will stimulate the acupoints, regulate the balance of Yin and Yang in the internal organs, and promote the dredging of meridians, Qi, and blood, to achieve the purpose of preventing and treating diseases. In Wu's research, 77 cases of diabetic high-risk foot patients were selected. Two groups of patients were given conventional basic intervention; the control group was treated using methylcobalamin oral treatment and the observation group in the control group had the addition of traditional

Chinese medicine acupoints paste intervention ^[37]. After 3 months of intervention, traditional Chinese medicine acupoint patch intervention for diabetic peripheral neuropathy can significantly improve the clinical efficacy, reduce the TCSS score, improve the peripheral nerve conduction velocity, and have a high degree of clinical treatment satisfaction. Chen *et al.* used acupoint plasters (saffron, cinnamon sticks, Chuanxiong, and Xinxin were powdered and made into a paste, which was applied to the foot Sanli and Sanyinjiao points) for the treatment of diabetic at-risk feet, which could effectively promote the improvement of clinical symptoms of the patients ^[39]. Li *et al.* applied Chinese medicine hard paste heat paste to treat 40 cases of diabetic foot, applying it to bilateral Yongquan and Sanyinjiao points. Each time, the paste was applied for 4h, once a day ^[40]. The results showed that the patients' TCM evidence score and inflammatory factor decreased after treatment compared with before treatment.

In clinical practice, acupuncture point dressing is mostly used as an adjunctive therapy. Its limited effectiveness may be due to the short application duration, which may not allow the medication to fully exert its therapeutic effects. Typically, acupuncture point dressings are applied for 4–6 hours, a duration that may be insufficient for optimal drug absorption ^[39]. At the same time, the adhesive tape of the acupressure points for the elderly is also easy to trigger allergic reactions. Elderly people's skin is more sensitive and less tolerant to adhesive materials such as adhesive tape, which is prone to allergic symptoms such as redness, swelling, and itching. This will not only affect the patient's experience but also may interrupt the treatment due to allergic symptoms, thus affecting the overall effect of acupoint taping. Allergy prevention can be achieved by cleansing the skin with mild medical cleansing products to remove dirt, oil, and stratum corneum build-up on the skin surface to facilitate better penetration and absorption of the medication, as well as to reduce the risk of allergy due to unclean skin. After cleansing, a small amount of moisturizer such as petroleum jelly can be applied to keep the skin moisturized and enhance the skin barrier function, but care should be taken to not apply too much so as not to affect the effect of the medication application ^[40].

5.3. Acupoint injection

Acupoint injection is a combination of chemical stimulation of drugs and mechanical stimulation of needling acting on meridians to produce the effect of promoting nerve repair and nerve nutrition. Zhu randomly divided 120 patients with diabetic high-risk feet into a study group and a control group ^[41]. The control group received basic symptomatic treatment with Western medicine, while the research group received acupoint injections of Lanxessin in addition to the same Western medical treatment. Based on the basic symptomatic treatment of Western medicine, the efficacy of acupoint injection for the treatment of diabetic peripheral neuropathy of the splenic phlegm-dampness type was obvious. It can inhibit inflammation, improve oxidative stress, and reduce the damage of vascular endothelial function. Zhao divided 70 patients with type 2 diabetes mellitus high-risk foot into two groups ^[42]. For the conventional treatment of diabetes, the control group was treated with microprobe, and the treatment group was treated with saffron injection acupoint injection for the control group.

Acupoint injection of traditional Chinese medicine can significantly reduce the MDNS scores and signs and symptoms scores of DPN patients and improve the quality of life. Although acupoint injection can promote the recovery of nerve function, repeated needling of the affected limbs of diabetic high-risk feet has a potential risk of infection. These include an increased risk of infection, aggravation of pain due to repeated needling, and occasional bleeding at the injection site. In patients with existing skin damage, the likelihood of developing foot ulcers is significantly higher ^[43]. Apply light pressure to the needle puncture site for a few moments with a sterile

dry cotton ball to prevent bleeding and hematoma formation. If bleeding occurs, apply pressure until bleeding stops. Advise the patient to keep the site clean and dry within 24 hours after the needling and avoid water to prevent infection. If there is slight redness, swelling, pain, and other reactions at the site of needling, it is generally a normal phenomenon and cold compresses can be applied locally.

5.4. Moxibustion

Moxibustion is divided into direct moxibustion and indirect moxibustion. Direct moxibustion can be divided into scar moxibustion and no scar moxibustion. Indirect moxibustion can be divided into interstitial ginger moxibustion, interstitial garlic moxibustion, interstitial salt moxibustion, and interstitial appendage cake moxibustion^[44]. The clinical effectiveness of moxibustion in treating DPN has been widely recognized. Recent studies showed that moxibustion can increase serum superoxide dismutase concentration, reduce free-radical production, prevent impairments of nerve tissues resulting from free-radical accumulation, and alleviate neuro-inflammation possibly by inhibiting NF- κ B and activating Nrf2^[46]. Zheng treated 70 cases of DPN patients with pave moxibustion therapy^[45]. The treatment group used methylcobalamin treatment plus pave moxibustion therapy and found that pave moxibustion therapy significantly improved clinical symptoms and nerve conduction velocity after 2 courses of treatment. Wei Xiang *et al.* observed 60 cases of diabetic peripheral neuropathy patients who were hospitalized and found that thunder fire moxibustion therapy can achieve the effect of warming meridians and opening collaterals through the meridian and acupoints through the meridian sensory transmission together and treat diabetic peripheral neuropathy^[47].

Elderly people have thinner skin and lower tolerance to high temperatures and are prone to burns when moxibustion is performed. Secondly, symptoms of diabetes are manifested by dry mouth and thirst, which are aggravated by moxibustion (fire). Moxibustion treats diseases through warm and hot stimulation, but elderly people are weak and prone to Yin deficiency and fire^[48]. When performing moxibustion treatment, symptoms such as dry mouth, fire, or allergic skin reactions such as rashes may result from warm and hot stimulation. Reducing the incidence of burns can be achieved by increasing rounds and observing the skin for 5–10 minutes.

5.5. Acupressure

Acupressure can mobilize local meridian Qi, improve the function of the five organs, dredge the meridians, increase the temperature and sensitivity of the skin at the end of the limbs, enhance circulation, promote nerve repair, and have a good overall effect. Chinese acupressure can effectively improve the clinical symptoms of DPN patients, such as limb pain, coldness, numbness, soreness, and weakness, and alleviate patients' abnormal pain, warmth, vibration, and pinprick tactile sensations^[49]. Guo considered that acupressure is a simple and easy means to provide a suitable, convenient, and effective intervention method for patients who cannot come to outpatient follow-up on time^[50]. One hundred and twenty patients with diabetic high-risk feet were divided into three groups: the control group, the methylcobalamin group, and the acupressure group. All three groups were given conventional basic treatment, and the control group was given no other treatment; the methylcobalamin group was given oral methylcobalamin tablets, 0.5 mg each time, 3 times a day. The acupressure group was given ten acupressure points, including Qiaogong, Neiguan, Blood Sea, Huizhong, Chengshan, Ashigangsanli, Sanyinjiao, Taixi, Taichong, Neitin. In the acupressure group, 10 specific acupoints were selected, with each point stimulated for 3 minutes, followed by continuous massage lasting approximately 20 minutes. Treatments were administered five times per week over a period of two weeks.

This intervention resulted in significant improvements in clinical symptom scores and Toronto Clinical Scoring System (TCSS) scores. However, no significant differences were observed in nerve conduction velocity between the groups. Ma's trial was divided into two groups, with 59 cases in each group^[51]. The test group used conventional intervention + acupressure, and the control group used conventional intervention. In the results, the sensory and motor nerve conduction velocities of the peroneal nerve in the test group were higher than those in the control group, and the difference was statistically significant ($P < 0.05$) proving that acupressure care can help to improve the patient's condition, and to prevent and control the progression and deterioration of DPN.

Although acupressure is convenient, patients may lack a correct understanding of acupressure. Elderly diabetic high-risk feet will have lower limb vascular lesions, and the extrusion during massage may damage the inner wall of blood vessels, leading to thrombosis. Those with venous thrombosis already formed, blind massage may lead to thrombus dislodgement, triggering serious complications such as pulmonary embolism^[52]. When patients continue self-massage at home after discharge, improper techniques, such as incorrect acupoint location, inappropriate methods, or excessive pressure, may lead to discomfort, lower limb pain, or even injury^[53]. Therefore, proper training in acupoint identification and massage intensity is essential. It is recommended that massage be performed by trained professionals, as incorrect application may compromise therapeutic outcomes and fail to achieve the desired results.

6. Discussion

Diabetic high-risk foot patients belong to the category of “gangrene”, “tendon gangrene”, “pulse paralysis”, etc^[54, 55]. Chinese medicine believes that this condition is primarily attributed to a deficiency of Qi and blood, as well as a depletion of bodily fluids and Qi, thus the meridians can't run normally and circulate^[56]. In the later stages of the condition, external pathogenic factors, such as fire and toxic foreign evils, invade the limbs. As the disease becomes prolonged, turbid toxins accumulate and cause obstruction, leading to a deficiency of Qi and blood, an imbalance of Yin and Yang, and damage to the meridians. Over time, this results in long-standing blood stasis, a loss of nourishment to the foot, and progression to a high-risk diabetic foot. Therefore, treatment should primarily focus on regulating Qi and blood, unblocking the meridians, and dispersing turbid toxins. At this stage of diabetic high-risk foot, actively improving peripheral neuropathy and other conditions through the combination of Chinese and Western medicine treatment can prevent and slow down the progression of the disease. Existing studies have demonstrated that Traditional Chinese Medicine (TCM) interventions based on the principle of “treating illness before it arises” can effectively improve clinical symptoms and increase nerve conduction velocity in patients with high-risk diabetic foot, while also exhibiting a favorable safety profile^[57, 58].

However, there is still some room for improvement. It is recommended to provide a more specific and scientific treatment plan for high-risk diabetic foot based on evidence-based medicine. That is, external treatment methods should be selected based on the patient's specific condition, with strict adherence to indications and standardized operating procedures. In addition, greater attention should be given to the regulation and control of herbal formulation and drug compounding. At present, the research of TCM external treatment for diabetic foot is mostly based on clinical observation. The research of the mechanism of action is relatively small, and its biological research should be strengthened to explore the key links and targets of the specific mechanism of action. Furthermore, review of the literature has found that the length of the TCM external intervention program is relatively short. The length of the intervention can be increased or followed up to observe the changes of patients'

long-term indicators, to improve the application and treatment of external Chinese medicine in the clinical management of high-risk foot in elderly diabetes.

7. Conclusion

The application of external Chinese medicine nursing methods based on the idea of treating the future disease in the high-risk foot stage 0 (without ulcers but with risk factors), i.e., early intervention to slow down the progression of the disease, embodies the idea of ‘prevention is more important than cure’, whose core lies in the idea of ‘preventing disease before it occurs, and preventing changes in the case of existing disease’. External Chinese medicine treatments such as herbal fumigation, acupoint stimulation, and topical ointment can improve local blood circulation, promote tissue repair, relieve pain and swelling, and inhibit infections, thus slowing down the progression of the disease through multi-dimensional interventions, and lowering the risk of foot ulcers and amputations. At present, whether it is massage or Chinese medicine external treatment, there is a lack of clinical big data research as a support point. It is difficult to standardize the implementation and treatment. The method to apply traditional Chinese medicine theories and techniques in a more targeted and effective manner for the prevention and treatment of diabetic high-risk feet in the elderly population is the problem that needs to be solved urgently.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] National Centre for Geriatrics, Chinese Society of Geriatrics, Diabetes Committee of the Chinese Association of Geriatrics, 2024, Guidelines for the Diagnosis and Treatment of Diabetes Mellitus in the Elderly in China (2024 Edition). *Concord Medical Journal*, 2024(4): 771–800.
- [2] International Diabetes Federation, 2021, IDF Diabetes Atlas. International Diabetes Federation, 2021(8th Edn).
- [3] Tong T, Yang C, Tian W, et al., 2020, Phenotypes and Outcomes in Middle-Aged Patients With Diabetic Foot Ulcers: A Retrospective Cohort Study. *Journal of Foot and Ankle Research*, 13: 1–8.
- [4] Edmonds M, Manu C, Vas P, 2021, The Current Burden of Diabetic Foot Disease. *Journal of Clinical Orthopaedics and Trauma*, 17: 88–93.
- [5] Lyundup AV, Balyasin MV, Maksimova NV, et al., 2022, Misdiagnosis of Diabetic Foot Ulcer in Patients With Undiagnosed Skin Malignancies. *International Wound Journal*, 19(4): 871–887.
- [6] Song Z, Ou J, Shu L, et al., 2022, Fall Risk Assessment for the Elderly Based on Weak Foot Features of Wearable Plantar Pressure. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 30: 1060–1070.
- [7] Al-Mohaithef M, Abdelmohsen SA, Algameel M, et al., 2022, Screening for Identification of Patients at High Risk for Diabetes-Related Foot Ulcers: A Cross-Sectional Study. *Journal of International Medical Research*, 50(3): 03000605221087815.
- [8] Bus S, Van Netten S, Lavery L, et al., 2016, IWGDF Guidance on the Prevention of Foot Ulcers in At-Risk Patients With Diabetes. *Diabetes/Metabolism Research and Reviews*, 32(S1): 16–24.
- [9] Monteiro-Soares M, Hamilton EJ, Russell DA, et al., 2024, Guidelines on the Classification of Foot Ulcers in People

With Diabetes (IWGDF 2023 Update). *Diabetes/Metabolism Research and Reviews*, 40(3): e3648.

- [10] Shi XQ, Li HY, Zhou J, et al., 2023, Analysis of the Current Status of the Application of Evidence Quality Evaluation and Recommendation in Chinese Medicine/Integrated Chinese and Western Medicine Clinical Practice Guidelines and Expert Consensus. *Journal of Traditional Chinese Medicine*, 2023(6): 581–586.
- [11] Du YQ, Liu YL, Li YS, et al., 2020, Based on “Surgery Zhengzong – Degeneration of Gangrene” to Explore the Characteristics of Identification and Use of Medicines in External Treatment of Diabetic Foot in Different Stages. *World Science and Technology – Modernisation of Traditional Chinese Medicine*, 2020(8): 2969–2974.
- [12] Yan X, Song JF, Zhang L, et al., 2022, Analysis of Risk Factors for Multi-Drug-Resistant Organisms in Diabetic Foot Infection. *BMC Endocrine Disorders*, 22(1): 46.
- [13] Nguyen AT, Pham HQ, Nguyen TX, et al., 2020, Knowledge, Attitude and Practice of Elderly Outpatients With Type 2 Diabetes Mellitus in National Geriatric Hospital, Vietnam. *Diabetes, Metabolic Syndrome and Obesity*, 2020: 3909–3917.
- [14] Mariadoss AVA, Sivakumar AS, Lee CH, et al., 2022, Diabetes Mellitus and Diabetic Foot Ulcer: Etiology, Biochemical and Molecular Based Treatment Strategies via Gene and Nanotherapy. *Biomedicine & Pharmacotherapy*, 151: 113134.
- [15] Seth A, Attri AK, Kataria H, et al., 2019, Clinical Profile and Outcome in Patients of Diabetic Foot Infection. *International Journal of Applied and Basic Medical Research*, 9(1): 14–19.
- [16] Silva LB, Silva PAB, Santos JFG, et al., 2019, Risk Strata and Quality of Care for the Elderly in Primary Health Care. *Revista Latino-Americana de Enfermagem*, 27: e3166.
- [17] Andersson E, Persson S, Hallen N, et al. 2020, Costs of Diabetes Complications: Hospital-Based Care and Absence From Work for 392,200 People With Type 2 Diabetes and Matched Control Participants in Sweden. *Diabetologia*, 63: 2582–2594.
- [18] Williams R, Karuranga S, Malanda B, et al., 2020, Global and Regional Estimates and Projections of Diabetes-Related Health Expenditure: Results From the International Diabetes Federation Diabetes Atlas. *Diabetes Research and Clinical Practice*, 162: 108072.
- [19] Park J, Zhang P, Wang Y, et al., 2021, High Out-of-Pocket Health Care Cost Burden Among Medicare Beneficiaries With Diabetes, 1999–2017. *Diabetes Care*, 44(8): 1797–1804.
- [20] Wang L, Lauren BN, Hager K, et al., 2023, Health and Economic Impacts of Implementing Produce Prescription Programs for Diabetes in the United States: A Microsimulation Study. *Journal of the American Heart Association*, 12(15): e029215.
- [21] Sari Y, Upoyo AS, Isworo A, et al., 2020, Foot Self-Care Behavior and Its Predictors in Diabetic Patients in Indonesia. *BMC Research Notes*, 13: 1–6.
- [22] Kaewput W, Thongprayoon C, Mungthin M, et al., 2019, Temporal Trends in Optimal Diabetic Care and Complications of Elderly Type 2 Diabetes Patients in Thailand: A Nationwide Study. *Journal of Evidence-Based Medicine*, 12(1): 22–28.
- [23] Macdonald KE, Stacey HJ, Harkin G, et al., 2020, Patient Perceptions of Phage Therapy for Diabetic Foot Infection. *PLoS One*, 15(12): e0243947.
- [24] Bekele F, Chelkeba L, 2020, Amputation Rate of Diabetic Foot Ulcer and Associated Factors in Diabetes Mellitus Patients Admitted to Nekemte Referral Hospital, Western Ethiopia: Prospective Observational Study. *Journal of Foot and Ankle Research*, 13: 1–8.
- [25] Liu R, Pang B, Hou W, et al., 2023, Practices and Thoughts on Chinese Medicine’s “Treatment of Future Diseases” in Tumour Research. *Beijing Chinese Medicine*, 37(12): 1146–1148.

- [26] Qin J, Tsui WR, 2020, Discussion on the Prevention and Treatment of Hypertension by External Treatment of Traditional Chinese Medicine Based on the Theory of “Treating the Future Disease”. *Journal of Liaoning University of Traditional Chinese Medicine*, 22(3): 203–206.
- [27] Navarro-Flores E, Cauli O, 2020, Quality of Life in Individuals With Diabetic Foot Syndrome. *Endocrine, Metabolic & Immune Disorders-Drug Targets*, 20(9): 1365–1372.
- [28] Lauwers P, Hendriks JM, Van Bouwel S, et al., 2021, Malnutrition According to the 2018 GLIM Criteria Is Highly Prevalent in People With a Diabetic Foot Ulcer but Does Not Affect Outcome. *Clinical Nutrition ESPEN*, 43: 335–341.
- [29] He M, Chen T, Lv Y, et al., 2022, The Role of Allogeneic Platelet-Rich Plasma in Patients With Diabetic Foot Ulcer: Current Perspectives and Future Challenges. *Frontiers in Bioengineering and Biotechnology*, 10: 993436.
- [30] Bai X, Song Z, Duan Y, et al., 2022, Progress of Chinese Medicine Speciality Treatment of Diabetic Foot. *Journal of Hainan Medical College*, 2022(3): 235–240.
- [31] Lai WY, He CH, Zhang JY, 2023, Clinical Observation on the Treatment of Diabetic Foot by Chinese Medicine Fumigation. *Bright Chinese Medicine*, 2023(23): 4618–4620.
- [32] Zhong H, Wang Y, Xue M, 2023, Effects of Chinese Medicine Fumigation on Clinical Symptoms and Nerve Conduction Function in Patients With Diabetic Peripheral Neuropathy. *Medical Theory and Practice*, 2023(24): 4300–4302.
- [33] Wang K, Zhang P, Luo T, et al., 2023, Clinical Study on the Treatment of Diabetic Peripheral Neuropathy With Yin Deficiency and Blood Stasis by Adding Flavour to *Paeonia lactiflora* and *Glycyrrhiza glabra* Soup and Combining With Traditional Chinese Medicine Fumigation. *Journal of Liaoning University of Traditional Chinese Medicine*, 2023(9): 212–216.
- [34] Wang J, Liu JW, 2022, An Overview of the Research on the Treatment of Diabetic Peripheral Neuropathy by External Treatment Based on Chinese Medicine Fumigation. *Chinese Ethnic Folk Medicine*, 2022(22): 60–63.
- [35] Zhang Y, Jiang H, 2022, Application of Chinese Medicine Fumigation in Diabetic Foot. *Chinese Medicine Clinical Research*, 2022(16): 86–88.
- [36] Ding M, Huang HR, He LH, 2023, Meta-Analysis of Acupoint Patch Therapy for Patients With Diabetic Constipation. *Chinese Medical Science*, 2023(15): 94–97,140.
- [37] Wu Q, Sun S, Wang J, et al., 2023, Clinical Efficacy of Traditional Chinese Medicine Acupoint Patch External Therapy in Intervening Diabetic Peripheral Neuropathy. *Journal of Practical Clinical Medicine*, 2023(20): 137–141.
- [38] Yao YH, Zhang H, Li J, et al., 2021, Efficacy and Effect on Serum MyD88/I κ B Signalling Pathway in the Treatment of Diabetic Peripheral Neuropathy With Qi and Yin Deficiency in Combination With Auricular Acupoint Pressure Beans by Adding Flavoured Huangqi and Turtle Soup. *Chinese Journal of Experimental Formulas*, 2021(11): 98–105.
- [39] Xia F, Xu M, Zhao Y, et al., 2023, Analysis of Medication and Point Selection Pattern of Acupoint Patch for the Treatment of Diabetic Peripheral Neuropathy. *Evidence-Based Nursing*, 2023(1): 122–128.
- [40] Wang A, Li H, Shi Y, et al., 2021, Net Meta-Analysis and Safety Evaluation of Acupuncture for Diabetic Peripheral Neuropathy. *World TCM*, 2021(21): 3225–3236.
- [41] Zhu YA, Zhang Y, Cao L, et al., 2023, Observations on the Efficacy of Acupoint Injection in the Treatment of Spleen Deficiency Phlegm-Dampness Type Diabetic Peripheral Neuropathy. *Shanghai Journal of Acupuncture and Moxibustion*, 2023(9): 910–916.
- [42] Zhao JD, Li Y, Ni YQ, et al., 2018, Clinical Observation of Chinese Medicine Acupoint Injection for the Treatment of Peripheral Neuropathy in Type 2 Diabetes Mellitus. *Journal of Anhui University of Traditional Chinese Medicine*, 2018(1): 50–52.
- [43] Wang J, Yu Y, Zhang HL, et al., 2020, Effects of Ginkgo Biloba Extract Injection at the Foot-Sanli Acupoint on

- Lower Limb Arterial Blood Flow, Blood Rheology and Angiogenesis Indexes in Patients With Diabetic Peripheral Vasculopathy. *Chinese Medicine Herald*, 2020(18): 81–86.
- [44] Fei AH, 2012, Effect of Moxibustion for Tonifying Kidney and Activating Blood on the Efficacy and NO of Early Diabetic Nephropathy. *Shanghai Journal of Acupuncture and Moxibustion*, 2012(12): 891–892.
- [45] Zheng XY, 2017, Clinical Observation on 70 Cases of Diabetic Peripheral Neuropathy Treated With Pave Moxibustion Therapy. *Chinese Medicine Herald*, 2017(19): 94–97.
- [46] Luo X, Fei A, Hao L, et al., 2020, Mild Moxibustion of Dorsal Yu Points Combined With Acupuncture in the Treatment of Diabetic Peripheral Neuropathy in 31 Cases. *Journal of Jiangxi University of Traditional Chinese Medicine*, 2020(2): 62–64.
- [47] Wei X, Xu YZ, Wei LL, et al., 2019, Clinical Observation on the Treatment of Diabetic Peripheral Neuropathy by Thunder Fire Moxibustion. *China Modern Distance Education of Traditional Chinese Medicine*, 2019(21): 83–85.
- [48] Tang N, Ban Y, Song B, et al., 2018, Clinical Observation of Thunder Fire Moxibustion to Improve Pain in Painful Diabetic Peripheral Neuropathy With Qi Deficiency and Blood Stasis. *China Traditional Chinese Medicine Modern Distance Education*, 2018(16): 122–124.
- [49] Yang J, Qin L, 2024, Meta-Analysis of the Effects of Acupressure on Postoperative Pain and Knee Function in Patients Undergoing Total Knee Arthroplasty. *Evidence-Based Nursing*, 2024(6): 992–999.
- [50] Guo L, Tian Y, Pendulum X, et al., 2024, Clinical Observation on Acupoint Massage for the Treatment of Blood Stasis Diabetic Peripheral Neuropathy. *Chinese Journal of Traditional Chinese Medicine*, 2024(7): 3853–3856.
- [51] Ma HM, Zhang W, Sun S, et al., 2023, Study on the Effect of Acupressure Care on Patients With Diabetic Peripheral Neuropathy. *Chinese Health Care*, 2023(23): 154–156.
- [52] Zhao Q, Li H, Ji M, et al., 2018, A Systematic Review and Meta-Analysis of the Efficacy and Safety of Tui Na for the Treatment of Essential Hypertension. *Journal of Traditional Chinese Medicine*, 2018(18): 1568–1573.
- [53] Yan H, Zhang C, Wang Y, et al., 2020, Effectiveness of High-Intensity Interval Training Combined With Acupressure in Patients With Type 2 Diabetes Mellitus. *Nursing Research*, 2020(19): 3394–3400.
- [54] Huang ZY, Zou S, Wu JL, et al., 2022, Research Progress of Chinese Medicine in the Treatment of Diabetic Foot. *Chinese Folk Therapy*, 2022(21): 121–125.
- [55] Zhang H, Geng S, 2022, Staged and Stratified Treatment Strategy for Diabetic Foot With External Chinese Medicine. *Beijing Traditional Chinese Medicine*, 2022(7): 769–772.
- [56] Shao R, He Q, 2022, Progress in the Understanding and Treatment of Diabetic Foot in the Elderly. *Journal of Tianjin Medical University*, 2022(4): 452–455.
- [57] Xu XY, Yang BH, Zhao JX, et al., 2021, On the External Treatment of Diabetic Foot in Chinese Medicine and Its Practice. *Beijing Traditional Chinese Medicine*, 2021(12): 1336–1339.
- [58] Zhang YX, Jiang H, 2022, Application of Chinese Medicine Fumigation in Diabetic Foot. *Chinese Medicine Clinical Research*, 2022(16): 86–88.

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Efficacy Study of Molecular Diagnostic Techniques for Monitoring Tuberculosis Relapse

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Abstract: The purpose of this article is to analyze the efficacy of molecular diagnostic techniques for monitoring tuberculosis relapse. After analyzing the connotation of molecular diagnostic techniques and their specific application process in tuberculosis relapse monitoring, a total of 200 cured tuberculosis patients were selected (100 in the experimental group and 100 in the control group). During the 12-month follow-up period, the experimental group was monitored by molecular diagnostic techniques, while the control group was monitored by traditional techniques. Finally, by comparing the performance indicators of the two monitoring methods, as well as the relapse situations and outcomes of patients, it was demonstrated that molecular diagnostic techniques have higher efficacy in tuberculosis relapse monitoring.

Keywords: Molecular diagnosis; Tuberculosis; Relapse monitoring; Target amplification

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1. Introduction

Tuberculosis is a prevalent disease, and monitoring patients for relapse after treatment is crucial for safeguarding their health and quality of life. On the one hand, monitoring for tuberculosis relapse can identify patients as early as possible, block potential sources of infection, and reduce the risk of infection. On the other hand, by monitoring the evolution of the patient's condition, it can provide data support for optimizing the patient's subsequent treatment and healthcare strategies, and generate personalized treatment plans. Mastering scientific, effective, and accurate monitoring methods is a key factor in improving the efficiency of relapse monitoring, controlling monitoring costs, and maximizing public health benefits.

2. Introduction to molecular diagnostic techniques and their application in tuberculosis relapse monitoring

2.1. Overview of molecular diagnostic techniques

Molecular diagnostic techniques belong to a type of precision medicine technology that can achieve disease typing, diagnosis, and prognosis assessment by detecting nucleic acids (DNA/RNA), proteins, or other biological molecular markers in biological samples. Its principle is to reveal the essence of diseases at the molecular level, and it has the characteristics of high specificity, high sensitivity, and early diagnosis.

Specifically, the core technical processes of molecular diagnostic techniques include target identification, signal amplification and conversion, and signal detection and analysis. Among them, target identification is to amplify DNA/RNA fragments through technologies such as polymerase chain reaction (PCR) to improve detection sensitivity, and then use labeled probes for specific binding to target sequences for the detection of protein markers. Signal amplification and conversion use PCR amplification technology to amplify target DNA exponentially and detect it using fluorescence signals or electrophoresis. Signal detection and analysis use chemiluminescence or fluorescence technology to monitor the amplification products in real-time, such as quantitative PCR (qPCR).

By utilizing the characteristics of DNA polymerase synthesizing new DNA strands during the PCR process, combined with a fluorescently labeled probe or dye, the progress of the PCR reaction can be measured by monitoring the increase of fluorescence signals in real-time. The entire molecular diagnosis process usually involves technologies such as gene chips, PCR technology, next-generation sequencing (NGS) high-throughput testing technology, microfluidics, and lab-on-a-chip technology.

2.2. Application of molecular diagnostic techniques in tuberculosis relapse monitoring

In the monitoring of tuberculosis relapse, the application process of molecular diagnostic techniques includes sample collection and pretreatment, nucleic acid extraction and purification, target amplification and detection, rapid drug-resistance detection, data analysis, and result interpretation.

2.2.1. Sample collection and pretreatment

For the dynamic monitoring of tuberculosis patients, samples are collected after treatment and then compared and analyzed. In this process, sample processing is a key step to improve the quality of analysis. Medical institutions use N-acetylcysteine-sodium hydroxide for liquefaction and decontamination to remove interfering bacteria. Subsequently, a high-speed centrifuge is used to enrich *Mycobacterium tuberculosis*, ensuring higher accuracy of the sample in subsequent detections. In terms of quality control, internal reference DNA, such as the human β -actin gene, is introduced to monitor the efficiency of nucleic acid extraction.

2.2.2. Nucleic acid extraction and purification

Nucleic acid extraction and purification are basic steps of molecular diagnostic techniques. Based on the pretreated samples, efficient extraction is achieved through magnetic bead methods or silica membrane adsorption methods. At the same time, specific capture probes are designed for MTB DNA drug-resistance genes, such as *rpoB* and *katG*, to further improve the detection accuracy.

2.2.3. Target amplification and detection

In the target amplification and detection stage, real-time fluorescence quantitative PCR (qPCR) technology is used

to distinguish *Mycobacterium tuberculosis* from non-*Mycobacterium tuberculosis* using labeled probes. At the same time, based on the loop-mediated isothermal amplification (LAMP) technology targeting the MPB64 gene, amplification can usually be completed within 1 hour, and the result can be judged by color development.

2.2.4. Rapid drug-resistance detection

For drug-resistance detection, the Xpert MTB/RIF system is mainly used in combination with real-time fluorescence PCR and melting curve analysis to detect *rpoB* gene mutations within 2 hours and report MTB positivity and rifampicin resistance. On this basis, based on current probe technology, after PCR amplification, hybridization probes are used, and reverse dot-blot hybridization is used to read the drug-resistance genotypes of rifampicin and isoniazid.

2.2.5. Data analysis and result interpretation

Data analysis and result interpretation aim to comprehensively understand threshold determination and the analysis of drug-resistance gene mutations. In the threshold determination link, the Ct value is used to determine the number of cycles required for the fluorescence signal in qPCR to reach the threshold. A lower Ct value corresponds to a higher bacterial load. Subsequently, based on the melting curve peak pattern, the purity of the bacterial species in the sample is revealed. For the analysis of drug-resistance mutations, the sequencing results are compared with the data in the existing *Mycobacterium tuberculosis* drug-resistance gene database (such as the TBDrea database). Finally, the types of drug-resistance mutations can be clarified, supporting the assessment of clinical relapse risks and the fine-tuning of subsequent treatment plans. Under the monitoring results, if MTB DNA remains positive or drug-resistance genes appear, it indicates an increased probability of tuberculosis relapse in patients, and consideration should be given to changing to second-line drugs, such as delamanid and bedaquiline^[1].

3. Influence mechanism of molecular diagnostic techniques on the efficacy of tuberculosis relapse monitoring

3.1. Precise identification and dynamic tracking of molecular markers

In the monitoring of tuberculosis relapse, the identification and dynamic tracking of molecular markers are the keys to assessing the relapse risk of tuberculosis patients. Based on high-throughput sequencing and real-time PCR fluorescence technology, medical institutions can accurately identify specific gene fragments of *Mycobacterium tuberculosis* (such as IS6110 and RD9). The presence and dynamic changes in the expression levels of these markers are important indicators for monitoring tuberculosis relapse. At the same time, combined with target amplification and specific probe hybridization, sequence comparison before and after patient treatment can be achieved, and then the tracking of drug-resistance mutations, such as *rpoB* and *katG*, can be realized. Compared with traditional culture methods, molecular diagnostic techniques can provide rapid and sensitive means for disease course and dynamic monitoring, effectively identifying signs of relapse and guiding medical institutions to implement targeted and precise intervention management for patients.

3.2. Multidimensional analysis of molecular heterogeneity

The molecular heterogeneity of *Mycobacterium tuberculosis* has a direct impact on the relapse risk and drug-resistance characteristics of tuberculosis. The application of molecular diagnostic techniques can reveal the

mutation spectra inside and outside the strain and the heterogeneity of gene expression in multiple dimensions through whole-genome sequencing and single-cell RNA sequencing. Multidimensional analysis methods can provide medical institutions with a comprehensive and in-depth understanding of the strain lineage and drug-resistance mechanisms, especially for different drug-resistance gene mutations, such as the distribution of katG S315T and inhA. Precise analysis of heterogeneity can not only promote the optimization of standard treatment plans but also provide personalized targeted treatment for different patients. At the same time, by using the analysis of molecular heterogeneity, it is possible to quickly determine whether the relapse strain and the primary strain are homologous, and then accurately judge whether the patient's condition is a primary infection or a relapse infection.

3.3. Visualization of host-microenvironment interactions

From the perspective of host-microenvironment interactions, the use of molecular diagnostic techniques in tuberculosis relapse monitoring enables visual monitoring. Using multiple chromatography-mass spectrometry and cell imaging technology, medical institutions can quickly analyze the interactions between the host immune response and pathogens, thereby assessing the immune homeostasis of the host after treatment. Such interactions can effectively reveal the regulatory mechanisms of cytokines such as interferon and tumor necrosis factor during relapse. At the same time, combined with RNA in situ hybridization and multispectral imaging technology, medical institutions can effectively observe the co-localization of pathogen distribution and host cell responses in tissue sections. Visual analysis can promote a deeper understanding of tuberculosis reactivation in medical institutions and provide strong support for the research and development of new medical treatments and therapies^[2].

4. Analysis of the application effect of molecular diagnostic techniques in tuberculosis relapse monitoring

To objectively understand the efficacy of molecular diagnostic techniques in tuberculosis relapse monitoring, two hundred cured tuberculosis patients were selected from a public tertiary-grade A hospital in this study. Among them, one hundred patients were monitored by traditional relapse monitoring methods after treatment and set as the control group, and 100 patients were monitored by molecular diagnostic techniques after treatment and set as the experimental group. This article will demonstrate that molecular diagnostic techniques have higher efficacy than traditional monitoring methods by comparing the relapse monitoring results of the two groups of patients.

4.1. Research subjects

The research subjects of this study were 200 cured tuberculosis patients from a public tertiary-grade A hospital, aged 18–65 years old, including 100 male patients and 100 female patients. The samples were selected through strict case screening to ensure that all 200 subjects had no serious complications. In terms of monitoring methods, a 100 patients in the control group were monitored by traditional relapse monitoring methods, that is, sputum smear microscopy + Lowenstein-Jensen culture. Another hundred patients in the experimental group were monitored by molecular diagnostic techniques after treatment, that is, Xpert MTB/RIF combined with CRISPR-Cas detection.

The follow-up period of this study was set to 12 months after the patients received treatment and follow-up visits were conducted on average every 3 months. The main follow-up data included the tuberculosis relapse rate,

detection sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). In terms of data collection, the etiological test results, clinical symptoms, imaging features, and treatment history of the patients in the control group and the experimental group were recorded^[3-5].

4.2. Comparison of the effects of different monitoring methods

4.2.1. Comparison of performance indicators

The detection rates, sensitivities, specificities, PPVs, NPVs, detection time, and single-test costs of traditional monitoring methods and molecular diagnostic techniques were compared, as shown in **Table 1**.

Table 1. Comparison of performance indicators between traditional monitoring methods and molecular diagnostic techniques for tuberculosis recurrence

Indicators	Traditional monitoring method (Control group)	Molecular diagnosis (Experimental group)
Detection rate	72% (72/100)	95% (95/100)
Sensitivity	65%	98%
Specificity	89%	97%
Positive predictive value (PPV)	75%	96%
Negative predictive value (NPV)	85%	98%
Detection time cost	Sputum smear: 24 hours Culture: 21 days	2 hours
Single-test cost (Yuan)	150 (sputum smear) 300 (culture), total 450 yuan	500 yuan

By comparing the two monitoring methods, the molecular diagnostic technique used in the experimental group has a sensitivity 33 percentage points higher than that of the traditional monitoring method and its specificity is significantly better than that of the traditional method (97% for molecular diagnosis vs. 89% for the traditional method). At the same time, the PPV and NPV of the molecular diagnostic technique reach 96% and 98%, respectively, which are much higher than 75% and 85% of the traditional monitoring method. In addition, in terms of time cost, molecular diagnosis only takes 2 hours, while the entire process of the traditional monitoring method takes 21 days. Although the cost of molecular diagnosis is slightly higher than that of the traditional monitoring method, considering the indicator performance and time cost, molecular diagnosis actually has a lower cost^[6-8].

4.2.2. Comparison of patient relapse rates and clinical outcomes

Table 2 shows the comparison of relapse rates and clinical outcome data of 100 patients in the control group and the experimental group, including the relapse rates within 12 months, early relapse situations, and symptom remission times of the two groups of patients.

Based on the data comparison in **Table 2**, among the 100 patients in the experimental group using molecular diagnostic techniques, the relapse rate within 12 months is just 5%, with the early relapse rate controlled at 2%. This is significantly lower compared to the relapse rates observed with traditional monitoring methods. This shows that molecular diagnostic techniques, with an average of one test every 3 months, can quickly detect the signs of tuberculosis relapse. In addition, the imaging abnormality rate and symptom remission time of the experimental group are much lower than those of the control group^[9, 10].

Table 2. Comparison of recurrence rates and clinical outcomes between the control group and the experimental group

Indicators	Molecular diagnostic technique (Experimental group)	Traditional monitoring method (Control group)	<i>P</i> -value
Relapse rate within 12 months	5% (5/100)	18% (18/100)	< 0.01
Early relapse (≤ 6 months)	2% (2/100)	12% (12/100)	< 0.05
Imaging abnormality rate	8% (8/100)	25% (25/100)	< 0.01
Symptom remission time (days)	14 \pm 3	21 \pm 5	< 0.001

5. Conclusion

Based on this study, it can be concluded that compared with traditional tuberculosis relapse monitoring methods, molecular diagnostic techniques can comprehensively improve the early-warning level of tuberculosis relapse based on highly sensitive pathogen detection and rapid drug-resistance gene analysis, reducing the probabilities of early and long-term relapse. In the future, medical and health institutions can promote the large-scale and popularized application of molecular diagnostic techniques in areas with limited medical resources through medical insurance policies and the technical training of medical staff, to achieve high-quality relapse monitoring of tuberculosis patients and improve the patients' living standards.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Zhao Y, Tu X, Wang N, et al., 2024, Comparison and Application Analysis of the Positive Detection Contributions of Three Etiological Detection Methods for Pulmonary Tuberculosis Patients. *Chinese Journal of Antituberculosis*, 2024: 1–12.
- [2] Gu J, Zhang P, 2025, Evaluation of the Application Value of Three Mycobacterium Tuberculosis Detection Methods in a General Hospital. *Journal of Tuberculosis and Lung Diseases*, 6(1): 68–72.
- [3] Ke Z, Tao X, Zhang X, et al., 2024, Application Progress of Molecular Biology Techniques in the Diagnosis of Multidrug-Resistant/Rifampicin-Resistant Tuberculosis. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, 34(11): 1073–1077.
- [4] Mairihaba K, Maiwulajiang Y, Alimire A, et al., 2024, Analysis of the Spatial Clustering and Influencing Factors of Tuberculosis Relapse Among Patients in Kashgar Region, Xinjiang From 2013 to 2020. *Modern Preventive Medicine*, 51(14): 2501–2506.
- [5] Sun Q, Wang X, Fu J, et al., 2024, Analysis of the Relapse Situation and Influencing Factors of Newly Treated Tuberculosis Patients After Successful Treatment in Nantong City, Jiangsu Province From 2013 to 2020. *Disease Surveillance*, 39(10): 1270–1275.
- [6] Zhao Y, Tu X, Wang N, et al., 2024, Comparison and Application Analysis of the Positive Detection Contributions of Three Etiological Detection Methods for Pulmonary Tuberculosis Patients. *Chinese Journal of Antituberculosis*, 2024: 1–12.
- [7] Yan G, Wang X, Wang Y, et al., 2025, Diagnostic Value of Metagenomic Next-Generation Sequencing for Suspected Osteoarticular Tuberculosis Patients. *Chinese Journal of Antituberculosis*, 47(2): 175–180.

- [8] Ke Z, Tao X, Zhang X, et al., 2024, Application Progress of Molecular Biology Techniques in the Diagnosis of Multidrug-Resistant/Rifampicin-Resistant Tuberculosis. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, 34(11): 1073–1077.
- [9] Shang Y, Li Q, Feng M, et al., 2023, Analysis of the Results of the Proficiency Testing of Molecular Diagnostic Techniques for Tuberculosis in Shanxi Province. *Journal of Shanxi Health Vocational College*, 33(5): 64–65.
- [10] Li S, Wang Y, Shu W, et al., 2023, New Progress in the Research and Development of Tuberculosis Laboratory Diagnostic Techniques. *Chinese Journal of Antituberculosis*, 45(5): 446–453.

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Influence of Personalized Nursing on Improving the Satisfaction of Emergency Pediatric Nursing

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Abstract: Personalized nursing is a necessary means to improve the satisfaction of emergency pediatric nursing. It can enhance the responsiveness of nursing services, strengthen the emotional connection between nurses and patients, and provide a theoretical basis for clinical practice. Therefore, in the context of the new era, it is necessary to deeply analyze the essence and connotation of personalized nursing, and analyze the existing deficiencies in current emergency pediatric personalized nursing, so as to develop effective improvement plans. Research shows that personalized nursing can significantly improve the satisfaction of emergency pediatric nursing, largely avoid nursing risks, and has strong clinical application value. This article summarizes and explores the research on the influence of personalized nursing on improving the satisfaction of emergency pediatric nursing, and puts forward corresponding views.

Keywords: Personalized nursing; Emergency pediatric nursing; Satisfaction; Influence; Research

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1. Introduction

Since the new era, exploring personalized nursing has been the key to promoting the development of clinical nursing work^[1]. The emergency pediatric department is one of the many departments in most hospitals, and it undertakes the important responsibility of treating critically ill children. However, due to the complex and changeable conditions of children and the anxiety of some parents, the nursing work in the emergency pediatric department is quite difficult. In response to this situation, the application of personalized nursing in emergency pediatric nursing is crucial for improving satisfaction. Personalized nursing is more comprehensive and targeted. Its focus is to strive for perfection in the nursing process, pursue high-quality nursing, and provide patients with a good nursing service experience^[2].

2. The essence and characteristics of personalized nursing

At present, the public's requirements for clinical nursing are escalating and personalized nursing is being

increasingly applied to different departments of clinical nursing. Through analysis, personalized nursing is a new patient-centered nursing concept. It emphasizes that nursing should meet the different detailed needs of patients. During the nursing process, high-quality and comprehensive personalized nursing services are provided for patients from physiological, psychological, social and other levels^[3]. Considering the characteristics of the emergency pediatric department, personalized nursing covers in-depth and scientific observation and treatment of children's conditions, as well as health education and psychological support for children and their families. For example, the emergency degree of the condition can be quickly judged according to the children's complaints, symptoms, and signs, and the children can be divided into three categories: critical, urgent, and non-urgent. The possible causes can be judged according to the children's symptoms (such as fever, vomiting, diarrhea, dyspnea, convulsions, etc.). Moreover, at the level of psychological support, nursing staff also need to communicate with children and parents with a good attitude, and timely grasp their psychological dynamics, to relieve the anxiety of children and their families and ensure the treatment^[4].

3. The intrinsic value of the application of personalized nursing

3.1. Effectively improving the overall quality of nursing

Personalized nursing significantly improves the quality and safety of nursing work, reduces the occurrence of nursing errors and risk events and ensures that children receive high-quality and efficient nursing services^[5]. This can bring a good nursing experience to children, reduce their physical and psychological burdens, and also relieve the psychological pressure of their families.

3.2. Improving the satisfaction of children and their families

Nursing services that pay more attention to details can make children and their families feel the care and professionalism of nursing staff, enhance their trust and recognition of nursing work, and thus improve their satisfaction with nursing services. In addition, personalized nursing also pays more attention to the psychological changes of children and their families. If unstable emotions occur, nursing staff will adjust the nursing methods in the shortest possible time, which can further improve the satisfaction of children and their families^[6].

3.3. Promoting the recovery of children

Through practice, it is not difficult to find that personalized nursing plays a role in psychological care, nutritional support, rehabilitation guidance, etc. It helps to relieve children's negative emotions, enhance their body immunity, and promote their early recovery.

4. A brief description of common risks in emergency pediatric nursing

4.1. Factors affecting personalized nursing

4.1.1. Insufficient competence of nursing staff

Personalized nursing requires medical staff to take into account the situation of children. Moreover, the diseases of children in the emergency pediatric ward are diverse, and there are few cases of a single disease. Therefore, in the treatment process, multiple drugs need to be used in combination, and there are many nursing operations. From these two perspectives, nursing staff should have strong practical ability, adaptability, and application ability.

At the same time, they also need to have a certain understanding of first-aid, personalized nursing, psychological analysis, and other knowledge, be proficient in using various advanced rescue equipment, and have certain insight. However, analyzing the emergency pediatric nursing situation in some hospitals, the professional knowledge of some nursing staff does not meet the standards, and their overall professional level is low. For example, when observing the patient's condition, some nursing staff do not understand the symptoms of the patient, resulting in frequent delays in diagnosis and even missing the best treatment time. Secondly, they cannot skillfully use the latest diagnostic and treatment equipment. Some nursing staff have difficulty operating the latest treatment equipment, and their adaptability is poor, which often leads to disputes with the patient's family.

4.1.2. Excessive overall pressure on nursing staff

Since the new era, China's people's livelihood medical system has been further improved and the number of emergency pediatric patients has continued to increase. Based on this, to meet the nursing needs of emergency pediatric patients, clinical nursing technology and basic nursing workload have also increased further, resulting in a shortage of clinical nursing staff, and even failing to meet the bed-to-nurse ratio stipulated by relevant departments. For example, in 2021, the bed-occupancy rate of hospitals nationwide was 74.6%, and that of public hospitals was 80.3%. In 2024, the number of registered nurses per 1,000 population in China reached 4^[7]. In such a situation, the workload of nursing staff has further increased and they are often in a state of fatigue, which increases the nursing risk to a certain extent and some negligent behaviors occur from time to time. Moreover, due to the lack of staff, some hospitals directly require interns to engage in front-line work. Due to the lax management of some hospitals, the nursing risk has been further increased.

4.2. Internal hospital factors

At present, more medical technologies and drugs are applied to medical nursing. In order to improve the effect of emergency pediatric nursing and meet the basic needs of users, it is necessary to train relevant nursing staff to minimize the internal risks of nursing. However, some hospitals have not implemented this, resulting in insufficient training for nursing staff and difficult improvement of their abilities. For example, some medical equipment has certain potential hazards. The more prominent problem is the hardware facilities. A depressing environment is not conducive to the recovery of children and will also affect the emotions of children and their parents to a certain extent^[8].

5. Strategies for applying personalized nursing to improve the satisfaction of emergency pediatric nursing

5.1. Strengthening risk assessment and improving nursing ability

Personalized nursing requires medical staff to have strong management, nursing, and service abilities, and be able to develop effective nursing plans according to the actual situation. Therefore, the hospital needs to assist medical staff to further strengthen risk control and effectively improve the comprehensive abilities of nursing staff, to fully implement personalized nursing in the emergency pediatric department. First, the hospital needs to organize medical staff to conduct a nursing risk assessment of the emergency pediatric patients in the hospital. In this process, various assessment forms can be used, such as infection risk assessment forms, nursing quality assessment forms, psychological nursing assessment forms, etc., and corresponding risk prevention measures can be implemented around these assessment contents, to develop an effective safety management system^[9]. Second,

the hospital needs to organize the nursing staff to regularly analyze the nursing risk events that have occurred in the department recently, based on the integrated clinical data. If the problem lies with the nursing staff, they need to be trained to strengthen their comprehensive management abilities, to avoid the occurrence of safety events and enable them to fully master the application methods and precautions of personalized nursing. Finally, anonymous reporting management can be carried out for adverse events in nursing, encouraging each department to report various adverse phenomena, and organizing medical staff to implement effective management countermeasures for the causes of risks. At the same time, relevant management systems should be established to ensure that medical staff work in strict accordance with the standards.

5.2. Gradually improving the nursing service process around personalized nursing

From the perspective of personalized nursing, scientific and accurate nursing services can significantly improve the nursing efficiency of the emergency pediatric department. Combining the needs of the reform and development of emergency pediatric nursing, a new nursing service system can be constructed from the following aspects: First, appropriately simplify the admission process for children according to the actual situation. Apply intelligent and big-data technologies to timely input and transmit children's information, to save more time for children and their families^[10]. Moreover, nursing staff should quickly assess the condition of children when they are admitted to the hospital, and arrange the nursing priority according to the severity of the condition to ensure that critically ill children can receive timely treatment. Second, scientifically set the nursing operation process. Adjust and improve various nursing operations according to the standards, develop detailed operation processes and precautions, and strengthen the operation assessment of nursing staff, so that they can proficiently master the correct operation methods and improve the accuracy and efficiency of nursing operations. For example, in the aspect of intravenous puncture, nursing staff should select the appropriate puncture site and puncture tool according to the age and vascular conditions of children, to improve the success rate of one-time puncture and reduce the pain of children^[11]. Third, establish a nursing shift-handover system. Nursing shift-handover is an important link to ensure the continuity and integrity of nursing work. A detailed shift-handover process and record form should be developed. Nursing staff are required to make a detailed handover of the children's conditions, treatment situations, nursing key points, etc. during the shift-handover and make records to ensure the accurate transmission of information. Through these methods, a new nursing process system can be constructed to effectively improve the nursing service quality.

5.3. Establishing a good nurse-patient relationship

In nursing work, in order to ensure the smooth progress of nursing work, nursing staff need to establish a good relationship with children and their families in line with the principles of personalized nursing, effectively reduce nursing risks, and ensure that children actively cooperate with nursing. In most cases, when nursing staff build a good communication relationship with patients, through communication, they can understand each other's situations. Children and their families will be more actively cooperate with the work of nursing staff and the nursing risk will be further reduced. In order to build a bridge of communication with patients, nursing staff need to treat everyone equally and should not discriminate against or neglect children for some special reasons. They need to establish a good and mutual-trust relationship with patients in actual work^[12]. At the same time, nursing staff need to use warm language and appropriate actions to make emergency pediatric patients feel their sincerity, to gain the trust of patients. Then, appropriate language can be selected according to different psychological states

to relieve the psychological barriers of patients as much as possible. Emergency pediatric patients may have fragile and sensitive psychological states due to their insufficient cognitive abilities and the strangeness of the hospital environment. They may be more likely to feel anxious, fearful, lonely and helpless, and this psychological state will directly affect their attitude and cooperation degree towards nursing. Therefore, nursing staff should be keenly aware of these psychological signals in their work and take corresponding measures to win the trust of children. After that, nursing staff can better understand the psychological states of patients and then take targeted psychological nursing measures. For children who are anxious due to illness, nurses can explain the condition and treatment plan in plain language to help them reduce their psychological burden. For children who feel lonely due to long-term hospitalization, nurses can appropriately increase the accompanying time or organize some in-ward interaction activities to make them feel the warmth of the group^[13].

5.4. Continuously guiding children and their families

To ensure the smooth progress of nursing work and improve management efficiency, it is particularly important to effectively guide children and their families. First, for young patients with relatively weak self-care abilities, medical staff need to communicate with their families in a timely manner and clearly inform the families to ensure that they can accompany the children throughout the day, or assign professional caregivers for accompaniment. This is because young patients often have fear, anxiety, and other negative emotions when facing the strange hospital environment and complex treatment process, and the accompaniment of family members can provide them with necessary psychological support and a sense of security^[14]. Moreover, strengthening the psychological guidance of young patients is also a key link in improving nursing quality. During the long-term treatment of chronic diseases in the internal medicine department, not only the children themselves but also their families are prone to various negative emotions, such as anxiety, irritability, and even loss of confidence in treatment. Based on this situation, medical staff should actively communicate with patients and their families, and grasp the patients' worried psychology through careful observation. When negative emotions are found in children or their families, nursing staff need to actively comfort and guide them in a timely manner^[15].

6. Future prospects

First, the integration of intelligent and personalized nursing services. With the rapid development of science and technology, artificial intelligence and big data technologies will be more widely applied in the medical field. In emergency pediatric nursing, with the help of intelligent devices such as smart bracelets and smart temperature patches to monitor the vital signs of children in real-time, dynamic tracking of children's health conditions can be achieved. Medical staff can predict the changes of the condition in advance based on these accurate data and adjust the treatment and nursing plans in a timely manner.

Second, multi-disciplinary collaboration. Emergency pediatric nursing involves multi-disciplinary knowledge and skills. In the future, multi-disciplinary collaboration will be further strengthened. A multi-disciplinary nursing team centered on children will be established, including pediatricians, nurses, dietitians, psychologists, etc., to jointly develop comprehensive and systematic treatment and nursing plans for children. In nursing management, advanced management concepts and methods such as project management and PDCA cycle will be introduced to improve the nursing quality.

7. Conclusion

In summary, in the context of the new era, combined with the current situation of emergency pediatric nursing, taking corresponding intervention measures around personalized nursing can significantly reduce clinical nursing adverse events, improve the nursing quality of nursing staff, and promote the continuous and good development of the pediatric department and even the entire hospital. Therefore, in the new era, hospitals and nursing staff need to base on the actual situation, explore new emergency pediatric nursing methods, deeply explore the connotation and main application methods of personalized nursing. By analyzing the existing problems in current emergency pediatric nursing, a new nursing system can be constructed from aspects such as strengthening the work ability of nursing staff, improving the nursing management system, and strengthening the psychological intervention of children, to improve the overall service quality.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Xu L, Ma R, 2024, Application Analysis of Nurse Hierarchical Management in Pediatric Nursing Management. *China Health Industry*, 21(20): 111–113.
- [2] Xing Q, Zhao Q, Zhao L, 2024, Application Effect Analysis of Detail Management in Pediatric Nursing Management. *China Health Industry*, 21(11): 145–148.
- [3] Du P, 2024, Application of High-quality Nursing Model in Pediatric Outpatient Infusion Children. *Proceedings of the 7th National Academic Exchange Conference on Rehabilitation and Clinical Pharmacy (IV)*, Nanjing Rehabilitation Medicine Association, 2024: 3.
- [4] Li N, 2024, Application of Targeted Nursing in Emergency Nursing of Infantile Convulsion. *Guide of Women's and Children's Health*, 3(2): 133–136.
- [5] Yan M, 2023, Influence of Family-like Nursing Model on Symptom Improvement of Children with Severe Pneumonia and Family Satisfaction. *Guide of China Medicine*, 21(25): 144–146.
- [6] Zhang Y, Xie A, Jing X, et al., 2023, Analysis of the Partnership between Parents of Children and Pediatric Nurses and Its Influencing Factors. *Journal of Nursing Science*, 38(15): 67–70.
- [7] Liu H, Hu Y, 2023, Application Effect Analysis of Personalized Nursing Model in the Nursing of Children with Severe Diarrhea in Pediatrics. *Guizhou Medical Journal*, 47(5): 821–822.
- [8] Chen M, 2023, Influence of Fun-based Nursing on the Compliance Behavior of Children in Infusion Nursing and the Nursing Satisfaction of Their Families. *Guide of China Medicine*, 21(9): 151–154.
- [9] Sun D, 2022, Improvement Effect of Nursing Communication Skills Applied in Pediatric Infusion Nursing on the Nursing Satisfaction of Children's Families. *Guide of China Medicine*, 20(32): 139–141, 145.
- [10] Fang Q, 2022, Clinical Significance of Non-verbal Communication Combined with Personalized Nursing in Infantile Gastroenteritis. *China Foreign Medical Treatment*, 41(08): 180–184.
- [11] Xie Y, 2021, Discussion on the Application of Personalized Nursing in Pediatric Patient Nursing. *Primary Medical Forum*, 25(21): 2997–2999.
- [12] Liu R, 2020, Clinical Application of Personalized Nursing in Neonatal Septicemia Nursing. *Modern Diagnosis & Treatment*, 31(21): 3493–3495.

- [13] Li F, Liu H, Chen C, 2020, Effect Study of Personalized Nursing Model in Pediatric Nursing. *Electronic Journal of Practical Clinical Nursing Science*, 5(19): 141–142.
- [14] Li H, 2020, Exploration of the Application Experience of Humanized Nursing in Pediatric Nursing. *Electronic Journal of Cardiovascular Disease Integrating Traditional Chinese and Western Medicine*, 8(10): 114–115.
- [15] Xu Y, 2017, Application of Personalized Intervention in Pediatric Nursing. *Journal of Modern Medicine & Health*, 33(10): 1557–1559.

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Research Progress on Unplanned Readmission of Enterostomy Patients

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Abstract: From the perspective of unplanned readmission in patients with enterostomy, this study reviewed the incidence, influencing factors and intervention measures, to provide reference for increasing the attention of medical staff, early detection of risk factors and formulation of personalized intervention measures.

Keywords: Enterostomy; Unplanned readmission; Influencing factors; Overview

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1. Introduction

An enterostomy is created when normal anal function cannot be retained due to intestinal disease, creating a new opening in the abdomen that draws part of the intestine out of the body for excretion of feces ^[1]. Although an ostomy saves a patient's life, it results in unplanned readmissions due to various complications. Therefore, it is important to clarify the unplanned readmission rate of patients with enterostomy, arouse the attention of medical staff, and carry out effective intervention measures to reduce the economic burden of patients and improve the prognosis. At present, there are few studies on the unplanned readmission of enterostomy patients in our country. This study summarized the relevant factors for the unplanned readmission of enterostomy patients, and laid the foundation for future targeted intervention.

2. Unplanned readmission rate of enterostomy patients

Based on the national readmission database, Sanaiha *et al.* reviewed 376,693 patients with colostomy, of whom 41.6% were readmitted within the first week of discharge ^[2]. Through a 6-month follow-up of 316 patients with colostomy in Henan, Hou found that the incidence of unplanned readmission was 25.4%, and most of them occurred within 3 months after discharge ^[3]. At present, there is no relevant study on the unplanned readmission of enterostomy patients in China, and there is a lack of statistical analysis of the relevant data.

3. Influencing factors

3.1. Patient factors

3.1.1. Demographic data

Age and sex were the factors influencing the unplanned readmission of enterostomy patients. Older patients are more likely to have unplanned readmissions, which may be related to decreased immune function and increased complications in elderly patients. Some studies have shown higher rates of unplanned readmissions in men, while others have shown a higher risk of readmissions in women ^[4, 5]. In contrast, the study of Plonkowski *et al.* study found that readmissions were gender-neutral ^[6]. The relationship between gender and unplanned readmission is inconsistent and needs to be further verified.

3.1.2. Comorbidity

Patients who have complications before surgery have a higher chance of developing unplanned readmissions ^[7]. Zhang *et al.* followed up 750 elderly patients with heart failure, and the results showed that 22.3% of the patients had readmitted to hospital ^[8]. Infection was associated with unplanned readmissions ^[9]. Poor blood sugar control in patients with combined diabetes can affect wound healing and increase the risk of infection, leading to unplanned readmissions ^[10]. In addition, co-existing respiratory conditions can also lead to complications and increase unplanned readmissions ^[7]. Studies have shown that congestive heart failure is associated with readmission in patients with ileostomy ^[6], however, there was no statistical significance between respiratory and diabetes comorbidities and readmissions.

3.1.3. Obesity

Obesity is more likely to lead to unplanned readmissions. Obese patients had a 50 percent and 20 percent chance of being readmitted to the hospital within 30 months and six months, respectively, compared with non-obese patients, according to a study ^[11]. It may be that obese patients have higher intra-abdominal pressure due to fat involvement, less muscle in the abdominal wall, lower elasticity, and less tight skin adhesion to the ostomy bag, which increases the occurrence of complications and leads to unplanned readmitted hospital visits ^[12].

3.1.4. Frailty

Frailty not only increases the risk of an enterostomy, but also increases the financial burden on the patient, leading to higher unplanned readmissions ^[13]. Braschi *et al.* conducted a survey of enterostomy patients ≥ 65 years of age using five modified frailty indexes, showing that frailty was an independent risk factor for unplanned readmission and had a 1.4-fold higher incidence of complications in frailty patients compared to non-frailty patients ^[14]. At present, the relationship between frailty and unplanned readmission in enterostomy patients has not been investigated in China.

3.2. Disease factors

3.2.1. Ostomy type

Patients with ileostomy have a higher rate of unplanned readmissions ^[10]. But the study of Plonkowski *et al.* study showed no significant difference in readmission rates between ileostomy patients and colostomy patients, with an increased readmission correlation among loop ileostomy patients ^[6]. Therefore, the effect of the mode of ostomy on readmission still needs further study.

3.2.2. Ostomy complications

Patients with long recovery time after ostomy and lack of knowledge about ostomy after discharge are likely to lead to complications such as infection and increase unplanned readmission^[4]. Leakage of ostomy excrement can also cause a series of common complications, such as prolapse, edema, and stenosis of the stoma, increasing the risk of unplanned readmission^[15]. This is consistent with previous research by Wang^[10].

3.3. Other factors

Ying *et al.* used a cohort design to analyze the relationship between hospital stay and unplanned readmission and the results showed that the risk of unplanned readmission increased with the extension of hospital stay, while the reduction of hospital stay did not increase the rate of unplanned readmission^[16].

4. Intervention measures

4.1. Strengthening discharge guidance can help reduce unplanned readmissions

Lin *et al.* implemented a routine nursing plus nursery-led discharge plan for colorectal cancer patients receiving ostomy and conducted a 6-month follow-up. The results showed that compared with the control group, the incidence of complications and unplanned readmissions was lower in the intervention group^[17]. This suggests that effective discharge planning can improve the quality of discharge teaching, reduce the length of stay and the occurrence of complications, and reduce unplanned readmission. The discharge warning tool is an auxiliary tool to prevent unplanned readmission. Yun *et al.* divided the patients with permanent enterostomy into an intervention group and a control group, and used the discharge warning tool on the basis of the control group^[18]. The results show that this method can effectively reduce the complications of patients with permanent enterostomy and reduce the incidence of patients with unplanned readmission.

4.2. Enhancing ostomy education to reduce unplanned readmissions

Forsmo *et al.* selected 122 patients undergoing enterostomy for intervention, and the results showed that stomy education based on the theory of accelerated rehabilitation surgery could significantly reduce the length of hospital stay, but could not reduce the readmission of patients^[19]. The intervention based on the concept of accelerated rehabilitation can reduce the length of hospital stay of patients, but patients may have insufficient knowledge of stomostomy and increase the rate of unplanned readmission. Therefore, health education guided by the accelerated rehabilitation theory needs to be investigated with large samples in the future.

4.3. Implementing effective nursing measures can reduce the risk of unplanned readmissions

Cluster nursing is an evidence-based nursing model that combines a series of related nursing measures and has been widely used in clinical practice^[20]. Ozata *et al.* selected 104 patients who underwent ostomy surgery for intervention, including in-hospital ostomy care, education, and structured post-discharge follow-up, and the results showed that cluster care significantly reduced the readmission rate of patients after ostomy^[21]. With the rapid development of information technology, the application of the “Internet +” information medical care platform in the field of medical services is increasingly widespread. Based on the “Internet +” information medical care platform, Mei *et al.* selected 233 patients with permanent colostomy for continuous care, and found that the “Internet

+” continuous care service model can effectively improve patients’ stomostomy-related knowledge and reduce the rate of unplanned readmission ^[12].

5. Conclusion

Effective interventions are able to reduce the rate of unplanned readmissions for patients. At present, the research on the unplanned readmission of enterostomy patients in China is relatively insufficient, and no targeted risk prediction model has been established. In addition, considering the differences in cultural background, Chinese scholars should learn from foreign experience in the future to construct intervention measures suitable for the unplanned readmission of enterostomy patients in China.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Wang H, 2023, Correlation Research on Disease Benefit Finding, Resourcefulness and Quality of Life of Patients with Enterostomy, thesis, Yanbian University.
- [2] Sanaiha Y, Xing H, Morchi R, et al., 2020, National Study of Immediate and Delayed Readmissions After Colostomy Creation. *Journal of Surgical Research*, 246: 457–463.
- [3] Hou M, 2020, Research on the Current Situation and Factors of Unplanned Readmission of Colorectal Cancer Ostomy Patients, thesis, Henan University.
- [4] Sun L, 2021, Analysis of Risk Factors for Unplanned Readmission within 3 Months after Colorectal Cancer Surgery. *Nursing Practice and Research*, 18(09): 1290–1293.
- [5] Justiniano C, Temple L, Swanger A, et al., 2018, Readmissions With Dehydration After Ileostomy Creation: Rethinking Risk Factors. *Diseases of the Colon & Rectum*, 61(11): 1297–1305.
- [6] Plonkowski A, Allison C, Philipson P, et al., 2023, Risk Factors Associated with Readmission within 30 Days Following Stoma Surgery: Development of a ‘Traffic Light’ Prediction Model. *Colorectal Disease*, 25(4): 747–756.
- [7] Yang J, Feng J, Li K, 2015, Analysis of Influencing Factors of Unplanned Readmission within 1 Year after Colorectal Cancer Surgery. *Journal of Nurses Training*, 30(06): 551–552.
- [8] Zhang J, Wu Q, Li C, et al., 2025, Prediction Study of Symptom Perception during the Acute Episode on Short-Term Health Outcomes in Elderly Patients with Heart Failure. *Journal of Nursing Science*, 40(01): 74–78.
- [9] He Y, Yang J, Jiang L, 2019, Research Progress on Unplanned Readmission after Colorectal Cancer Surgery. *Nursing Research*, 33(2): 290–293.
- [10] Wang Z, Xu H, Li J, et al., 2018, Research on the Current Situation and Influencing Factors of Unplanned Readmission after Emergency Enterostomy. *Chinese Journal of Nursing Education*, 15(11): 860–864.
- [11] Patel K, Krishna S, Porter K, et al., 2020, Diverticulitis in Morbidly Obese Adults: A Rise in Hospitalizations with Worse Outcomes According to National US Data. *Digestive Diseases and Sciences*, 65(9): 2644–2653.
- [12] Dai L, 2019, A Brief Analysis of the Impact of Body Mass Index on Complications of Enterostomy. *Journal of Colorectal & Anal Surgery*, 25(05): 626–628.
- [13] Ebrahimian S, Lee C, Tran Z, et al, 2022, Association of Frailty with Outcomes of Resection for Colonic Volvulus: A

National Analysis. PLoS One, 17(11): e0276917.

- [14] Braschi C, Salzman G, Russell M, 2024, Association of Frailty With Post-operative Outcomes of Older Adults Undergoing Elective Ostomy Reversal. *American Surgeon*, 90(1): 75–84.
- [15] Huang A, Meng Y, Wang X, et al., 2023, Construction and Application of a Continuing Nursing Service Model for Ostomy Patients Based on the “Internet+” Information-based Medical Care Platform. *Journal of Nursing Administration*, 23(5): 350–354.
- [16] Yuan Y, Zhang S, Sun S, et al., 2025, Causal Association Analysis of Hospitalization Duration and Readmission Rate in Patients with Mental Disorders. *Journal of Shandong University (Medical Edition)*, 63(3): 99–109.
- [17] Lin L, Fang Y, Wei Y, et al., 2024, The Effects of a Nurse-led Discharge Planning on the Health Outcomes of Colorectal Cancer Patients with Stomas: A Randomized Controlled Trial. *International Journal of Nursing Studies*, 155: 104769.
- [18] Shen Y, Wang Z, Hou M, et al., 2021, The Application of Discharge Warning Tools in Preventing Unplanned Readmission of Enterostomy Patients. *Journal of Qilu Nursing*, 27(6): 1–3.
- [19] Forsmo H, Pfeffer F, Rasdal A, et al., 2016, Pre- and Postoperative Stoma Education and Guidance within an Enhanced Recovery After Surgery (ERAS) Programme Reduces Length of Hospital Stay in Colorectal Surgery. *International Journal of Surgery*, 36(Pt A): 121–126.
- [20] Li C, Hu J, Su X, et al., 2017, Research Progress of the Concept of Cluster Nursing and Its Application in Surgical Nursing. *Chinese Journal of Modern Nursing*, 23(30): 4.
- [21] Ozata I, Tufekci T, Aksan T, et al., 2024, Reducing Dehydration-induced Readmissions Post-colorectal Surgery: The Impact of a Prevention Bundle. *International Journal of Colorectal Disease*, 39(1): 138.

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Role of Tisp40/Smad2 Protein in High Glucose-induced Renal Interstitial Fibrosis

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Abstract: *Objective:* To observe the effect of high glucose staining on human renal tubular epithelial cells (HKC) and to investigate the role of Tisp40/Smad2 protein in diabetes-induced renal fibrosis. *Methods:* Human renal tubular epithelial cells (HKC) were cultured in vitro and cells were incubated with a final concentration of 25, 50, and 100 mM high glucose for 24 h. The cell viability was detected by the CCK-8 assay; cells were treated with a final concentration of 50 mM high glucose for 6, 8, 12, 24, 48, and 72 h, and the degree of cell damage by high glucose at different time points was detected. Cells were treated with final concentrations of 25, 50, and 100 mM glucose for 24 h. Tisp40 protein expression was detected by enzyme-linked immunosorbent assay (ELISA) and Tisp40 mRNA expression was detected by polymerase chain reaction (RT-PCR). To observe the effect of high glucose on Tisp40/Smads signaling proteins, the Tisp40 cells were divided into six groups: (1) the normal control group; (2) the 25 mM high glucose group; (3) 50 mM high glucose group; (4) 100 mM high glucose group; (5) Tisp40-positive control group; (6) Tisp40-stimulated group (100 mM high glucose + 50 mM Tisp40), and the expression level of phosphorylated Smad2 protein (p-Smad2) was detected by immunoblotting (Western blot). *Results:* Compared with the control group, the survival rate of HKC cells decreased significantly with the increase of high glucose staining dose and time ($P < 0.05$) in a dose-dependent and time-dependent manner. ELISA results showed that the expression of Tisp40 protein was elevated to 44.3, 63.7, and 82.6 $\mu\text{g/ml}$ after 24 h of high glucose action on HKC cells and the induction was in a dose-dependent manner. RT-PCR showed that the expression level of Tisp40 mRNA increased significantly with increasing glucose concentration, which was 2.75, 5.42 and 9.67 times higher than that of the control group, respectively, and the induction was in a dose-dependent manner ($P < 0.05$). The Western blot showed that the expression level of p-Smad2 protein increased significantly after 24h of glucose action in the cells at concentrations of 25, 50 and 100 mM glucose ($P < 0.05$), and the amount of p-Smad2 protein reached the maximum under the co-stimulation of 100 mM high glucose + 50 mM Tisp40 given to the cells ($P < 0.05$). *Conclusion:* Abnormal expression of Tisp40 and p-Smad2 was involved in the process of high glucose-induced HKC cell injury and Tisp40-induced high expression of Smads proteins played an important role in high glucose-induced renal fibrosis.

Keywords: HKC cells; Renal interstitial fibrosis; Tisp40/Smad protein

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1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia, which has become one of the most lethal chronic diseases, with the most prominent and significant renal damage^[1]. Diabetic nephropathy (DN) presents early with persistent microalbuminuria and proteinuria and eventually progresses to renal failure^[2]. It is the most common single etiology in patients with nephropathy in the United States and Europe, up to 44.5%, and about 25% in China^[3]. Pathological findings show that interstitial fibrosis and glomerulosclerosis have become the first manifestation and the mechanism of high glucose-induced renal fibrosis is unknown so far. Renal fibrosis is characterized by fibroblast (FB) proliferation and excessive deposition of extracellular matrix (extracellular matrix, ECM), which leads to changes in normal renal tissue organization and loss of function^[4]. It is characterized by interstitial collagen deposition, inflammatory cell infiltration, loss of renal tubular cell damage, fibroblast accumulation, and peritubular microvascular sparing. Smads play an important role in cell proliferation, development, differentiation, apoptosis, immunomodulation, and regulation of ECM accumulation. The most sensitive receptor-regulated protein in Smad protein is Smad2, and its phosphorylation marks the activation of this protein^[5]. Based on this, this study intends to simulate the model of diabetes-induced renal fibrosis by culturing HKC cells in vitro, to detect the expression of key gene proteins after different high-glucose staining, to elucidate the expression of Tisp40/Smads in the renal fibrosis induced by diabetes, and to provide a theoretical basis for patients with diabetes-induced renal injury in the later stage.

1.2. Research questions

Diabetic renal fibrosis (DNF) is a key pathological process in the progression of diabetic nephropathy to end-stage renal disease, and its core mechanisms include cellular injury, inflammatory response, and extracellular matrix deposition. However, the roles of Tisp40 and p-Smad2 in the development of DNF are still not fully elucidated. The present study focuses on the following questions.

- (1) What are the expression changes and interrelationships of Tisp40 and p-Smad2 in diabetic renal fibrosis?
- (2) Is the expression of Tisp40 and p-Smad2 up-regulated in HKC cells and renal tissues of patients with diabetic renal fibrosis in a high-glucose environment?
- (3) Does Tisp40 contribute to the activation of the Smads signaling pathway through direct or indirect regulation of p-Smad2?

1.3. Objectives

Diabetic renal fibrosis is a key pathology in the progression of diabetic nephropathy to end-stage renal disease and its development involves the regulation of multiple signaling pathways. Among them, the specific roles and interrelationships of Tisp40 and p-Smad2 in renal fibrosis have not been fully clarified. This study aimed to investigate the expression changes of Tisp40 and p-Smad2 in diabetic renal fibrosis and to analyze the expression levels and localization of Tisp40 and p-Smad2 in a high glucose-induced renal tubular epithelial cell (HKC) model. To assess the correlation between Tisp40 and p-Smad2 and to explore their possible roles in diabetic renal fibrosis.

2. Materials and methods

- (1) Human renal tubular epithelial cells (HKC) (Cell Resource Center, Shanghai Institutes for Life Sciences,

Chinese Academy of Sciences)

- (2) Glucose, CCK-8 cell proliferation kit (4980-050k, Trevigen)
- (3) DMSO (Sigma Aldrich)
- (4) Fetal bovine serum (Sigma Aldrich)
- (5) DMEM medium (Sigma Aldrich)
- (6) Penicillin-streptomycin antibiotic (HyClone Cell Culture and Bioprocessing)
- (7) Rabbit anti-human Phospho-Smad2 antibody
- (8) Rabbit anti-human Smad2 antibody
- (9) TRIzol kit
- (10) Sigma-Aldrich quantitative PCR kit
- (11) Taq DNA polymerase probe kit (Wuhan Doctoral Biotechnology Co., Ltd.)
- (12) ELISA reagent test kits (Wuhan Doctoral Biotechnology Co., Ltd.)
- (13) Whole protein extraction Kit (Beijing Solebao Technology Co., Ltd.)
- (14) Bio-Rad DC Protein Assay Kit (Beijing Boao Sen Biotechnology Co., Ltd.)
- (15) Primers (Shanghai Sangon Bioengineering Co., Ltd.)

2.1. Methods

2.1.1. Cell culture

HKC cells are cultured using F12/DMEM (1: 1) medium (37 °C constant temperature incubator with 5% CO₂, Thermo Fisher) for 3–7 generations for experiments. After 24 hours of incubation, the cells are digested using pre-formulated trypsin to make a cell suspension, which is counted under the microscope and evenly distributed into two culture flasks according to the ratio of 1: 2~3. Logarithmic proliferating cells were selected (to prove no mycoplasma contamination) and continued to be incubated for 24 hours using DMEM to prepare for the experiments. HKC cells were divided into six groups: (1) Normal control group (control); (2) 25 mM high glucose group; (3) 50 mM high glucose group; (4) 100 mM high glucose group; (5) Tisp40 positive control group; and (6) Tisp40 stimulation group (100 mM high glucose + 50 mM Tisp40), and the proteins were extracted as described above.

2.1.2. CCK-8 detection of cell viability

The ultra-clean bench is sterilized and disinfected before and after the operation, and after the working conditions are reached, the cells are removed from the incubator to observe the cell growth. According to the cell growth status, the logarithmic growth phase cells that are favorable for the experiment are selected. Trypsin (0.25% by mass) is used to digest the adherent cells, and the cells are mixed from the bottom of the dish with a micropipette repeatedly. All the cells are resuspended under the microscope, counted, and then cultured for the experiment (1: 3 or 4), and counted under the microscope. The cell density is adjusted using 100 µl/well inoculation in a sterilized 96-well cell culture plate in a 5% CO₂ incubator incubation, at 37 °C for 24h, the plate is removed and the cell growth status is observed under the microscope, to observe if it is fused around 80%–90%, then the plate waste is discarded. Around 100 µL of the intervention reagent is added to each well, so that the cells are exposed to the final concentration of 0 (blank control), 25, 50, and 100 mM of high-sugar DMEM medium, respectively, and incubated at 37°C in a 5% CO₂ incubator. After 24 h of incubation, the intervention solution in each well was discarded, and then 80 µl of fresh DMEM medium and 20 µl of CCK-8 reagent with a mass volume fraction of 5

μg/μL (which had been prepared 4 h in advance), are added to each well of each experimental group and shaken at a low speed for 3 min, and the absorbance (OD) are detected by the enzyme marker at 490 nm. The average OD value of each group is quoted. Cell inhibition rate = (mean value of OD in the solvent control group - mean value of OD in the intervention group)/(mean value of OD in the solvent control group - mean value of OD in the blank control group) × 100%. Five parallel samples are set up in each group and the experiment was repeated thrice.

2.1.3. Protein extraction

The culture solution is poured out and the bottle is held upside down on the blotting paper to allow the blotting paper to absorb the culture solution. Around 3 ml of 4°C pre-cooled PBS (0.01M pH = 7.2–7.3) is added to each bottle of cells. The cells are washed by gently shaking for 1 min on a flat surface and then the washings are discarded. The above operation is repeated twice, and the cells are washed three times in total to wash away the culture fluid. The culture flask is placed on ice after discarding the PBS. Around 10 μl of PMSF (100 mM) is added to 1 ml of lysate and shaken well on ice. Around 400 μl of lysate containing PMSF is added to each bottle of cells and lysed on ice for 30 min. To make the cells fully lysed, the culture bottle is shaken back and forth frequently. After lysis, a clean scraper is used to scrape the cells on one side of the culture flask, and the cell fragments are quickly transferred to a 1.5 ml centrifuge tube with a pipette. The cells are centrifuged at 12000 rpm for 5 min at 4°C. The supernatant is transferred after centrifugation to a 0.5 mL centrifuge tube and stored at -20°C.

2.1.4. Western blot detection of Tisp40, p-Smad2 protein expression

The preparation of the SDS-PAGE gel electrophoresis includes: Preparation of separator gel (10% PAGE gel, 4 ml) (Solution A: 0.5 ml; Solution B: 0.75 ml); deionized water: 1.75 ml (10% APS: 30 μl; TEMED: 10 μl). After mixing thoroughly, the solution is transferred into the gel-making tank to the corresponding scale and seal with deionized water. A total of 40 μg of protein is extracted into 80 ml of buffer solution, which needs to be denatured for 11 min at 100 °C. Pre-prepared PVDF membranes with the same quality as the separator gel are immersed into the solution containing 1 × Transfer Buffer for 16 min. Previously prepared separator gels are placed in the 1 × Transfer Buffer solution at 4 °C. Drops of pre-prepared rabbit anti-human p-Smad2 (1: 200), rabbit anti-human Smad2 (1:200), rabbit anti-human Tisp40 primary antibody are added, refrigerated overnight at 4°C, washed 3 times with TBST for 5 min and then incubated with (HRP)-labeled IgG secondary antibody (1:1000) for 1 h. In addition to the ECL liquid, Solution A and Solution B of the above ECL kit are taken, mixed well, and put on the plastic wrap. The membrane is placed with the protein side facing up. Add ECL solution to the top of the membrane and incubate for 6 minutes. After incubation, the excess ECL solution is discarded and the membrane is wrapped in clean plastic wrap and set aside. The plastic wrap, completed in the above process, is put into the Kodak Gel Imaging Image Station 4000MM imager, the gray and dark bands are observed and the clear bands are selected to take pictures.

2.1.5. RNA extraction and reverse transcription synthesis of cDNA

According to the pre-determined groups, the concentration of high glucose staining required for the experiment is added and incubated for 24h. The cells are collected after and 1 ml of Trizol reagent is added for digestion. The cells are lysed after the staining at a low temperature for 5 minutes and trichloromethane is added before mixing repeatedly with a pipette. The above homogenate is left at room temperature for 5 min to allow nucleic acids and proteins to fully dissociate. Around 0.2 ml of chloroform per 1 ml of TRIzol reagent dosage of homogenate

is added and the cap of the tube is closed tightly, manually shaken vigorously for 15 s, before being left to stand at room temperature for 2–3 min and centrifuged at 10,000 g at 4°C for 10 min. The carefully aspirated upper aqueous phase (colorless) is added it to a new tube and the volume of the aspirated aqueous phase is calculated at the same time. An equal volume of pre-cooled isopropanol is added to the aspirated aqueous phase, the tube tightly is capped tightly, and gently shaken. The RNA is left to settle by centrifugation at 10,000 g for 10 min at 4°C. The supernatant is discarded, each tube is rinsed with 1 ml of 75% ethanol, cap tightly, and gently shaken to remove residual isopropanol and salts. The tubes is centrifuged at 7,500 g for 5 min at 4°C. The supernatant is disposed, the tubes are un capped and the RNA precipitates are dried (either by evaporation at room temperature or by vacuum drying). The RNA precipitate is dissolved in an appropriate amount of RNase-free water. The appropriate amount of DEPC is added and fully dissolved. An A260 /A280 ratio assay is performed and the sample is placed between 1.8 and 2.1, before being stored at -80°C for backup. Extracted RNA is subjected to agarose gel electrophoresis, and the following mixture is prepared in RNase-free centrifuge tubes, reacted at 65°C for 5 min, and cooled in an ice bath. The reverse transcription reaction conditions are set up as follow: 30°C, 10 min; 42°C for 30 min; 95°C for 5 min, then cooled in an ice bath. The product is stored in the refrigerator at -20°C.

2.1.6. Real-time fluorescence quantitative reverse transcription-polymerase chain reaction (Real-time PCR)

The frozen lysed cells are taken and left at room temperature for 5 minutes to make them completely soluble. The cDNA sequences of the target gene and the internal reference β -actin are obtained from Genbank NCBI Reference Sequences (RefSeq), and the primer design software Primer Premier 5.0 (primer5) and Primer blast are used to design primers based on the genomic reference assemblies of the selected organisms. Primer5 is used to verify the characteristics of the primers themselves, hairpin structure, primer self-dimerization, mismatch, and inter-primer dimerization, and the absolute value of ΔG .

The upstream primer sequence for Tisp40 is 5'-TTACGATCGGTACGAC-3', and the downstream primer is 5'-AATCTAGGCTATGCTG-3'. For the internal reference gene β -actin, the upstream primer is 5'-TCACACCCACGATAATGGC-3' and the downstream primer is 5'-CGGAGTTATCGACTGATCG-3'. For each sample, 1 μ L of cDNA was used. PCR is conducted with an initial denaturation at 93°C for 2 minutes, followed by 40 cycles of 93°C for 1 minute, 55°C for 1 minute, and 72°C for 1 minute. A final extension is carried out at 72°C for 7 minutes. The peak plot of the solubilization curve is used to determine the presence of non-specific amplification: the GC content of the products and the order of the bases make each product have different peaks, which can distinguish the specific products. The $\Delta\Delta C_t$ method is used to analyze the concentration of template DNA, based on the principle that the C_t value is linearly related to the logarithm of the initial template copy number.

2.2. Statistical processing

SPSS 22.0 software is applied to analyze the data statistically, and the test results are expressed as ($\pm s$). ANOVA is used for multiple group comparisons, and SNK and Fisher LSD-t tests are used for group comparisons of multi-sample means. The results are expressed as $P < 0.05$ to indicate that the differences are statistically significant.

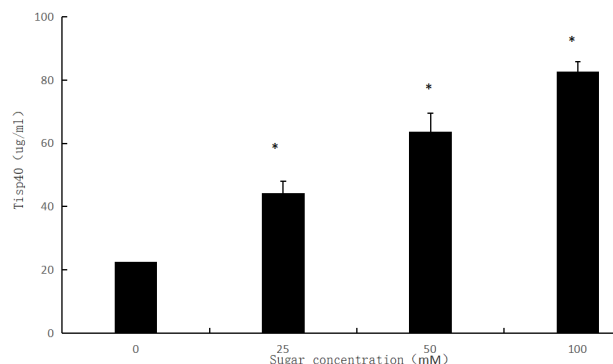
2.3. Ethics approval

Research ethics provided by the Ethics Committee of Ningxia Medical University (License No.: 2024-N066) is used.

3. Results

3.1. Effects of different high glucose staining on HKC cell viability

HKC cells were treated with glucose at final concentrations of 25, 50, and 100 mM for 24 hours. The resulting cell survival rates were 91.7%, 79.5%, and 49.3%, respectively. The differences were statistically significant ($P < 0.05$) when compared with the control group. A dose-dependent pattern was observed, with the higher the staining concentration, the lower the survival rate of the cells (refer to **Figure 1**).

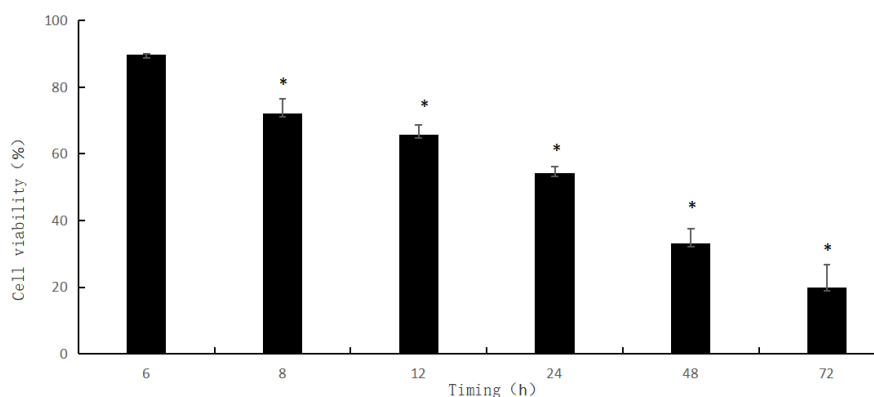


Note: * indicates that the difference between the high glucose group and the control group was statistically significant ($P < 0.05$)

Figure 1. Changes in 24h relative cell survival of HKC cells stained with different concentrations of high sugar.

3.2. Effect of the duration of high glucose staining on the survival of HKC cells

The cells were stained with glucose at a final concentration of 100 mM, and HKC cells were stained for 6 h, 8 h, 12 h, 24 h, 48 h, and 72 h. The survival rate of HKC cells decreased to 89.7%, 72.1%, 65.8%, 54.3%, 33.1%, and 19.9%, respectively, when compared with that of the control group (the survival rate of the control group was set to 1). The differences were all statistically different ($P < 0.05$) when compared with the control group. A time-dependent pattern was observed, with longer dyeing time, lower cell survival, and greater damage (refer to **Figure 2**).



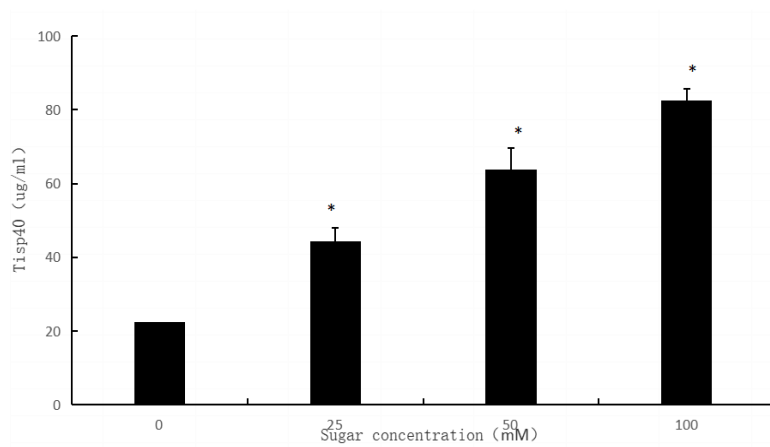
Note: * indicates that the difference between the intervention group and the control group was statistically significant ($P < 0.05$)

Figure 2. Changes in relative survival of HKC cells at different time points under 100 mM concentration staining.

3.3. Different concentrations of glucose-induced Tisp40 protein and Tisp40 mRNA expression

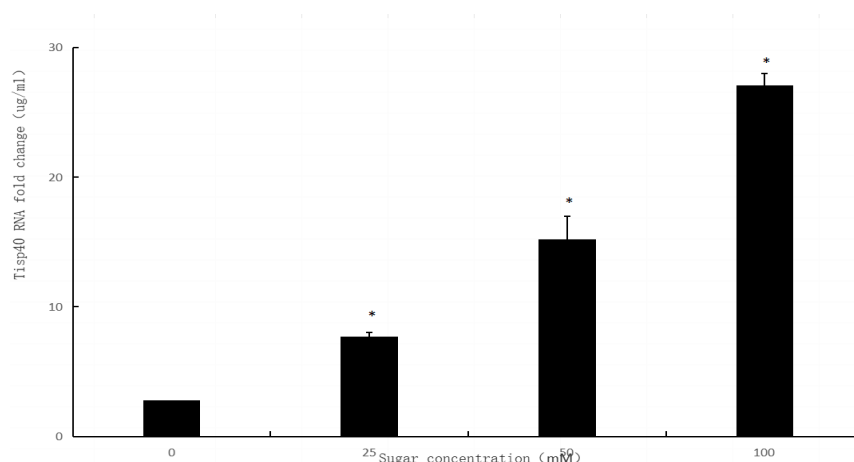
After acting on HKC cells at final concentrations of 25, 50, and 100 mM high glucose for 24 h, the expression of

Tisp40 protein and Tisp40 mRNA was significantly increased compared with that of the control group, and the difference was statistically significant ($P < 0.05$), as shown in **Figure 3** and **Figure 4**.



Note: * indicates that the difference between the intervention group and the control group was statistically significant ($P < 0.05$)

Figure 3. Different concentrations of high glucose induced Tisp40 protein expression



Note: * indicates that the difference between the intervention group and the control group was statistically significant ($P < 0.05$)

Figure 4. Different concentrations of high glucose induced Tisp40 gene expression

3.4. High sugar-induced p-Smad2 protein expression

Compared with the control group, high glucose 25, 50 and 100 mM toxicity doses were able to induce an increase in p-Smad2 protein in HKC cells, and the cell survival rate decreased with the increase of the concentration in a dose-dependent manner ($P < 0.05$). When cells were given Tisp40 stimulation alone, the amount of cellular expression of p-Smad2 protein was very small, whereas when cells were given 100 mM high glucose + 50 mM Tisp40 co-stimulation, the cells expressed the maximum amount of p-Smad2 protein ($P < 0.05$) (refer to **Figure 5**).

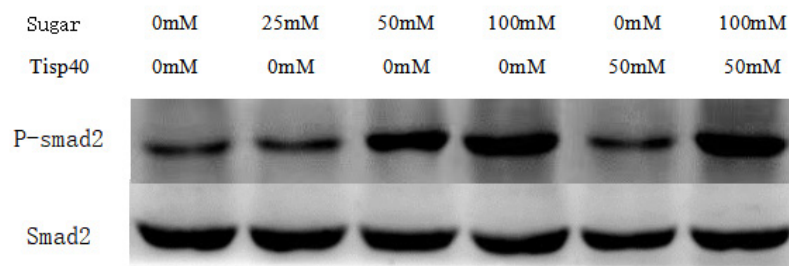


Figure 5. p-Smad2 protein expression in each group of cells

4. Discussion

The pathogenesis of renal fibrosis in diabetic patients is unknown so far. Studies have shown that Tisp40 is closely related to apoptosis, proliferation, and differentiation ^[6]. In hepatocellular carcinoma tissues, the expression level of Tisp40 is also upregulated compared with normal tissues ^[7]. Xiao *et al.* found that the expression of Tisp40 protein was significantly higher than that of the control group in animal models, both in I/R-induced human renal tubular epithelial cell (HK-2) fibrosis and in TGF- β 1 stimulation-induced renal tubular epithelial cells ^[8]. In addition to this, the process of Smad2 phosphorylation, including promoter gene 4 (URG4), transforming growth factor (TGF- β I), zinc finger transcription protein (Snail I), α -smooth muscle actin (α -SMA), epithelial calreticulin (E-cadherin), and inhibition of E-cadherin expression were also regulated.

To further verify whether renal tubular fibrosis is involved in the development of the disease, this study took human renal tubular epithelial cells (HKC) as the research object. The results of this study showed that different concentrations of high glucose, as well as different time interventions in HKC cells could significantly elevate the expression levels of Tisp40 protein and Tisp40 mRNA, and showed a positive correlation between the time and the dose of expression. The high expression of Tisp40 induced morphological changes in the cells, remodeling the microenvironment of HKC cells to make it suitable for new HKC cell survival and proliferation sites. The main changes were α -smooth muscle actin (α -SMA) expression and fibronectin (FN) in the renal tubule-mesenchyme, which were transformed into myofibroblasts that characteristically expressed α -SMA in the presence of high glucose-stimulating factor, and the expression of Tisp40 mRNA was significantly increased.

TGF- β 1 is a key signal transduction factor that plays a critical role in the activation of Smads. However, it is a “double-edged sword,” and some studies to validate the role of TGF- β 1 in fibrosis have found that mice were killed by systemic inflammatory infections after genetically silencing TGF- β 1 ^[9, 10]. To further verify whether Tisp40 could affect the expression of TGF- β 1, Tisp40 knockout mice and I/R-induced mice were constructed, which showed that TGF- β 1 protein expression was not differential, and it was hypothesized that Tisp40 could not directly induce the expression of TGF- β 1.

The Smad family of proteins are common signaling protein factors that induce fibrosis, especially the presence of Smad2 protein as a key factor. Smad2 is composed of the highly conserved MH1 and MH2 linked by a proline-rich strand region. Smad2 has 2 more amino acid fragments than Smad3. Its activation can be phosphorylated by the T β RI receptor on the membrane of downstream cell lines, and the phosphorylated P-Smad2 separates from the receptor T β RI at this time and is transcriptionally activated with target genes on the other copolymer. The results of this study showed that comparing the different concentrations of the high glucose staining group with the control group, the intervention of staining with concentrations of 25mM, 50mM, and

100mM could make the p-Smad2 protein highly expressed, and the difference was statistically significant.

Without high glucose stimulation, simply giving cells Tisp40 intervention, the cells expressed less amount of p-Smad2 protein. Whereas, giving cells 100mM high glucose + 50mM Tisp40 combined intervention, HKC cells showed a significant increase in p-Smad2, which was the highest among all groups, indicating that P-Smad2 was due to high expression of Tisp40 protein and was positively correlated with the dose. Smad2 is overactivated in both experimental animal models and human renal fibrosis ^[11]. In previously constructed models of renal fibrosis, knockdown of the Smad2 gene significantly alleviated the degree of renal fibrosis ^[12], and overexpression of Smad2 was shown to inhibit the activity of MMP-1 in fibroblasts ^[13].

In summary, activation of the Tisp40 protein plays an important role in renal tubular fibrosis caused by high glucose intervention. Based on this, explicitly inhibiting the expression activity of Tisp40, p-Smad2, in this signaling protein, may be a new way to treat renal fibrosis in diabetic patients. However, there may be numerous intermediate synergistic intervention pathways for the high expression of p-Smad2 induced by Tisp40, and it is particularly urgent to explore and precisely inhibit the activating factors affecting its synergistic pathways.

5. Conclusion

Aberrant expression of Tisp40 and p-Smad2 is significantly involved in HKC cell injury under a high glucose environment. It was shown that high glucose conditions induced the upregulation of Tisp40 expression and further promoted the activation of the Smads signaling pathway, especially the aberrant phosphorylation of p-Smad2. Tisp40 may play an important role in key pathological processes, such as renal tubular epithelial cell-to-fibroblast transition (EMT), extracellular matrix (ECM) deposition, and inflammatory response through enhancing the expression of Smads and its signaling, inflammatory response and other key pathological processes. This mechanism may accelerate the process of high glucose-induced renal fibrosis, which ultimately leads to renal impairment. Therefore, Tisp40 may be an important target to regulate the Smads-mediated renal fibrosis signaling pathway, which may provide a new theoretical basis and potential therapeutic strategy for the intervention of diabetic nephropathy (DN) and other related diseases.

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Disclosure statement

The authors declare no conflict of interest.

References

- [1] Zoccali C, Mallamaci F, De Caterina R, 2023, Pharmacokinetic Relevance of Glomerular Hyperfiltration for Drug Dosing. *Clinical Kidney Journal*, 16(10): 1580–1586. <https://doi.org/10.1093/ckj/sfad079>
- [2] Han YC, Tang SQ, Liu YT, et al., 2021, AMPK Agonist Alleviates Renal Tubulointerstitial Fibrosis via Activating

- Mitophagy in High Fat and Streptozotocin Induced Diabetic Mice. *Cell Death & Disease*, 12(10): 925. <https://doi.org/10.1038/s41419-021-04184-8>
- [3] Liu M, Peng T, Hu L, et al., 2020, UVA Influenced the SIRT1-miR-27a-5p-SMAD2-MMP1/COL1/BCL2 Axis in Human Skin Primary Fibroblasts. *Journal of Cellular and Molecular Medicine*, 24(17): 10027–10041. <https://doi.org/10.1111/jcmm.15610>
 - [4] Su Q, Huang W, Huang Y, et al., 2024, Single-cell Insights: Pioneering an Integrated Atlas of Chromatin Accessibility and Transcriptomic Landscapes in Diabetic Cardiomyopathy. *Cardiovascular Diabetology*, 23(1): 139. <https://doi.org/10.1186/s12933-024-02233-y>
 - [5] Giha HA, Alamin OAO, Sater MS, 2022, Diabetic Sarcopenia: Metabolic and Molecular Appraisal. *Acta Diabetologica*, 59(8): 989–1000. <https://doi.org/10.1007/s00592-022-01883-2>
 - [6] Xiao C, Zhao H, Zhu H, et al., 2020, Tisp40 Induces Tubular Epithelial Cell GSDMD-Mediated Pyroptosis in Renal Ischemia-Reperfusion Injury via NF- κ B Signaling. *Frontiers in Physiology*, 11: 906. <https://doi.org/10.3389/fphys.2020.00906>
 - [7] Zhang X, Hu C, Ma ZG, et al., 2023, Tisp40 Prevents Cardiac Ischemia/Reperfusion Injury through the Hexosamine Biosynthetic Pathway in Male Mice. *Nature Communications*, 14(1): 3383. <https://doi.org/10.1038/s41467-023-39159-0>
 - [8] Xiao CC, Zhang J, Luo PC, et al., 2017, Identification of Tisp40 as an Essential Regulator of Renal Tubulointerstitial Fibrosis via TGF- β /Smads Pathway. *Cellular Physiology and Biochemistry*, 42(2): 697–712. <https://doi.org/10.1159/000477887>
 - [9] Cohen AJ, Nikbakht N, Uitto J, 2023, Keloid Disorder: Genetic Basis, Gene Expression Profiles, and Immunological Modulation of the Fibrotic Processes in the Skin. *Cold Spring Harbor Perspectives in Biology*, 15(7): a041245. <https://doi.org/10.1101/cshperspect.a041245>
 - [10] Liu W, Wang F, Huang Q, et al., 2023, N-glycosylation-mediated CD147 Accumulation Induces Cardiac Fibrosis in the Diabetic Heart through ALK5 Activation. *International Journal of Biological Sciences*, 19(1): 137–155. <https://doi.org/10.7150/ijbs.77469>
 - [11] Zhang J, Li Y, Liu Q, et al., 2021, Sirt6 Alleviated Liver Fibrosis by Deacetylating Conserved Lysine 54 on Smad2 in Hepatic Stellate Cells. *Hepatology*, 73(3): 1140–1157. <https://doi.org/10.1002/hep.31418>
 - [12] Abdel MM, Pauklin S, 2021, TGFB1/INHBA Homodimer/Nodal-SMAD2/3 Signaling Network: A Pivotal Molecular Target in PDAC Treatment. *Molecular Therapy*, 29(3): 920–936. <https://doi.org/10.1016/j.ymthe.2021.01.002>
 - [13] Jiang SB, Lu YS, Liu T, et al., 2020, UVA Influenced the SIRT1-miR-27a-5p-SMAD2-MMP1/COL1/BCL2 Axis in Human Skin Primary Fibroblasts. *Journal of Cellular and Molecular Medicine*, 24(17), 10027–10041. <https://doi.org/10.1111/jcmm.15610>

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Research on Predicting the Nephrotoxicity Mechanism of Lianqiao-4 Based on Network Pharmacology and Molecular Docking

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Abstract: *Objective:* To predict the nephrotoxicity mechanism of Lianqiao-4 through network pharmacology and molecular docking methods. *Methods:* The main chemical components of Lianqiao (Forsythia suspensa), Bistortae rhizoma, Ophiopogonis radix, and Clematidis radix et rhizoma, as well as nephrotoxicity-related targets, were screened through databases such as TCMSP, Swiss Target Prediction, GeneCards, and ETCM. Venny 2.1.0 was used to identify the main components of Lianqiao-4 and nephrotoxicity targets. The STRING platform and David database were utilized to construct a protein-protein interaction (PPI) network diagram, while gene function (GO) enrichment analysis and KEGG pathway analysis were conducted. The “Lianqiao-4 active ingredients-nephrotoxicity targets-signaling pathways” network model was constructed using Cytoscape 3.9.1 software. *Results:* Network pharmacology and molecular docking analysis revealed that the core active ingredients responsible for the nephrotoxicity mechanism of Mongolian medicine Lianqiao-4 include steroidal saponins such as ophiopogonin A, flavonoids like kaempferol and quercetin, steroidal compounds such as β -sitosterol and sitosterol, and other key regulatory targets including STAT3, ABCG2, HSP90AA1, MMP9, PTGS2, and EGFR. Major pathways involved include lipid and atherosclerosis, chemical carcinogenesis - DNA adducts, and arachidonic acid metabolism. *Conclusion:* Mongolian medicine Lianqiao-4 exerts its therapeutic effect on nephrotoxicity through multiple components, targets, and pathways, pending experimental verification.

Keywords: Network pharmacology; Molecular docking; Lianqiao-4; Nephrotoxicity

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1. Introduction

Lianqiao-4, a commonly used Mongolian medicine compound, is also known as Yindarixi Tang or Yindari-4 Wei Tang, and is recorded in the “Four Tantras of Medicine.” This compound consists of four herbal ingredients:

Lianqiao (*Forsythia suspensa*), *Bistortae rhizoma*, *Ophiopogonis radix*, and *Clematidis radix et rhizoma*. Classified as a cooling formula, it exhibits antidiarrheal and heat-clearing properties, primarily used to treat intestinal heat dysentery, abdominal pain, diarrhea, and other ailments. Clinically, Lianqiao-4 is often employed in the treatment of infantile diarrhea ^[1]. Studies have demonstrated its significant protective effects against CCL4-induced acute liver injury and its hepatoprotective and enzyme-lowering effects in models of pylorus ligation-induced liver injury ^[2,3]. Additionally, research has revealed its remarkable gastroprotective effects against gastric and duodenal ulcers ^[4].

The kidney is a crucial organ in the human body, and drugs and their metabolites can potentially cause harm to it ^[5]. Due to its abundant blood flow, high oxygen consumption, elevated enzymatic activity, and high tissue metabolic rate, the kidney is susceptible to the influx of drugs and metabolites, which can affect its normal functioning and, in severe cases, be life-threatening ^[6]. Therefore, this study aims to investigate the preliminary effects of Lianqiao-4 on nephrotoxicity using network pharmacology methods.

2. Experimental methods

2.1. Collection of active ingredients and target prediction for Mongolian medicine Lianqiao-4

The main active ingredients of Lianqiao, *Ophiopogonis radix*, *Bistortae rhizoma*, and *Clematidis radix et rhizoma* were collected through literature searches and databases such as TCMSP and HERB. These ingredients were screened based on oral bioavailability ($OB \geq 30\%$) and drug-likeness ($DL \geq 0.18$). The two-dimensional molecular structures of the active ingredients were searched using the PubChem database and then imported into the Swiss Target Prediction database for target prediction. The target names were corrected using the Uniprot database.

2.2. Acquisition of disease targets

Using “nephrotoxicity” as the keyword, disease targets for nephrotoxicity were screened from the GeneCards and DisGeNET databases. After removing duplicates, the targets were corrected using the UniProt database.

2.3. Construction of PPI network for potential nephrotoxicity targets of Mongolian medicine Lianqiao-4

Venny 2.1.0 software was used to find the intersection of drug active targets and disease targets, and a Venn diagram was drawn. The intersecting targets were then imported into the STRING database, with the protein species set to “Homo sapiens” for protein-protein interaction analysis. The analysis results were imported into Cytoscape 3.9.1 software to construct a PPI network diagram and screen for core targets.

2.4. GO enrichment and KEGG pathway analysis

The intersecting targets were imported into the DAVID database for GO enrichment and KEGG pathway analysis, respectively. GO covers three aspects: biological process (BP), cellular component (CC), and molecular function (MF). Subsequently, the Microbiome Online Platform was used to sort the top 10 rankings based on *P*-value from smallest to largest and create bar charts and bubble charts.

2.5. Construction of “Active ingredient-target-signal pathway” network diagram

The active ingredients of Mongolian medicine Lianqiao-4, renal toxicity-related targets, and related pathways were imported into Cytoscape 3.9.1 to construct an “Active ingredient-target-signal pathway” network diagram, further exploring the mechanism of action of Mongolian medicine Lianqiao-4 on renal toxicity.

2.6. Molecular docking

Using AutoDockTools 1.5.6 software, molecular docking was performed on the key active ingredients and core protein targets of Lianqiao-4 for treating renal toxicity based on the Degree value. Visualization analysis was assisted by PYMOL 3.11 software.

3. Experimental results

3.1. Analysis of screening results for main components of Lianqiao-4

Using the TCMSP and HERB platforms, all chemical components contained in the four Mongolian medicines were evaluated for ADEM properties. There were 19 chemical components in Lianqiao, 31 in *Ophiopogon japonicus*, 3 in *Clematis armandii*, and 6 in *Bistortae rhizoma*. The two-dimensional molecular structural formulas of the active ingredients were searched using the PubChem database, and then imported into the Swiss Target Prediction database for target prediction of the active ingredients (226 targets). The names of the drug active ingredient targets were then corrected using the Uniprot database.

3.2. Acquisition of disease targets

Using “nephrotoxicity” as a keyword, renal toxicity targets were screened from the GeneCards and DisGeNET databases. After merging and removing duplicates, 612 renal toxicity-related targets were obtained. The disease target names were then corrected using the UniProt database.

3.3. Construction of PPI network for potential targets of Mongolian medicine Lianqiao-4 in treating renal toxicity

There were 184 main component targets and 612 disease targets. Using Venny 2.1.0 software, 39 intersecting targets of Lianqiao-4 for treating renal toxicity were obtained (**Figure 1**).

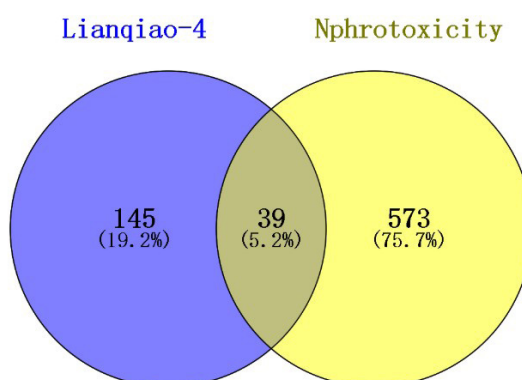


Figure 1. Venn diagram of targets for Forsythia-4 in treating renal toxicity.

After importing the intersecting targets into the STRING database to obtain protein-protein interaction information, there were 39 nodes and 232 edges, with an average node degree of 11.9. The PPI network diagram was drawn using Cytoscape 3.9.1 software, as shown in **Figure 2**. In the PPI protein interaction network diagram, the top 7 target proteins ranked by Degree value are PTGS2 (Prostaglandin-Endoperoxide Synthase 2, COX-2), BCL2 (B-cell lymphoma 2 protein), ABCG2 (ATP-binding cassette transporter G2), HSP90AA1, MMP9 (Matrix Metalloproteinase 9), STAT3 (Signal Transducer and Activator of Transcription 3), and EGFR (Epidermal Growth Factor Receptor). These are all core targets in the PPI protein interaction network diagram.

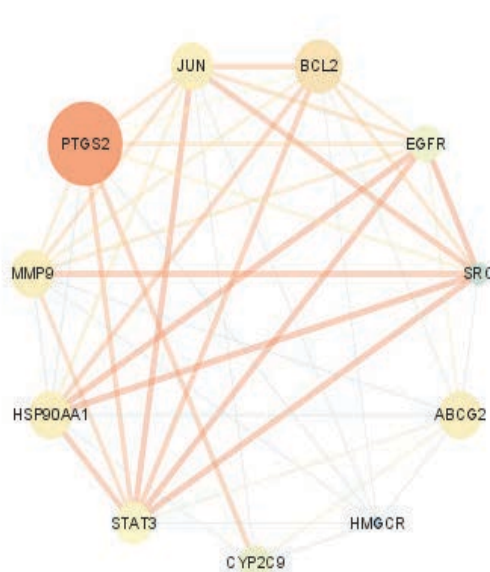


Figure 2. Intersection target PPI network diagram.

3.4. GO enrichment and KEGG pathway analysis

The intersecting targets were imported into the DAVID database for GO enrichment and KEGG pathway analysis. The analysis results were screened with a P -value < 0.05 as the criterion, resulting in 115 biological processes (BP), 21 cellular components (CC), and 48 molecular functions (MF). The top 10 results were plotted in a bar chart, as shown in **Figure 3**. BP mainly includes the cytochrome P450 epoxigenase pathway, xenobiotic metabolic process, steroid metabolic process, etc. CC mainly includes endoplasmic reticulum membrane, membrane-bounded intracellular organelles, caveolae, cytoplasm, etc. MF mainly includes heme binding, aromatase activity, etc. KEGG pathway analysis yielded 87 pathways, and the top 10 were plotted in a bar chart (**Figure 4**). Pathway analysis suggests that Forsythia-4 may exert its effects through pathways such as lipid and atherosclerosis, chemical carcinogenesis - DNA adducts, and arachidonic acid metabolism. These results indicate that Forsythia-4 regulates and treats renal toxicity through multiple biological processes.

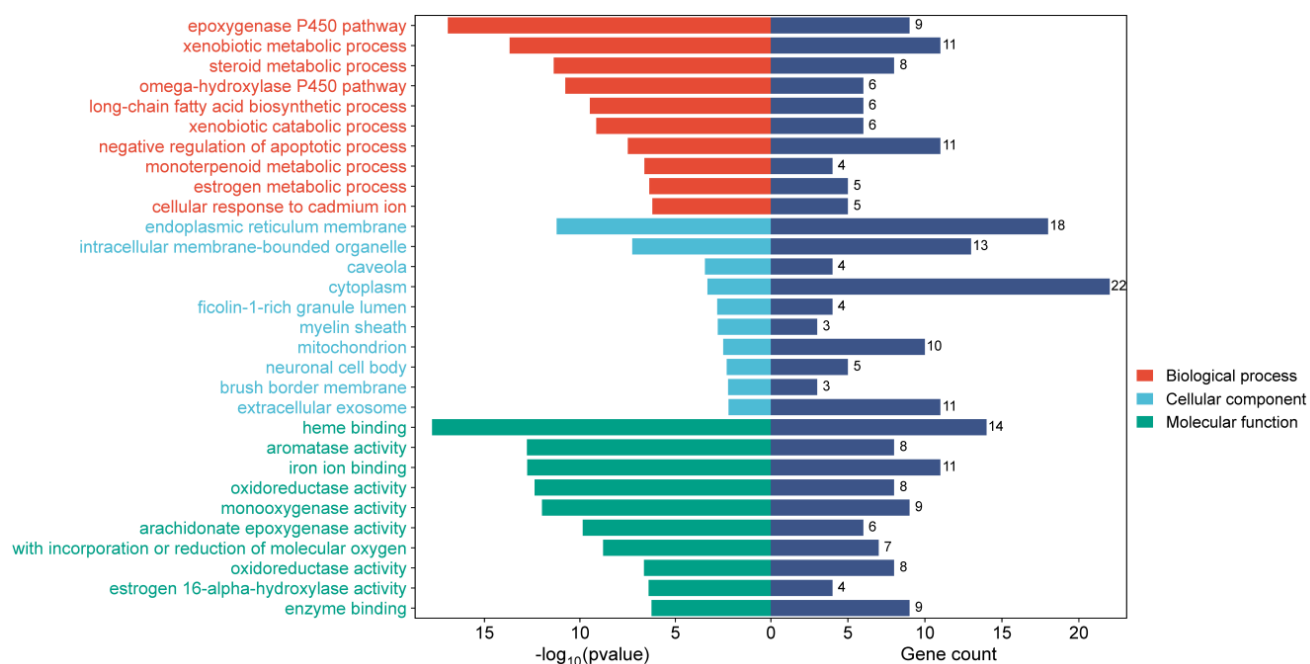


Figure 3. GO enrichment analysis diagram.

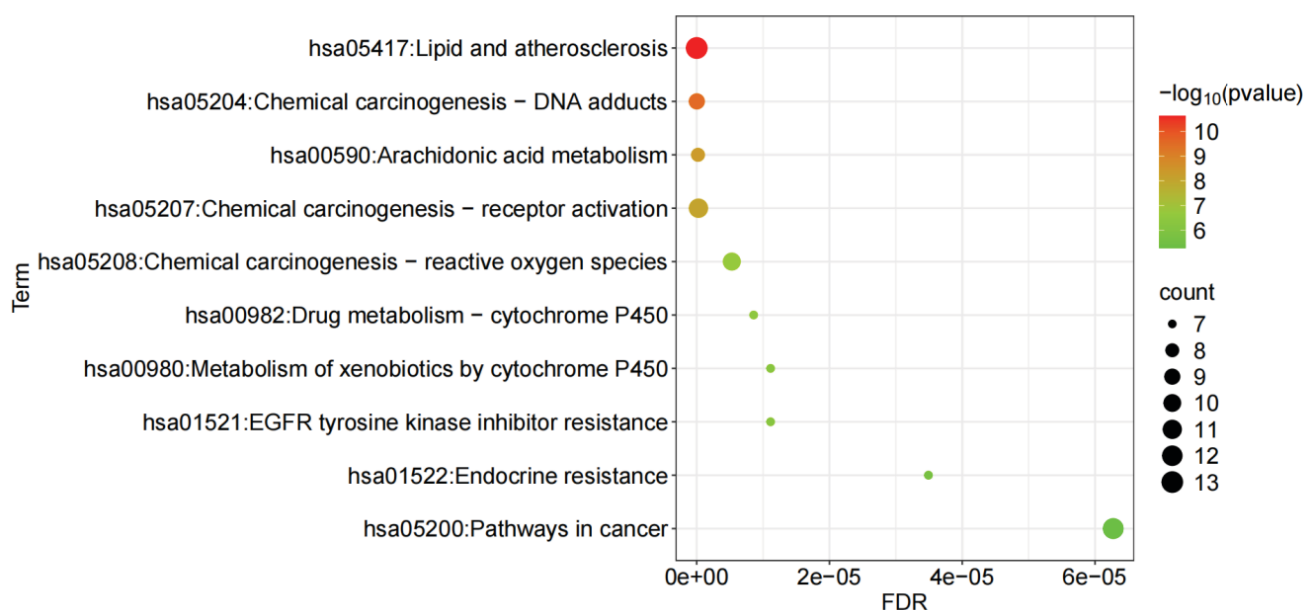


Figure 4. KEGG pathway enrichment analysis.

3.5. Construction of the “Active ingredient-target-signal pathway” network diagram

The “Active ingredient-target-signal pathway” network diagram was constructed using Cytoscape 3.9.1 software. With the Degree value as a reference, the core components of Forsythia-4 include kaempferol, beta-sitosterol, ophiopogonin A, quercetin, and β -sitosterol. The core target proteins for the treatment of renal toxicity include Signal Transducer and Activator of Transcription 3, ATP-binding cassette transporter G2, HSP90AA1, Matrix Metalloproteinase 9, Prostaglandin-Endoperoxide Synthase 2, and Epidermal Growth Factor Receptor. The core pathways include drug metabolism - cytochrome P450, metabolism of xenobiotics by cytochrome P450, EGFR

tyrosine kinase inhibitor resistance, and arachidonic acid metabolism (**Figure 5**).

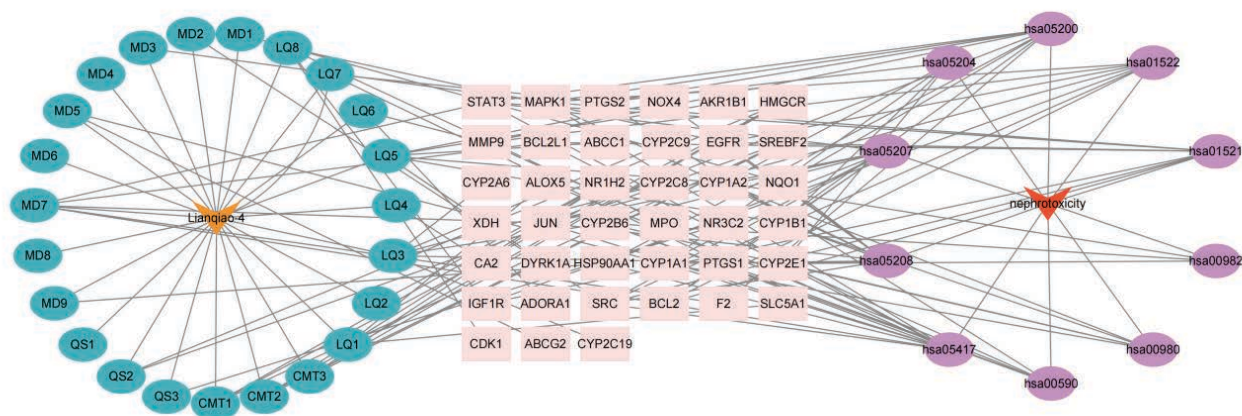


Figure 5. Active ingredient-target-signal pathway diagram. Note: Green circles represent drug active ingredients, blue circles represent pathways, and light squares represent targets.

3.6. Molecular docking

Using AutoDockTools 1.5.6 software, molecular docking was performed between the main active ingredients of Forsythia-4 (kaempferol, beta-sitosterol, ophiopogonin A, quercetin, β -sitosterol) and the core protein targets (Signal Transducer and Activator of Transcription 3, ATP-binding cassette transporter G2, HSP90AA1, Matrix Metalloproteinase 9, Prostaglandin-Endoperoxide Synthase 2, Epidermal Growth Factor Receptor) based on their Degree values. Visualization analysis of the high binding energy results was carried out using PYMOL 3.11 software (**Figure 6** and **Figure 7**).

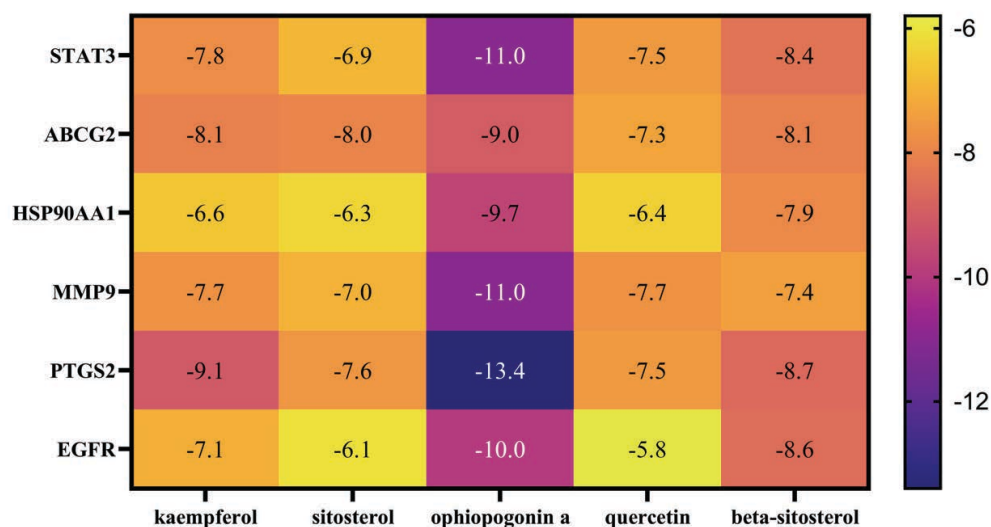


Figure 6. Molecular docking heatmap.

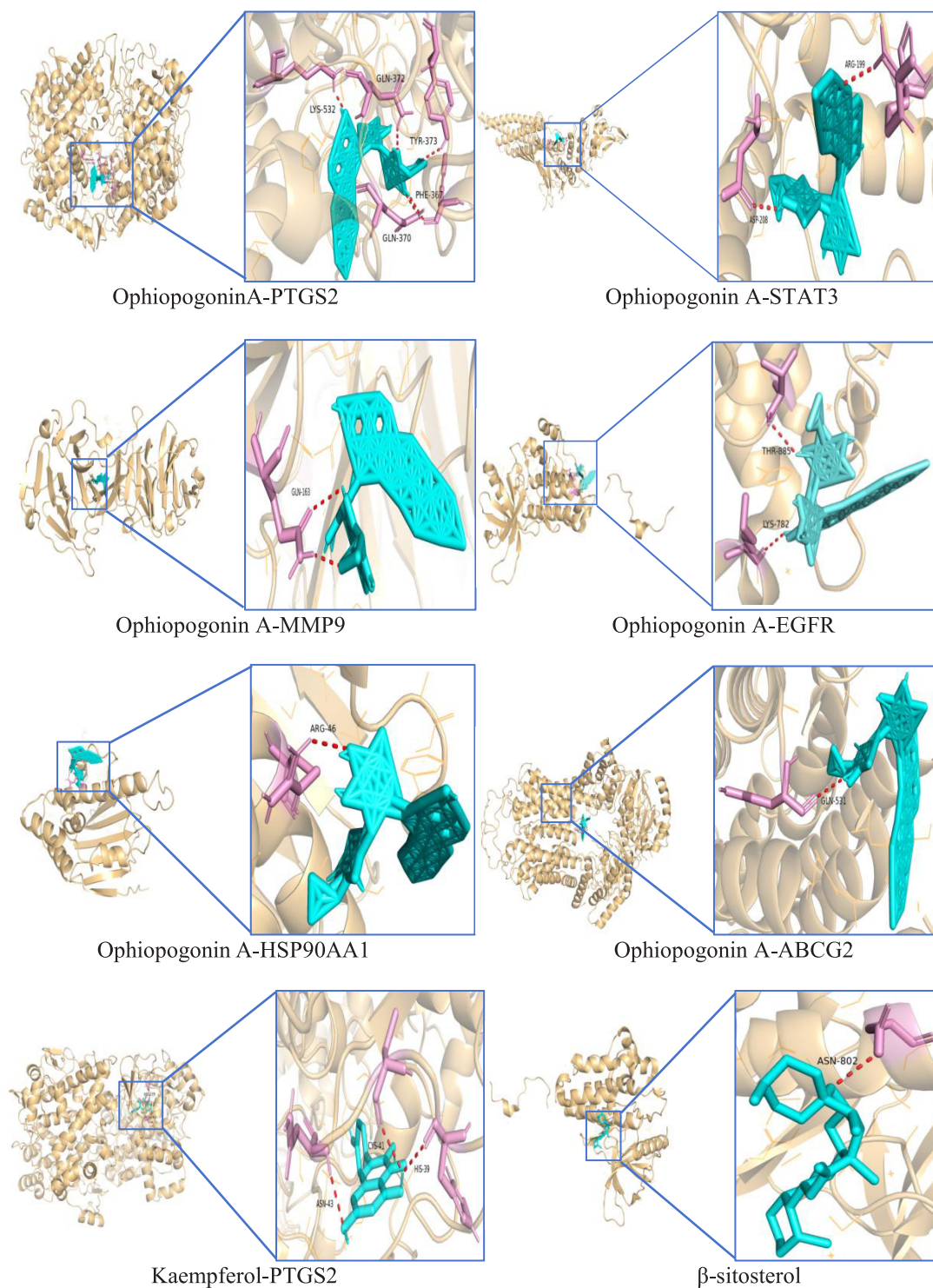


Figure 7. Molecular docking diagram.

4. Discussion

Through analysis of database screening results, it was found that Mongolian medicine Lianqiao-4 has 39 potential targets for the treatment of renal toxicity. The main active ingredients of Lianqiao-4 include ophiopogonin A,

kaempferol, β -sitosterol, quercetin, and other components. Core targets such as PTGS2, ABCG2, HSP90AA1, MMP9, STAT3, and EGFR may play a role in the treatment of renal toxicity.

Mongolian medicine Lianqiao-4 is composed of four herbal medicines: Forsythia, *Polygonum bistorta*, *Clematis armandii*, and *Ophiopogon japonicus*. According to literature reports ^[7–10], kaempferol and quercetin belong to flavonoids and are present in all four herbal medicines. Beta-sitosterol and sitosterol, which belong to steroid compounds, are also found in all four herbs of Lianqiao-4. *Ophiopogon japonicus* contains various steroidal saponins, flavonoids, polysaccharides, and other components, among which ophiopogonin A is one of the steroidal saponin compounds ^[10].

According to the literature, ophiopogonin A, as one of the key active ingredients in *Ophiopogon japonicus*, not only exhibits antioxidant and anti-inflammatory effects but also effectively reduces the expression levels of inflammatory markers such as TNF- α , IL-1 β , and IL-6 in renal tissue. This significantly alleviates hypoxia-induced apoptosis of renal tubular epithelial cells ^[11].

Both kaempferol and quercetin, flavonoid compounds, possess antioxidant and anti-inflammatory properties. Studies have revealed that kaempferol can reduce the activity of enzymes like MP-9 and COX-2, exerting an anti-tumor effect ^[12]. Kaempferol activates the AMPK/Nrf2 signaling pathway, effectively suppressing the oxidative stress state and the release of inflammatory factors in diabetic nephropathy rats, thereby promoting the recovery of renal function ^[13]. On the other hand, quercetin mitigates renal function damage and renal fibrosis by inhibiting the PI3K/Akt/NF- κ B signaling pathway ^[14].

Research indicates that prostaglandin-endoperoxide synthase 2 (PTGS2), also known as cyclooxygenase 2 (COX2), is widely distributed in the body ^[15]. Under normal physiological conditions, the expression level of PTGS2 is very low. However, it can be secreted in large amounts when activated in pathological states, promoting the synthesis of prostaglandins and leading to inflammatory responses ^[16, 17]. Yang *et al.* ^[18] found that renal inflammatory responses can be reduced by inhibiting the expression of inflammatory cytokines such as cyclooxygenase 2 (COX2). Additionally, Guo *et al.* ^[19] discovered that parecoxib sodium, a specific inhibitor of COX-2, can effectively block the expression of COX-2 and thus inhibit inflammatory responses caused by acute kidney injury. Furthermore, COX2 plays a key role in inflammation and tumor development ^[20]. Signal transducer and activator of transcription 3 (STAT3) is a core member of the JAK/STAT signaling pathway and is closely associated with kidney diseases ^[21]. Sun *et al.* ^[22] found that polysulfides and hydrogen sulfide can provide protective effects against nephrotoxicity by inhibiting NF- κ B-mediated renal inflammatory responses through sulfuration modification of STAT3 and IKK β . Lee *et al.* ^[23] showed that inhibiting the activity of STAT3 can reduce renal tubular epithelial cell apoptosis and oxidative stress, thereby improving renal function. Epidermal growth factor receptor (EGFR) is a member of the ErbB family of receptor tyrosine kinases. Research has found that EGFR protein expression is a key factor in kidney diseases in various animal models, including glomerulonephritis, hypertensive nephropathy, and diabetic nephropathy ^[24]. According to Singh *et al.* ^[25], DAM17-mediated EGFR ligand shedding can activate EGFR signaling, promote the release of proinflammatory cytokines, and exacerbate renal inflammation. Studies have demonstrated that matrix metalloproteinase 9 (MMP9) releases inflammatory factors through the NF- κ B pathway, causing glomerular injury ^[26], and thus inhibiting MMP9 can reduce renal injury ^[27].

KEGG pathway enrichment analysis revealed that the main pathways for Forsythia suspensa-4 to alleviate nephrotoxicity include lipid and atherosclerosis, chemical carcinogenesis - DNA adducts, and arachidonic acid metabolism. Among them, the metabolic process of the arachidonic acid pathway is mainly achieved through three

enzymes: cyclooxygenase, lipoxygenase, and cytochrome P450 enzymes ^[28]. Research has found that regulating the arachidonic acid metabolism pathway by inhibiting the activity of cyclooxygenase 2 (COX-2) and 5-LOX can effectively alleviate renal inflammation ^[29].

Molecular docking verified the core targets and components associated with nephrotoxicity in *Forsythia suspensa*-4. Active ingredients such as ophiopogonin A, kaempferol, β -sitosterol, and quercetin were found to tightly bind to core targets such as PTGS2, ABCG2, HSP90AA1, MMP9, STAT3, and EGFR. Studies have shown that ophiopogonin A can reduce the expression of inflammatory factors in renal tissue ^[11], and PTGS2 protein plays a key role in the treatment of nephrotoxicity ^[16–20]. Therefore, *Forsythia suspensa*-4 may have a protective effect on renal toxicity by inhibiting the expression of proteins such as PTGS2, STAT3, and MMP9, and its pathway may be the arachidonic acid metabolism pathway.

5. Conclusion

In summary, through network pharmacology and molecular docking studies, it is initially predicted that *Forsythia suspensa*-4 has a multi-component, multi-target, and multi-pathway mechanism of action in the treatment of nephrotoxicity. This study provides new targets and pathways for the experimental treatment of nephrotoxicity with *Forsythia suspensa*-4, but the exact mechanism of action still needs further validation in cellular and animal experiments.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Anggelima L, Gong J, et al., 2022, Research on the Etiology of Pyloric Ligation Liver Injury and the Hepatoprotective Substance Basis of *Forsythia*-4 Based on the Theory of ‘Decomposition of Essence and Dregs’. *Asia-Pacific Traditional Medicine*, 18(5): 32–35.
- [2] Wang H, Bai M, Bao M, et al., 2014, Screening Study on the Effective Parts of Mongolian Medicine *Forsythia*-4 Decoction for Hepatoprotective and Enzyme-Lowering Effects on Acute Liver Injury Caused by CCL4. *Chinese Journal of Ethnomedicine and Ethnopharmacy*, 20(10): 45–47.
- [3] Wang H, Tong S, Xiao M, et al., 2013, Protective Effect of Mongolian Medicine ‘*Forsythia*-4 Decoction’ on Pyloric Ligation Liver Injury. *Chinese Journal of Experimental Traditional Medical Formulae*, 19(20): 250–254.
- [4] Tong S, Wang H, Bai T, et al., 2021, Protective Effect and Mechanisms of Action of Mongolian Medicine *Sulongga*-4 on Pyloric Ligation-Induced Gastroduodenal Ulcer in Rats. *World Journal of Gastroenterology*, 27(16): 1770–1784.
- [5] Feng X, Fang S, Gao Y, et al., 2018, Research Status of Renal Toxicity of Traditional Chinese Medicine at Home and Abroad. *China Journal of Chinese Materia Medica*, 43(3): 417–424.
- [6] Yang L, Wurilaga, Saqilatu, et al., 2023, Research Progress on the Nephrotoxic Components of Traditional Chinese Medicine and Their Toxicity Mechanism. *Chinese Herbal Medicine*, 54(23): 7934–7952.
- [7] Sun L, Sun N, Xu P, et al., 2025, Research Progress on the Chemical Constituents of *Forsythia* and Its Anti-Respiratory Virus Mechanism. *Journal of Traditional Chinese Medicine and Pharmacology*, 31(3): 146–154.
- [8] Chen Y, Tu Y, Bao L, et al., 2025, Research Progress on Chemical Constituents and Pharmacological Effects of

- Polygonum bistorta and Predictive Analysis of Quality Markers. *Information on Traditional Chinese Medicine*, 42(1): 76–83.
- [9] Li Z, Tang B, Duan Z, et al., 2024, Study on the Chemical Constituents of Chuanmutong Standard Decoction Based on HPLC Characteristic Spectrum and Preparative Separation Technology. *Asia-Pacific Traditional Medicine*, 20(9): 42–47.
 - [10] Wan M, Yuan J, Zhang Y, et al., 2023, Research Progress on the Pharmacological Effects of Extracts and Active Ingredients from *Ophiopogon japonicus*. *Drug Evaluation Research*, 46(08): 1819–1826.
 - [11] Sheng X, Yang Y, Liu J, et al., 2021, *Ophiopogonin A* Alleviates Hemorrhagic Shock-Induced Renal Injury via Induction of Nrf2 Expression. *Frontiers in Physiology*, 11: 619740.
 - [12] Ju P, Ho Y, Chen P, et al., 2021, Kaempferol Inhibits the Cell Migration of Human Hepatocellular Carcinoma Cells by Suppressing MMP-9 and Akt Signaling. *Environmental Toxicology*, 36(10): 1981–1989.
 - [13] Guo Y, Liu Q, Guo H, et al., 2025, Therapeutic Effect and Mechanism of Kaempferol on Streptozotocin-Induced Diabetic Nephropathy Rats. *Natural Product Research and Development*, 1–13.
 - [14] Kong L, Lu H, Wang X, et al., 2024, Protective Effect and Mechanism of Quercetin on Cardio-Renal Function in Rats With Cardio-Renal Syndrome. *China Pharmacy*, 35(13): 1612–1617.
 - [15] Mahboubi S, Zarghi A, 2019, Selective COX-2 Inhibitors as Anticancer Agents: A Patent Review (2014–2018). *Expert Opinion on Therapeutic Patents*, 29(6): 407–427.
 - [16] Chen Y, Xu X, Yang J, 2024, Correlation Analysis Between the Expression Level of Prostaglandin Endoperoxide Synthase 2 in Lung Adenocarcinoma Tissue and the Mutation of Epidermal Growth Factor Receptor Gene. *Journal of Clinical Psychosomatic Diseases*, 30(4): 6–10.
 - [17] Flach S, Scarfe G, Dragone J, et al., 2016, A Phase I Study to Investigate the Absorption, Pharmacokinetics, and Excretion of [(14)C]Prucalopride After a Single Oral Dose in Healthy Volunteers. *Clinical Therapeutics*, 38(9): 2106–2115.
 - [18] Yang F, Shi X, Yang W, et al., 2022, *Pueraria montana* (Kudzu Vine) Ameliorates the Inflammation and Oxidative Stress Against Fe-NTA Induced Renal Cancer. *Journal of Oleo Science*, 71(10): 1481–1492.
 - [19] Guo Y, Wu B, Chen Q, et al., 2022, Parecoxib Ameliorates Renal Toxicity and Injury in Sepsis-Induced Mouse Model and LPS-Induced HK-2 Cells. *Drug Development Research*, 83(3): 659–668.
 - [20] Aioub A, Abdelnour S, Shukry M, et al., 2022, Ameliorating Effect of the Biological Zinc Nanoparticles in Abamectin Induced Hepato-Renal Injury in a Rat Model: Implication of Oxidative Stress, Biochemical Markers, and COX-2 Signaling Pathways. *Frontiers in Pharmacology*, 13: 947303.
 - [21] Liu C, Zhu W, Tang Q, et al., 2016, Effect of Jin Kui Shen Qi Wan on p-STAT3 Protein in Renal Tissue of Rats With Unilateral Ureteral Obstruction. *Hunan Journal of Traditional Chinese Medicine*, 36(10): 22–26.
 - [22] Sun H, Leng B, Wu Z, et al., 2020, Polysulfide and Hydrogen Sulfide Ameliorate Cisplatin-Induced Nephrotoxicity and Renal Inflammation Through Persulfidating STAT3 and IKK β . *International Journal of Molecular Sciences*, 21(20): 7805.
 - [23] Lee S, Kim K, Lee S, et al., 2024, STAT3 Blockade Ameliorates LPS-Induced Kidney Injury Through Macrophage-Driven Inflammation. *Cell Communication and Signaling*, 22(1): 476.
 - [24] Yuan C, 2023, TIF1 γ Inhibits the Progression of Renal Tubular Interstitial Fibrosis by Promoting EGFR Ubiquitination Degradation, thesis, Huazhong University of Science and Technology.
 - [25] Singh S, Chauhan S, Kumar A, et al., 2022, Amphiregulin in Cellular Physiology, Health, and Disease: Potential Use as a Biomarker and Therapeutic Target. *Journal of Cellular Physiology*, 237(2): 1143–1156.

- [26] Meng F, Ren S, 2024, Identification of Hub Genes and Molecular Pathways in Keratoconus by Integrating Bioinformatics and Literature Mining at the RNA Level. *International Ophthalmology*, 44(1): 244.
- [27] Alomari G, Al-Trad B, Hamdan S, et al., 2021, Alleviation of Diabetic Nephropathy by Zinc Oxide Nanoparticles in Streptozotocin-Induced Type 1 Diabetes in Rats. *IET Nanobiotechnology*, 15(5): 473–483.
- [28] Wu D, Cui L, Xu F, et al., 2025, Research Progress on Multi-Target Anti-Inflammatory Drugs Based on Arachidonic Acid Metabolism Pathway. *Journal of China Pharmaceutical University*, 1–18.
- [29] Yuan Z, Yang L, Zhang X, et al., 2020, Mechanism of Huang-Lian-Jie-Du Decoction and Its Effective Fraction in Alleviating Acute Ulcerative Colitis in Mice: Regulating Arachidonic Acid Metabolism and Glycerophospholipid Metabolism. *Journal of Ethnopharmacology*, 2020(259): 112872.

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Study on the Influence of Nutrition Intervention on Children's Health during Follow-Up of High-Risk Infants

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Abstract: High-risk infants, from fetal stage to 3-year-old, face severe physical and mental development threats due to biological, psychological, or environmental factors. These threats can lead to developmental delay and cognitive impairment, affecting their future quality of life and social integration. Scientific health management, with nutritional intervention as a key part, is urgently needed. Nutritional intervention, through targeted supplementation and feeding guidance, can optimize their development, avoid nutritional-related deviations, reduce long-term disease risk, and lay a healthy growth foundation. This study analyzes the positive effects of nutritional intervention on high-risk infants' physical growth, neural development, and disease prevention, providing scientific evidence for optimizing clinical follow-up strategies.

Keywords: High-risk infants; Nutritional intervention; Physical growth; Neural development; Disease prevention

Online publication: June 4, 2025

1. Introduction

High-risk infants include premature, low-birth-weight, intrapartum-asphyxia, and genetic-metabolic-disorder cases. The first 1000 days of life are crucial for children's nutrition^[1], affecting catch-up growth and brain neural network construction^[2]. In China, high-risk infant incidence is rising, yet the current follow-up system over-emphasizes disease treatment and neglects nutritional intervention integration. Thus, analyzing nutritional intervention in high-risk infant follow-up is of great significance.

2. Materials and methods

2.1. Research subjects

From 2020–2023, 986 high-risk infants were initially selected. Inclusion criteria included preterm (gestational age

< 37 weeks), low birth weight (< 2500 g), perinatal hypoxia, and genetic metabolic disorders. Cases with severe congenital malformations were excluded. Finally, 812 high-risk infants were included in the cohort study, ensuring sample homogeneity and representativeness^[3].

2.2. Intervention methods

A three-level nutrition management network was constructed, with a clear division of labor and efficient collaboration. The staff of primary health care institutions, who have received professional training and maintain a serious and responsible attitude, regularly and accurately measure the growth indicators of high-risk infants, such as height, weight, and head circumference. The measuring tools used are all strictly calibrated. When observing the daily feeding behavior, detailed records are made of the exact values of food intake, the interval time of feeding frequency, whether the feeding posture is correct, and other details, leaving no potential problems overlooked. Secondary specialized hospitals, with advanced detection equipment such as high-precision biochemical analyzers and professional body composition analyzers, as well as professional evaluation tools such as the Child Nutritional Risk Assessment Scale^[4], comprehensively evaluate the nutritional status of high-risk infants from multiple dimensions, accurately identifying individuals at nutritional risk. Tertiary medical centers bring together multidisciplinary expert resources, including pediatricians, nutritionists, rehabilitation therapists, etc. Based on the detailed information provided by the first two levels of institutions and combined with the individual differences of each high-risk infant, such as genetic background, disease severity, and growth and development stage, a highly individualized nutrition plan is formulated for each high-risk infant. The specific intervention measures are as follows:

- (1) Stage-based Nutritional Supplementation Strategy: For very low birth weight infants, the ladder addition method of human milk fortifier is adopted. In the early stage, according to the tolerance of the infants, the amount of human milk fortifier is gradually increased to meet their high nutritional needs for rapid growth. When the corrected age reaches 4 months, hydrolyzed protein formula is introduced in a timely manner to provide a more suitable nutritional source for the infants and help them grow healthily^[5]. During the implementation process, the digestion and absorption status of the infants is closely monitored. According to indicators such as the weight gain rate and the properties of feces, the dosage and time of the human milk fortifier and hydrolyzed protein formula are flexibly adjusted.
- (2) Precise Micronutrient Supplementation: Based on the detection levels of key indicators such as serum ferritin and 25-hydroxyvitamin D, the doses of iron supplements and vitamin D3 are dynamically adjusted. For iron supplements, the dose is precisely controlled at 2-4mg/kg/d according to the weight of the infants; for vitamin D3, a dose of 800-1000IU/d is given^[6]. Through this precise supplementation method, it is ensured that high-risk infants obtain sufficient and appropriate micronutrients to maintain normal body metabolism and development. The serum indicators are regularly rechecked, and the supplementation dose is adjusted in a timely manner according to the changes in the indicators to avoid the situation of nutrient deficiency or excess.
- (3) Feeding Skill Training System: For infants with swallowing-respiratory coordination disorders, a comprehensive training program has been carefully designed. Oral motor intervention is adopted. Through professional manipulation to stimulate the oral muscles, the strength and coordination of the oral muscles are enhanced, and the swallowing function is improved. Combined with the food texture grading training, according to the swallowing ability of the infants, the texture of the food is gradually adjusted,

starting from liquid food, gradually transitioning to semi-liquid, soft food, and finally achieving a normal diet, improving the feeding efficiency and safety of the infants. During the training process, one-on-one guidance is provided by professional rehabilitation therapists, and the training program is continuously optimized according to the progress of the infants to ensure the training effect.

2.3. Evaluation indicators

Based on the corrected age, a comprehensive evaluation of high-risk infants is carried out every 3 months. The evaluation content covers multiple important aspects: In terms of physical development, the focus is on the weight Z score and the head circumference growth rate. These indicators can intuitively reflect the growth situation of high-risk infants. By comparing with normal children of the same age, it can be determined whether their growth meets the standard. In terms of neurobehavior, the Gesell Developmental Quotient is used for evaluation. The neurodevelopmental level of high-risk infants is comprehensively measured from multiple dimensions such as adaptive behavior, gross motor, fine motor, language, and personal social interaction. In terms of metabolic indicators, bone mineral density, hemoglobin, etc. are detected to understand the skeletal health status of high-risk infants and whether there are metabolic diseases such as anemia. A control group of healthy infants and young children in the same period is set up. By comparing the data of the two groups, the effect of nutritional intervention can be more accurately analyzed. In the data analysis process, advanced statistical methods such as the propensity score matching method are used to further eliminate the influence of confounding factors on the research results and ensure the accuracy and reliability of the research results.

3. Results

3.1. The trend of physical development catch-up

After nutritional intervention, at 12-month age, the intervention group had a significant physical development catch-up. The weight Z score increased by 0.82 ± 0.31 , and the head circumference growth rate reached 90% of normal children. In extremely preterm infants (< 32 -week gestational age), bone mineral content caught up with full-term standards at 6-month corrected age. The ladder addition of a human milk fortifier and a timely hydrolyzed protein formula significantly promoted infants with very low birth weight.

3.2. The characteristics of neural development outcome

High-risk infants with early nutritional intervention had an adaptive behavior score of (91.3 ± 6.2) at 18-month age, better than the conventional follow-up group (84.7 ± 7.1) . MRI diffusion tensor imaging showed that the fractional anisotropy of the corpus callosum in the group with enhanced DHA intake increased by 12%^[7]. Early sufficient protein intake was positively correlated with neurodevelopmental quotient improvement, especially in language and fine motor skills.

3.3. The effect of disease prevention

The incidence of anemia in the intervention group decreased to 8.3% (control group: 21.6%). For infants with bronchopulmonary dysplasia, the pulmonary function index FEV1 increased by 19%. Long-term follow-up showed that systematic nutrition management reduced the risk of metabolic syndrome by 42%. Precise micronutrient supplementation and dietary structure adjustment played key roles.

4. Discussion

4.1. The temporal effect mechanism of nutritional intervention

There is a crucial “window of opportunity” for high-risk infants’ brain development within 6 months after birth. Nutritional intervention can activate neuronal synaptic plasticity through the IGF-1 pathway. Every 1 g/kg/d increase in protein intake can increase hippocampal volume growth rate by 0.7 mm³/month. However, excessive catch-up growth should be avoided, and the muscle/fat ratio should be monitored. DHA and choline also play important roles in the brain development critical period.

4.2. Strategies for addressing special nutritional needs

Preterm infants with a 38% incidence of gastroesophageal reflux can use thickened emulsion and postural feeding to reduce reflux and increase intake efficiency by 60%. For phenylketonuria infants, a computer-aided dietary planning system formulates personalized dietary plans. The thickened emulsion formula and postural feeding method, as well as the dietary plan for genetic-metabolic-disease infants, are continuously optimized.

4.3. The family-medical collaborative management model

A “nutrition coach” follow-up system using a mobile APP was established. Parents record feeding logs, and the APP provides nutritional guidance. This increased parents’ compliance, with vitamin K compliance rate rising from 54% to 89%, and feeding behavior deviation correction cycle shortening by 2.3 weeks^[8]. The system can be improved by adding online consultation and video guidance, and by carrying out parent training.

5. Conclusion

This study shows that systematic nutritional intervention significantly improves high-risk infants’ physical and neural development. Its mechanism involves epigenetic modification and metabolic programming. To improve high-risk infant health management, an interdisciplinary nutritional support team (including pediatricians, nutritionists, and rehabilitation therapists) should be established^[9]. Individualized intervention programs based on biomarkers should be developed for precise nutritional intervention^[10]. Future research can explore different-region and different-background nutritional intervention models and the synergy between nutritional intervention and other rehabilitation methods.

Disclosure statement

The author declares no conflict of interest

References

- [1] Li L, Li N, Xing Y, 2024, Research Progress of Early Life Nutritional Risk Assessment of High-Risk Neonates. *Chinese Journal of Neonatology*, 39(12): 747–751.
- [2] Jiang J, Zhao L, 2014, *Infant Nutrition and Physical Growth Promotion*. People’s Medical Publishing House, Beijing.
- [3] Wang L, Li C, Lv P, et al., 2024, Effect of Standardized Follow-Up Monitoring Mechanism on the Growth and Development of High-Risk Infants. *International Medical Review*, 30(12): 2004–2008.
- [4] Hu Y, 2022, Thinking on Hot Issues of Nutrition Support for High-Risk Infants. *Chinese Journal of Child Health*, 30(2):

120–124.

- [5] Liu X, 2022, Nutrition Support and Health Management of High-Risk Infants. *Chinese Journal of Child Health Care*, 30(2): 120–124.
- [6] Wang X, 2017, Investigation on Nutritional Supplementation of High-Risk Neonates with Metabolic Bone Disease, thesis, Shanghai Jiao Tong University.
- [7] Zhang Y, 2020, Observation of Early Intervention Effect of Different Management Models on High-Risk Infants, thesis, North China University of Science and Technology.
- [8] Zhao Y, Sun H, 2022, Study on the Effect of Family Intervention on Nutrition and Feeding of Medium and High-Risk Preterm Infants. The 15th National Nutrition Science Conference of Chinese Nutrition Society, Tengzhou Maternal and Child Health Hospital.
- [9] Fang H, 2024, Follow-Up Results of Information Management of 163 Rural Full-Term Infants. *Jiangsu Health Care*, 2024(6): 1–25.
- [10] Yang Z, 2010, Effect of Early Intervention on Intelligence, Temperament and Physical Development of High-Risk Infants, thesis, Anhui Medical University.

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Multidimensional Strategies to Prevent and Control Risk Factors in Patients with Nonvalvular Atrial Fibrillation: Mechanistic Explorations and Advances in Clinical Practice

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Abstract: Background: Non-valvular atrial fibrillation (NVAf), the most prevalent cardiac arrhythmia globally, poses a dual challenge of thromboembolic and bleeding risks, with stroke being the most devastating complication. Despite advancements in anticoagulation and rhythm control, patient outcomes remain suboptimal. Aim: This review synthesizes current evidence on the pathophysiological mechanisms, multidimensional management strategies, and emerging innovations in NVAf to inform clinical practice and future research directions. *Methods:* A systematic literature search was conducted across nine databases (CNKI, Wanfang, SinoMed, VIP, PubMed, Web of Science, Cochrane Library, Embase, and MEDLINE) using combined Medical Subject Headings (MeSH) and free-text terms, including “atrial fibrillation,” “non-valvular atrial fibrillation,” “risk factors,” and “mechanism” (and their Chinese equivalents). Studies on NVAf pathogenesis, therapeutic interventions, and risk stratification tools were analyzed. *Results:* (1) Risk Factors and Pathophysiology: NVAf progression is driven by hemodynamic stress (e.g., hypertension), metabolic disorders (e.g., obesity, diabetes), chronic inflammation, and fibrosis. Biomarkers such as CRP and Galectin-3, along with TGF- β /Smad signaling, are central to atrial remodeling. (2) Anticoagulation Controversies: While NOACs reduce stroke risk compared to warfarin (HR = 0.79), challenges persist in extreme body weight populations and drug-drug interactions (e.g., with P-glycoprotein inhibitors). (3) Left Atrial Appendage Closure (LAAC): LAAC demonstrates non-inferiority to anticoagulation in stroke prevention (HR = 0.79) with reduced major bleeding (HR = 0.49), though device-related thrombosis (1.8–7%) remains a concern. (4) Precision Medicine: AI-driven models enhance stroke prediction (AUC = 0.71; sensitivity 92%), while genotype-guided warfarin dosing shortens INR stabilization by 40%. (5) Lifestyle Interventions: Combined Mediterranean diet and moderate exercise reduce AF burden (HR = 0.69) and reverse left atrial enlargement (LAVI reduced by 12%). (6) Multidisciplinary Care: Integrated “heart-brain team” approaches combining LAAC and PFO closure lower annual stroke recurrence from 8.2% to 2.1%, while comprehensive rehabilitation improves functional capacity (6MWD + 45 m) and quality of life (SF-36 + 12 points). *Conclusion:* NVAf management has evolved from isolated anticoagulation to a multidimensional paradigm integrating genomics, AI, and lifestyle modification. Future priorities include validating long-term outcomes of novel therapies, addressing evidence gaps in special populations, and implementing digitally enabled, cross-

disciplinary care models to mitigate the global burden of NVAF-related complications.

Keywords: Nonvalvular atrial fibrillation; Risk factors; Prevention and treatment; Mechanisms; Clinical practice; Advances

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1. Background

Bidirectional management of thromboembolic (especially stroke) and bleeding risks in non-valvular atrial fibrillation (NVAF), the most common arrhythmia globally, is a major challenge in the cardiovascular field^[1]. Epidemiological data show that the global incidence of NVAF has shown a substantial increase over the last three decades^[1]. A large number of studies have demonstrated a lifetime risk of approximately 33%, with high rates of disability and mortality^[2], with a stroke risk in patients with NVAF that is five times higher than that of the general population, and a high annual incidence of bleeding events related to anticoagulant therapy of 2–4%^[3]. Population aging and the prevalence of metabolic syndrome drive the continuous growth of NVAF prevalence, which is expected to exceed 30 million patients worldwide in 2030, becoming a major public health problem. The current aging population situation in China has intensified, and the China Blue Book of Self-Care shows that 85% of Chinese residents die of chronic diseases^[4], in which the risk of stroke, heart failure, and other serious complications in patients with NVAF is also significantly increased, which imposes a heavy burden on the patients' individuals, families, and society^[5]. Although several anticoagulants and rhythm control strategies have been used for NVAF treatment, the prognosis of patients is still unsatisfactory^[1,5–8]. In recent years, the research paradigm has shifted from single anticoagulation therapy to multidimensional risk management, covering the exploration of pathomechanisms, the application of novel technologies, and individualized intervention strategies. In this article, the study systematically reviews the biological mechanisms of NVAF risk factors, the evidence-based progress of prevention and treatment strategies, and the direction of future research, with a view to providing a scientific basis for clinical practice.

2. Methods

The author searched a total of nine databases, including China Knowledge Network (CNKI), Wanfang Database, China Biomedical Literature Database (SinoMed), VIP, PubMed, Web of Science, Cochrane Library, Embase, and MEDLINE, on the computer. A combination of subject terms and free words was used for the search. The Chinese search terms were “atrial fibrillation,” “non-valvular atrial fibrillation,” “risk factors,” and “mechanisms.” The English search terms were “Atrial Fibrillation,” “Non-valvular atrial fibrillation,” “Risk Factor,” “Mechanism,” and “Machine.”

3. Current research on patients with atrial fibrillation (AF)

A part of scholars have conducted a lot of research in terms of risk factors and the occurrence mechanisms of AF. Some scholars have shown that the prevalence of AF is 2% in the general population and 10–12% in people aged 80 years and above^[10]. It has been concluded that: epidemiology confirms that AF is associated with a

variety of factors, which individually or in combination can contribute to the initial development of arrhythmias and the onset of disease features^[11,12], aging is a major factor contributing to the pathogenesis of arrhythmias^[11], arterial hypertension, obesity, diabetes mellitus, and genetics are notable predisposing factors to AF, and a variety of dietary components have a protective effect that may reduce the AF incidence^[2,13]. A large prospective study involving 24,734 female participants investigated the relationship between inflammatory markers such as CRP, fibrinogen and intercellular adhesion molecule 1 and the incidence of AF, and the results suggested that inflammation is a strong indicator of the incidence of AF. In addition, some studies have confirmed that fibrosis is also an important factor in maintaining AF, and atrial remodeling caused by fibrosis is associated with AF promotion^[6,14]. Meanwhile, most of the scholars also studied in terms of the complications of AF. Some scholars found that: the incidence and morbidity of AF are related to the redox potential of glutathione and cysteine, which are markers of oxidative stress, and that for every 10% increase in glutathione, the incidence of AF is 30% higher, and the same change leads to a 40% increase in the risk of AF^[6,14]. Another study showed that the risk of stroke in patients with AF is five times higher than in normal subjects and 90% of cardiogenic embolic emboli originate from the atria or auricles^[15]. With the increase in the incidence of AF has led to a continuous increase in the number of AF-related emergencies and hospitalizations, an increase in the number of sudden acute AF in various types of patients with acute and critical illnesses, which has seriously increased the economic pressure on the affected parties and the imbalance in the distribution of medical resources. Based on the existing research base of foreign scholars, it has been shown that the estimated lifetime risk of AF varies according to patient-level factors such as age, gender, ethnicity, and the burden of clinical risk factors, etc. In addition to genetic factors, risk factors for AF include hypertension, type 2 diabetes mellitus, and physical inactivity, which are the main factors that can increase the lifetime risk of AF^[2,3]. However, interventions on risk factors can reduce the occurrence of AF^[2,5,10–15], and play an important role in the secondary prevention of AF episodes.

Chinese-related studies have less data compared with foreign studies. The Chinese emergency management guidelines for acute atrial fibrillation (2024)^[1] mentioned that the increase in the incidence of AF is likely to lead to a sustained increase in the number of related emergencies and hospitalizations, and seriously increase the economic pressure, and other views are consistent with the views of foreign scholars' studies^[16]. Some epidemiological studies show that men are more likely to suffer from AF than women^[17,18]. A multicenter prospective cohort study based on a Chinese community^[9] reported the incidence of AF among people over 60 years of age in a Chinese community. Among 18738 subjects, 351 (1.87%) had new-onset AF during the four-year follow-up period; and the overall incidence rate of AF was 5.2/1000 person-years during the observation period of 67704 person-years. A study enrolling 80 patients with NVAf who were to undergo catheter ablation or electrical cardioversion for AF showed that left atrial volume index (LAVI), parietal emptying velocity (PEV), and the biomarker B-type brain natriuretic peptide (BNP) were independent risk factors for stroke risk in patients with NVAf, and PEV was more valuable in predicting stroke risk^[19,20]. As for the risk factors and comorbid symptoms of AF, a small number of scholars constructed a prediction model for dementia in AF patients^[21]. Meanwhile, a review study on AF showed that quality of life, physical activity, body weight, stress management, blood pressure, cardiovascular disease, heart failure, neurological disorders, cognitive dysfunction and dementia are the main influencing factors about the load of AF^[22], which suggests that the occurrence of AF and its clinical consequences can be altered to a large extent by changing the life style, which is in line with the conclusions of the research of foreign scholars^[2,3,5,10–15,20].

As a result, AF causes very high rates of disability and mortality, and has a poor prognosis. patients with

NVAF also have a significantly increased risk of serious complications, such as stroke and heart failure, which imposes a heavy burden on individuals, families and society, and has become an important challenge for global public health.

4. Current state of research on patients with non-valvular atrial fibrillation (NVAF)

In 2020, the European Society of Cardiology and the European Society for Cardiothoracic Anesthesia updated and published the 2020 European Society of Cardiology Guidelines for the Management of Atrial Fibrillation ^[5], which suggested that the AF diagnosis and treatment process should be jointly participated by the doctor and the patient. Subclinical AF can be identified with the help of devices, and the “4S-AF” process-oriented assessment, i.e., considering the structured characteristics of AF for all AF patients, comprehensively evaluating the risk factors of AF, and emphasizing lifestyle intervention and risk factor management ^[5,6]. The guideline also proposes the “CC To ABC” management pathway, i.e., based on individual assessment, stroke prevention, optimization of symptom control, etc., focusing on the identification and management of concomitant diseases and risk factors, and exploring lifestyle interventions, etc., for comprehensive management ^[5-8]. Similarly, China’s “Healthy China 2030” Planning Outline and China’s Medium- and Long-term Development Plan for the Prevention and Treatment of Chronic Diseases (2017–2025) both emphasize good chronic disease work. The 2018 China Atrial Fibrillation Guidelines recommend opportunistic screening for atrial fibrillation in high-risk populations, and for patients with a high risk of concomitant stroke, recommending a No less than 72 hours of long-duration ECG monitoring is recommended for the diagnosis of AF ^[9], and the 2019 Technical Program for Graded Diagnosis and Treatment of Atrial Fibrillation proposes that hospitals at all levels should emphasize the initial identification of AF in the population, and encourages hospitals at all levels to set up a remote ECG network based on the “Internet Plus” and strengthen the management of single diseases in the region. In summary, although a variety of anticoagulants and rhythm control strategies have been used for NVAF treatment, the prognosis of patients is still unsatisfactory.

4.1. Pathophysiologic classification of major risk factors

The pathogenesis of non-valvular atrial fibrillation (NVAF) is complex, involving multiple interactions such as electrical remodeling, structural remodeling and neuroendocrine activation. Recent studies have categorized risk factors into the following four groups: (1) Hemodynamic abnormalities: uncontrolled hypertension and heart failure lead to elevated atrial pressure, which activates the RAS system through mechanical stress, promoting myocardial fibrosis and electrical conduction heterogeneity; (2) Metabolic disorders: obesity and diabetes mellitus accelerate atrial matrix remodeling through insulin resistance and lipotoxicity, and upregulation of inflammatory factors; (3) Organ dysfunction: patients with chronic kidney disease (CKD) exacerbate vascular endothelial dysfunction due to uremic toxin accumulation and calcium and phosphorus metabolism disorders; hepatic dysfunction affects the synthesis of coagulation factors and the metabolism of anticoagulant drugs; (4) Inflammation and fibrosis cascade: biomarkers such as C-reactive protein (CRP) and Galectin-3 are positively correlated with the degree of myocardial fibrosis, and activation of the TGF- β /Smad signaling pathway is the core molecular mechanism of atrial fibrosis ^[11]. These factors drive atrial electrical activity through the “calcium imbalance-oxidative stress-mitochondrial dysfunction” axis, resulting in a prothrombotic state. Studies have demonstrated that NVAF patients have increased vWF release and decreased expression of thrombomodulin (TM) in left atrial endothelial cells, further promoting platelet activation and fibrin deposition ^[22].

4.2. Pharmacologic basis and controversies of anticoagulation therapy

Based on Virchow's three-component theory of thrombosis, anticoagulation therapy reduces the risk of thromboembolism by intervening in the coagulation cascade. The advantages of novel oral anticoagulants (NOACs) over conventional warfarin are: (1) Specific target inhibition: rivaroxaban and dabigatran directly block key nodes of coagulation and reduce thrombin generation; and (2) Predictable pharmacokinetics: NOACs do not require routine monitoring of INR and have fewer food and drug interactions, but renal function-dependent metabolism leads to an increased risk of bleeding in CKD patients^[23]. However, the use of NOACs in specific populations remains controversial: (1) Patients with extreme body weight: those weighing < 50 kg or > 120 kg may have abnormal drug concentrations due to changes in the volume of distribution, but there is a lack of evidence-based rationale for dose adjustments; and (2) Multi-drug combination scenarios: when combined with P-glycoprotein inhibitors, NOACs blood concentrations are elevated by 30–40%, and bleeding complications need to be guarded against^[24].

4.3. Anatomical and clinical evidence for left auricular occlusion (LAAC)

90% of NVAf-associated thrombi originate in the left auricle (LAA), and its morphologic typing is strongly associated with embolic risk. Some studies have confirmed that LAAC is noninferior to warfarin in reducing stroke risk and significantly reduces major bleeding events (HR = 0.49). However, the incidence of postoperative device-related thrombosis (DRT) (approximately 3–7%) and residual shunting remains a clinical concern. In recent years, dual-disk occluders have reduced the risk of DRT to 1.8% by enhancing endothelial coverage and sealing^[25].

4.4. Intelligent innovation of risk stratification tools

4.4.1. Optimization of the CHA2DS2-VASc score

The CHA2DS2-VASc-IL score proposed in 2022 integrates interleukin-6 (IL-6) and fibrinogen levels to significantly increase stroke prediction efficacy (AUC from 0.64 to 0.71) in low-risk populations (score ≤ 1).

4.4.2. Artificial intelligence dynamic prediction system

The AF-SCORE model based on deep learning algorithms realizes real-time assessment of stroke risk by analyzing ambulatory electrocardiogram, electronic health record (EHR) and wearable device data (sensitivity 92%, specificity 88%).

4.5. Precision medicine exploration of individualized anticoagulation strategies

4.5.1. Gene-directed dose adjustment

Testing for polymorphisms in the CYP2C9 and VKORC1 genes guided the initial dose of warfarin, resulting in a 40% reduction in time to INR attainment (from 28 to 17 days).

4.5.2. Renal function-adapted regimens

For CKD patients with eGFR < 30 mL/min, apixaban dose-adjustment (2.5 mg bid) reduced the risk of major bleeding by 31% compared with the standard dose (RR = 0.69, *P* = 0.02).

4.5.3. Anticoagulation-antiplatelet combination therapy controversy

The COMPASS subgroup analysis showed that combining rivaroxaban (2.5 mg bid) with aspirin in patients with NVAf combined with coronary artery disease reduced cardiovascular events (HR = 0.74) but increased the risk of major bleeding (HR = 1.51), with the net clinical benefit needing to be individually weighed.

4.6. Technological innovation and device iteration

4.6.1. Pulsed electric field ablation (PFA)

Selective ablation of atrial tissue by destabilizing myocardial cell membranes through non-thermal electric fields, avoiding pulmonary vein stenosis and esophageal injury. The PULSED-AF trial showed a 25% reduction in AF recurrence rate 12 months after PFA compared to radiofrequency ablation (15% vs. 20%). The PULSED-AF trial showed a 25% reduction in AF recurrence rate 12 months after PFA compared to radiofrequency ablation.

4.6.2. Fourth-generation blocker design

The new generation WATCHMAN FLX device achieves a 96% complete block rate and a reduced incidence of device-related thrombosis (DRT) to 1.8% through a compressible skeleton design ^[25]. The intracardiac ultrasound (ICE)-guided zero-contrast implantation technique reduces the risk of contrast nephropathy (OR = 0.32), especially in patients with CKD. The WATCHMAN FLX device utilizes a fully occluded balloon structure, which improves the procedural success rate to 98% with a residual shunt rate of < 3%.

4.7. Lifestyle interventions

A Mediterranean diet (rich in omega-3 fatty acids and antioxidants) combined with 150 minutes of moderate-intensity exercise per week reduced atrial fibrillation load (HR = 0.69) and reversed left atrial enlargement (12% reduction in LAVI) ^[26].

4.8. Construction of multidisciplinary cooperative management model

The concept of “mind-brain co-management” promotes collaboration between neurology and cardiovascular medicine, and for patients with NVAf combined with cryptogenic stroke, the combined application of LAAC and patent foramen ovale occluder (PFO) blockage has reduced the annual stroke recurrence rate from 8.2% to 2.1%. In addition, a comprehensive intervention integrating nutrition and rehabilitation medicine improved patients’ exercise tolerance (6-minute walk distance increased by 45 meters) and quality of life scores (SF-36 score increased by 12 points) ^[27].

5. Discussion

The current study has some limitations, such as: the first aspect, the bottleneck of clinical application of risk prediction models. The CHA2DS2-VASc score does not sufficiently discriminate between intermediate-risk patients (scores 1–2), and about 30% of patients are misclassified. Most novel biomarkers lack standardized testing procedures and cost-effectiveness analyses, and there is insufficient data on racial variability. Secondly, there is a “gray area” controversy in anticoagulation therapy, and NOACs reversal agents have limitations. Although NOACs reversal agents can rapidly antagonize Xa inhibitors, the ANNEXA-4 study showed that their thrombotic event rate was as high as 10%. Although Idarucizumab and Andexanet alfa are approved, their short half-life (8–12 hours) and high cost limit clinical use. Evidence gaps in special populations: anticoagulation strategies for patients

with liver failure and solid tumors combined with NVAF lack high-quality RCT support. Thirdly, uncertainty about the long-term efficacy of device therapy. There is a lack of long-term data on LAAC, with most of the available studies having a follow-up period of ≤ 5 years, and scarce data on follow-up more than 5 years after LAAC, and the mechanism of the association between delayed pericardial effusion, the process of endothelialization of the blocker, and late thrombosis has not yet been elucidated. In addition, the long-term effects of PFA on the atrial autonomic plexus still need to be further evaluated. Fourthly, the practice of interdisciplinary integration is insufficient. Existing studies mostly focus on single interventions and lack full-cycle management programs that integrate cardiovascular, hematology, nephrology, and digital health technologies.

Future research directions can focus on several areas: (1) artificial intelligence and digital healthcare, where deep learning models achieve 98% sensitivity in AF screening by analyzing PPG signals from wearable devices; (2) remote monitoring platforms, integrating anticoagulation adherence reminders and INR self-measurement data to improve time to treatment window (TTR) to 72%; (3) novel anticoagulation strategies, dual factor XI/XI inhibitors, which showed antithrombotic efficacy equivalent to enoxaparin and a 50% reduction in the risk of bleeding in a phase II trial; and (4) to explore and standardize intervention programs based on daily living patterns.

6. Conclusion

NVAF risk management has moved from “single anticoagulation” to “multidimensional integration.” Individualized anticoagulation protocols based on genomics/epigenetics, AI-driven dynamic risk assessment systems, and intervention strategies targeting inflammation/oxidative stress will drive a paradigm shift in clinical practice. In the future, it is necessary to strengthen the long-term follow-up study and deepen the synergistic innovation between basic medicine and clinical translation, to ultimately realize the comprehensive prevention and control of NVAF-related complications.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

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References

- [1] Lippi G, Sanchis-Gomar F, Cervellin G, 2021, Global Epidemiology of Atrial Fibrillation: An Increasing Epidemic and Public Health Challenge. *Int J SImke*, 16(2): 217–221.
- [2] Elliott A, Middeldorp M, Gelder I, et al., 2023, Epidemiology and Modifiable Risk Factors for Atrial Fibrillation. *Nature Reviews Cardiology*, 20(6): 404–417.
- [3] January C, Wann L, Calkins H, et al., 2019, 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS

Guideline for the Management of Patients with Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration with the Society of Thoracic Surgeons. *Circulation*, 140(2): e125–e151.

- [4] Yang C, Hui Z, Zeng D, et al., 2021, A Community-Based Nurse-Led Medication Self-Management Intervention in the Improvement of Medication Adherence in Older Patients with Multimorbidity: Protocol for a Randomised Controlled Trial. *BMC Geriatrics*, 21: 1–15.
- [5] Hindricks G, Potpara T, Dagres N, et al., 2020, 2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*, 2020: ehaa612.
- [6] Sagris M, Vardas E, Theofilis P, et al., 2021, Atrial Fibrillation: Pathogenesis, Predisposing Factors, and Genetics. *International Journal of Molecular Sciences*, 23(1): 6.
- [7] Zhuang T, Zhang S, 2024, Interpretation on Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2024. *Medical Journal of Peking Union Medical College Hospital*, 15(4): 801–806.
- [8] Chen X, Liu H, 2024, Predictive Value of Essen Stroke Risk Score Combined with OX-LDL and UCH-1 for Short-Term Prognosis of Patients with First-Time Acute Ischemic Stroke in Non-Atrial Fibrillation Population. *Journal of Xinjiang Medical University*, 47(2): 254–258 + 263.
- [9] Huang C, Zhang S, Huang D, et al., 2018, Atrial Fibrillation: Current Understanding and Treatment Recommendations – 2018. *Chinese Journal of Cardiac Pacing and Electrophysiology*, 32(4): 315–368.
- [10] Staerk L, Sherer J, Ko D, et al., 2017, Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes. *Circulation Research*, 120: 1501–1517.
- [11] Sagris M, Antonopoulos A, Theofilis P, et al., 2021, Risk Factors Profile of Young and Older Patients with Myocardial Infarction. *Cardiovascular Research*, 2021.
- [12] Diavati S, Sagris M, Terentes-Printzios D, et al., 2021, Anticoagulation Treatment in Venous Thromboembolism: Options and Optimal Duration. *Current Pharmaceutical Design*, 2021.
- [13] Hinderer S, Schenke-Layland K, 2019, Cardiac Fibrosis—A Short Review of Causes and Therapeutic Strategies. *Advanced Drug Delivery Reviews*, 146: 77–82.
- [14] Samman T, Sandesara P, Hayek S, et al., 2017, Association Between Oxidative Stress and Atrial Fibrillation. *Heart Rhythm*, 14: 1849–1855.
- [15] Yoshimoto A, Suematsu Y, Kurahashi K, et al., 2021, Early and Middle-Term Results and Anticoagulation Strategy After Left Atrial Appendage Exclusion Using an Epicardial Clip Device. *Annals of Thoracic and Cardiovascular Surgery*, 27(3): 185.
- [16] Deshmukh A, Iglesias M, Khanna R, et al., 2022, Healthcare Utilization and Costs Associated with a Diagnosis of Incident Atrial Fibrillation. *Heart Rhythm*, 3(5): 577–586.
- [17] Wei Y, Zhou G, Wu X, et al., 2023, Latest Incidence and Electrocardiographic Predictors of Atrial Fibrillation: A Prospective Study from China. *Chinese Medical Journal (English)*, 136(3): 313–321.
- [18] Shi S, Tang Y, Zhao Q, et al., 2022, Prevalence and Risk of Atrial Fibrillation in China: A National Cross-Sectional Epidemiological Study. *The Lancet Regional Health – Western Pacific*, 23: 100439.
- [19] Ren Y, Li N, Lu J, et al., 2024, Study on the Evaluation of Stroke Risk in Patients with Non-Valvular Atrial Fibrillation by Echocardiography Combined with B-Type Natriuretic Peptide. *Journal of Bengbu Medical College*, 49(10): 1367–1370.
- [20] Zhao J, Chen M, Zhou X, et al., 2024, Diagnosis of Left Atrial Appendage Thrombus in Patients with Atrial Fibrillation

Using Dual-Energy CT. *Journal of Sun Yat-sen University (Medical Sciences)*, 45(5): 745–754.

- [21] Xing Y, Zhang Y, Yao Z, et al., 2024, Construction and Validation of a Predictive Model for Cognitive Frailty in Elderly Patients with Atrial Fibrillation. *Military Nursing*, 41(7): 38–42.
- [22] Zhao Y, 2017, The Effect of Behavioral Intervention Based on the Transtheoretical Model on Cardiac Rehabilitation and Quality of Life in Patients after Percutaneous Coronary Intervention. *International Medicine and Health Guidance News*, 23(15): 2456–2460.
- [23] Ruff C, Giugliano R, Braunwald E, et al., 2014, Comparison of the Efficacy and Safety of New Oral Anticoagulants with Warfarin in Patients with Atrial Fibrillation: A Meta-Analysis of Randomised Trials. *The Lancet*, 383(9921): 955–962.
- [24] Meid A, Wirbka L, Groll A, et al., 2022, Can Machine Learning from Real-World Data Support Drug Treatment Decisions? A Prediction Modeling Case for Direct Oral Anticoagulants. *Medical Decision Making*, 42(5): 587–598.
- [25] Reddy V, Doshi S, Kar S, et al., 2017, 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. *Journal of the American College of Cardiology*, 70(24): 2964–2975.
- [26] Neumann F, Jagemann B, Makarova N, et al., 2022, Mediterranean Diet and Atrial Fibrillation: Lessons Learned from the AFHRI Case–Control Study. *Nutrients*, 14(17): 3615.
- [27] Freixa X, Arzamendi D, Tzikas A, et al., 2014, Cardiac Procedures to Prevent Stroke: Patent Foramen Ovale Closure/ Left Atrial Appendage Occlusion. *Canadian Journal of Cardiology*, 30(1): 87–95.

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A Comprehensive Review of the Phenomenon of Nipple Confusion and Coping Strategies

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Abstract: Nipple confusion, a term that accurately describes the confusion that occurs between the mother's nipple and the artificial teat during feeding in newborns. Specifically, it refers to the fact that babies develop specific breastfeeding habits after birth, based on their initial feeding experience. For babies who are accustomed to their mother's nipple, they tend to show resistance to bottle feeding; on the contrary, those who have adapted to bottle feeding may refuse to accept their mother's nipple. This confusion is particularly common among mixed-feeding babies.

Keywords: Nipple confusion; Newborn; Breastfeeding; Breast versus bottle

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1. Introduction

Nipple confusion is a common problem in neonatal feeding, where infants are confused between the mother's nipple and the artificial teat due to early exposure to different feeding modalities (breast vs. bottle), resulting in a strong preference or resistance to one or the other. This phenomenon is particularly prominent among mixed-feeding infants, with approximately 30–50% of mixed-feeding infants worldwide experiencing varying degrees of nipple confusion. Data from the Chinese Centre for Disease Control and Prevention (CDC) 2021 show that mixed feeding rates are as high as 42% in urban areas and 35% in rural areas, with about 60% of mixed-fed infants experiencing breastfeeding-resistant behaviour. Breastfeeding is not only the best source of nutrition for infants, but it is also the core pathway of emotional bonding between mothers and infants. However, nipple confusion may lead to interruption of breastfeeding, affecting the health of the infant and the mother-infant relationship. Breastfeeding is not only the best source of nutrition for infants, but also a central means of emotional bonding between mothers and infants. However, nipple confusion may lead to breastfeeding interruption, affecting infant health and the mother-infant relationship. This article systematically reviews the research progress of nipple confusion from the perspectives of physiological mechanisms, influencing factors, socio-cultural background, and intervention strategies, aiming to provide a scientific basis for clinical practice and family care.

2. Advantages of breastfeeding

In terms of nutritional supply, breast milk is rich in a variety of nutrients, with an appropriate ratio of protein, fat and sugar, and contains all kinds of vitamins, minerals and immunologically active substances necessary for the growth of infants, which can perfectly satisfy the nutritional needs of infants aged 0–6 months, and help infants grow healthily ^[1]. In terms of strengthening the immune system of infants, immunoglobulins and lactoferrin in breast milk can not only meet the growth and development needs of infants in the first 4 to 6 months of life, but also effectively resist the attack of bacteria and viruses, which reduces the chances of infants suffering from respiratory infections, diarrhoea, gastrointestinal infections, otitis media, etc. ^[2]; for the digestive system of infants, breast milk is natural and gentle, which is easier to be digested and absorbed, and reduces gastrointestinal discomforts; from the emotional level, the close contact between mothers and infants when breastfeeding, and the exchange of eyes and skin, can greatly enhance parent-child From the mother's point of view, breastfeeding can promote post-partum uterine contraction, speed up physical recovery, and also reduce the risk of mothers suffering from breast cancer, ovarian cancer and other diseases; from the economic and environmental point of view, breastfeeding does not require the purchase of expensive milk powder and related supplies, saving the family's expenditure, and at the same time, avoiding the consumption of resources and environmental pollution brought about by the production of milk powder packaging, which is both affordable and environmentally friendly. At the same time, it avoids the consumption of resources and environmental pollution caused by the production and packaging of milk powder, which is both economical and environmentally friendly.

3. Physiological mechanisms and causes of nipple confusion

3.1. Data on infant “path dependency”

Studies have shown that sucking patterns developed by infants in the first 2–4 weeks of life are “path-dependent,” and that early exposure to the mother's nipple or bottle can lead to the solidification of oral muscle memory, with babies accustomed to the mother's nipple being reluctant to use a bottle, and babies accustomed to bottle feeding refusing to be fed from the mother's nipple ^[3]. The National Institutes of Health (NIH) 2022 study noted that 65% of infants introduced to a bottle within 1 week of birth showed breast milk resistance after 1 month, significantly higher than the delayed introduction group (22%). A Chinese cohort study (2020) of the cities of Beijing and Shanghai also showed a 58% incidence of nipple confusion among infants who used a bottle within 3 days after birth. It is important to note that in countries with breastfeeding rates of more than 80%, such as Norway and Sweden, the incidence of nipple confusion is less than 15%, while in the Philippines and Mexico, where formula prevalence is high, the rate is more than 40%. The situation is more complex in China, where mixed feeding rates in first-tier cities are close to those in developed countries, but insufficient support for breastfeeding in primary health care facilities has led to a nipple confusion correction rate in rural areas that is only half that of urban areas.

3.2. Differences in sucking patterns

In clinical practice, the main concern is for those babies who were first exposed to and accustomed to bottle feeding in the neonatal stage. Their early experience of bottle feeding, or frequent use of the bottle for feeding for various reasons, leads to weakness or incoordination of sucking and swallowing, misrhythmic sucking, and abnormal sucking response when subsequently confronted with breastfeeding ^[4]. The reason for this phenomenon is the significant difference in mechanical mechanisms between breast sucking and bottle sucking.

(1) Breastfeeding

The infant needs to wrap his tongue around the areola and squeeze the milk ducts through wave-like peristalsis to stimulate the milk ejection reflex. This process requires coordinated respiration, swallowing and jaw movements, with an average sucking frequency of 40–60 times per minute, which consumes a lot of energy. The flow rate of breastmilk is dependent on the milk array (average flow rate of 5–10 mL/min) and is intermittent; the flow rate of the bottle is constant and can be artificially adjusted by tilting the bottle at an angle, leading to the infant's dependence on "instant gratification."

(2) Bottle sucking

The fixed shape of the teat and gravity allow for a fast and steady flow of milk (about 20–30 mL/min), and the infant only needs to swallow passively, reducing the frequency of sucking to 10–20 sucks/minute with no need for force. There are significant differences in how the bottle and nipple feel in the baby's mouth. This includes several aspects such as length, softness, amount of milk produced and the amount of force required to suck. For example, when a baby sucks on its mother's nipple, it needs to mobilize its muscles, balance its breathing and trigger the milk ejection reflex through the sucking stimulus for milk to flow out in large quantities. With bottle feeding, on the other hand, as the nipple forms a completely closed space, the baby only needs to swallow easily and can access the milk without much effort. Therefore, once babies are used to bottle feeding, they may show different reactions when faced with nipples of different textures and lengths, as well as milk volume that comes in small and large quantities at different times and at different speeds. Some babies may be slightly patient and able to hold out until the milk bursts; while others may resist strongly and cry after two sucks; and some may even start crying as soon as they are carried to their mothers. All these reactions reflect the impact of the nipple confusion phenomenon on the feeding habits of babies. It is not surprising that children may show a more sensitive and reluctant attitude towards their mothers. It takes time for the child to adapt and change, and the mother should be patient and understanding when such resistance is encountered.

(3) Neural reflexes and behavioural learning

Infants' sucking reflexes are controlled by the brainstem, but feeding choices involve higher-level cortical learning mechanisms. Frequent switching of feeding tools may lead to "operant conditioning" - associating the bottle with easy feeding and the breast with hard sucking - and behavioural avoidance.

4. The multidimensional impact of nipple confusion

4.1. Direct impact on breastfeeding

The direct impact includes a decrease in lactation. The sucking action of the child, the most natural lactation stimulator, has a significant boosting effect on milk secretion. When nipple confusion occurs, the mother's milk production may gradually decrease due to the lack of direct breastfeeding stimulation. Data show that the average daily lactation of nipple-confused mothers is 30–40% lower than that of the exclusive breastfeeding group. The Chinese Association for Maternal and Child Health 2022 report states that insufficient breast milk due to nipple confusion accounts for 47% of the reasons for weaning at six months postpartum. Although breast pumps can play a similar role to some extent, and some mothers have had success in increasing milk production through breast pumps, prolonged use of breast pumps can lead to poor milk migration, recurrent milk stagnation, and even

irreversible damage to the breasts, which can further reduce milk production. It also increases breast health risks. Improper use of breast pumps can lead to obstruction or damage to the milk ducts, increasing the risk of mastitis (2–3 times more likely). A multicentre study in China (2021) found that 35% of nipple-confused mothers had experienced mastitis episodes, significantly higher than the 12% in the exclusive breastfeeding group.

4.2. Infant health and development

(1) Differences in nutritional intake

Immunoglobulins (e.g., sIgA), oligosaccharides, and active enzymes in breast milk are not fully retained by the bottle, and the risk of respiratory infections was 18% higher in mixed-fed infants compared to the exclusively breastfed group. Data from the Chinese Centre for Disease Control and Prevention (CDC) showed that the incidence of diarrhoea was significantly higher in mixed-fed infants (21.3%) than in exclusively breastfed infants (9.8%)^[5].

(2) Abnormalities in oral development

Long-term bottle feeding may affect mandibular development and increase the probability of dental caries and malocclusion. A study by Peking University Stomatological Hospital (2023) noted that 45% of children who used bottles for a long period of time before the age of 3 years had problems with anterior tooth mandibular problems.

4.3. Psychological and social consequences

Mother-infant attachment is weakened: skin-to-skin contact during breastfeeding promotes oxytocin secretion and strengthens the parent-child bond. Nipple confusion may reduce such interactions, leading to an increased incidence of infant separation anxiety. A survey by the Chinese Academy of Social Sciences in 2022 showed that nipple-confused infants had a 23% lower parent-child interaction score than the exclusive breastfeeding group. It also increases psychological stress for mothers, with about 70% of nipple-confused mothers reporting anxiety or self-blame, and 15% of them terminating breastfeeding early as a result. A study by the Chinese Maternal and Child Health Psychological Association 2023 noted that nipple confusion is one of the most important triggers of postpartum depression, with related cases accounting for 31% of postpartum depression clinic visits.

5. Geographical differences in nipple confusion

(1) High-income countries

Medicalized delivery patterns (e.g., rising caesarean section rates) are often accompanied by early bottle use, with mixed feeding rates as high as 58% and nipple confusion rates of 38% in the United States, according to the findings of relevant data; in European countries, breastfeeding rates are maintained at more than 80%, with nipple confusion rates at only 12–18%, due to stronger policy support (e.g., 18 months of paid breastfeeding leave in Sweden). Low-income countries: traditional breastfeeding culture is stronger and nipple confusion is less than 10%, but formula marketing is changing this trend^[6].

(2) Current situation in China

According to the China Child Development Report (2022), the national rate of exclusive breastfeeding within six months is 29.2%, far below the WHO-recommended target of 50%. The mixed feeding rate in first-tier cities (e.g., Beijing and Shanghai) exceeds 40%, and the incidence of nipple confusion reaches

52%. In rural areas, where traditional breastfeeding habits are retained to a greater extent, the mixed feeding rate is 35%, but medical resources are scarce for correcting nipple confusion, with only 28% of mothers receiving professional guidance. China's formula milk market is growing at an average annual rate of 12%, reaching RMB 50 billion in 2022. Excessive advertising has led to 30% of mothers believing that "formula milk is as nutritious as breast milk," indirectly exacerbating nipple confusion. Medical and healthcare professionals are concerned about hypoglycaemia in newborns and prematurely recommend formula supplementation, indirectly contributing to nipple confusion.

6. Comprehensive intervention strategies for nipple confusion

6.1. Golden window management

Immediate postnatal interventions are useful in solving nipple confusion in the infant. Biological Nurturing, which encourages mothers to breastfeed in a semi-reclining position and utilizes the infant's innate crawling reflexes to find the breast on their own^[7]. In Norway, legislation has been passed requiring hospitals to implement a "no bottle policy," banning the use of artificial teats within 72 hours of delivery, and increasing breastfeeding rates to 90%. China can learn from this experience and strengthen the implementation rules in the Breastfeeding Promotion Regulations.

6.2. Breastfeeding recommendations

Mothers facing the challenge of nipple confusion should take positive and effective measures:

- (1) Increase skin-to-skin contact with your child. For daily interactions, try face-to-face gentle dialogue with the baby, with gentle touch massage, or natural skin-to-skin contact during bathing^[8]. As these interactions gradually increase, the intimate position of chest-to-belly can be achieved naturally when breastfeeding. Through this gradual approach to contact, the baby can be given enough security while the mother gradually adapts to intimate parenting and eventually transitions to intimacy while breastfeeding.
- (2) Try to change the feeding position. When bottle feeding, the child is usually lying flat on his/her back with the bottle placed vertically. Milk flows out quickly due to gravity, causing the child to swallow quickly and complete the feeding. However, when switching to breastfeeding, as the milk flows out relatively slowly, the child may not be able to get enough milk in the same amount of time, resulting in irritability and restlessness. Therefore, during bottle feeding, attempts can be made to keep the child in a seated position with adequate back support so that the bottle remains essentially parallel to the floor to slow down the rate of milk outflow and bring it closer to what happens during breastfeeding^[9]. During bottle feeding, it is appropriate to insert short pauses between sucking and swallowing so that the baby can rest, and slowly the baby will learn that this is the normal state of milk drinking.
- (3) Stimulate milk formation before feeding. As bottle-feeding is more labour-saving, some babies may resist breastfeeding which requires a lot of sucking. For this reason, to counteract nipple confusion, the key is to let babies re-experience the convenience of breastfeeding. Mothers can stimulate the milk squirt reflex before breastfeeding to ensure that babies get enough milk as soon as they latch on to the breast. To do this, it is recommended to choose a quiet and comfortable environment and relax by taking deep breaths. Before breastfeeding, apply a warm towel to the breast for a few moments, and then gently roll the nipple with your fingertips to stimulate it by imitating the rhythm of the baby's sucking. At the same

time, imagining the picture of milk flowing or recalling the sound of the baby swallowing contentedly can promote oxytocin secretion through psychological suggestion^[10]. When a slight swelling of the breast is felt, milk oozes from the nipple, or when milk is observed to flow out in a jet, it means that the squirt reflex has been successfully triggered, and it is easier to establish a successful feeding experience by letting the baby latch on to the breast immediately at this time.

- (4) Try to hold the bottle under the armpit for feeding. Firstly, let the baby stay close to the mother, then place the bottle under the mother's armpit and adjust the height and direction of the bottle as much as possible to mimic the natural state of the breast. It is advisable to try it at a time when the baby is not fully awake, such as just before bedtime or when the baby has just woken up. Initially, the baby can suck a small amount of milk, after which the family can quietly remove the bottle from behind and quickly replace it with the breast. It is important to note that this method requires several attempts and patience.

7. Conclusion

In summary, nipple confusion is a complex problem at the intersection of biobehavioural, socio-cultural and medical practice. Although its challenges should not be underestimated, a breastfeeding-friendly society can be built through multidisciplinary collaboration between paediatricians and family and social support to promote policy innovation. As breastfeeding advocate Jack Newman says, "Babies are not machines, and breastfeeding is not a task - it's a two-way dialogue that requires patience and wisdom."

Disclosure statement

The authors declare no conflict of interest

References

- [1] Zhao Y, Wang X, 2024, Research Progress of Breastfeeding in Preterm Infants. *Chinese Community Physician*, 40(4): 4–6.
- [2] Wang Q, Wang H, Xiao M, et al., 2018, Analysis of the Current Situation of Breastfeeding and Nursing Countermeasures in China. *Chinese Journal of Reproductive Health*, 29(2): 200–202.
- [3] Zhang Y, Ma H, Ren M, et al., 2025, Research Progress of Scenario Simulation in Breastfeeding Health Education. *Frontiers of Medicine*, 15(9): 31–34.
- [4] Shao M, Luo P, Qin X, et al., 2022, Research Progress of Sucking Function Assessment Tool for Newborns. *Military Nursing*, 39(7): 17–20.
- [5] Chen D, 2023, Influence of Infant Health Care on Infant Growth and Development, Nutritional Diseases and Health Status. *Introduction to Women's and Children's Health*, 2(13): 73–75.
- [6] Hu H, 2017, Clinical Observation of Finger Training Combined with Biological Nourishment Method on Improving Nipple Confusion Rate After Mother–Infant Separation. *Everybody's Health (Late Edition)*, 11(8): 190–191.
- [7] Fang X, Zhang J, 2009, Nutritional Needs and Supply of Mothers and Infants During the Window Period. *Life Development Opportunities – Window Period Nutrition – Proceedings of the 12th Annual Conference of Danone Nutrition Centre, College of Life Sciences, Xuzhou Normal University*: 177–180.
- [8] Hu D, 2021, What to Do About Nipple Confusion. *Jiangsu Health Care*, 2021(11): 32–33.

- [9] Deng H, 2020, How to Master the Correct Breastfeeding Posture. Collection of Manuscripts from the 12th Academic Exchange Activity on Health Education and Health Promotion in Guangzhou, Guangzhou Municipal Health and Health Promotion and Education Centre: 1.
- [10] Bao X, 2019, Baby's Refusal of Nipple Is Not Mother's Fault. Jiangsu Health Care, 2019(6): 36.

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The Prevalence and Influencing Factors of Posttraumatic Stress Disorder in Patients with Myocardial Infarction: A Systematic Review and Meta-analysis

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Abstract: With the accelerated pace of population aging in China, the number of patients suffering from myocardial infarction (MI) is increasing annually. During disease progression, patients are at significantly higher risk of developing severe negative emotions, and emerging evidence suggests that post-traumatic stress disorder (PTSD) is significantly associated with cardiovascular disease, which seriously affects patients' quality of life. *Objective:* The aim of this study was to comprehensively assess the prevalence and influencing factors of PTSD in MI patients through systematic review and Meta-analysis. *Methods:* A computerized search of PubMed, the Cochrane Library, Embase, Web of Science, PsycINFO, China Knowledge Network (CNKI), WanFang Data, VIP, and China Biomedical Literature Database (CBM) was conducted to collect longitudinal studies, case-control studies, and cross-sectional studies related to PTSD prevalence rates and influencing factors in MI patients published up to August 1, 2024. Literature screening, data extraction and quality assessment were done independently by two researchers and Meta-analysis was done using Stata 16.0 software. This study has been registered on the PROSPERO platform, registration number: CRD42024577243. *Results:* A total of 16 papers were included, with a total sample size of 3,768 cases involving 8 influencing factors. The results of the Meta-analysis showed that the prevalence of PTSD in patients with MI was 20.4% (95% CI = 15.0–26.5%). Female ($OR = 3.12$, 95% CI = 1.97–4.97, $P < 0.001$), high neuroticism score ($OR = 2.21$, 95% CI = 1.20–4.07, $P = 0.011$), and high intrusive rumination score ($OR = 2.95$, 95% CI = 1.50–5.83, $P = 0.002$) were the risk factors for PTSD in MI patients. While age ($OR = 1.01$, 95% CI = 0.98–1.04, $P = 0.440$), education level ($OR = 0.55$, 95% CI = 0.07–4.48, $P = 0.574$), social support rating scale ($OR = 0.81$, 95% CI = 0.52–1.26, $P = 0.346$), Killip cardiac function classification ($OR = 2.29$, 95% CI = 0.91–5.80, $P = 0.080$) and creatine kinase isoenzyme ($OR = 1.03$, 95% CI = 0.99–1.05, $P = 0.124$) were not associated with the development of PTSD in MI patients. *Conclusion:* The prevalence of PTSD was higher in patients with MI. The prevalence varied by evaluation tool and study area. Risk factors were multifactorial, including general factors (female) and overall assessment (high neuroticism score, high invasive rumination score). Therefore, early intervention and proper

de-escalation of PTSD symptoms in patients with MI by medical staff are needed in clinical practice to reduce the risk of PTSD.

Keywords: Myocardial infarction; Post-Traumatic Stress Disorder; Prevalence; Influencing factors; Meta-Analysis

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1. Introduction

The Global Burden of Disease (GBD) study indicates that the total number of cases of cardiovascular disease (CVD) increased from 271 million in 1990 to 523 million in 2019, with the number of deaths from CVD increasing from 12.1 million to 18.6 million, posing a serious threat to people's health ^[1]. Myocardial infarction (MI) is a major cause of death in CVD, with rapid onset, fast progression, and high mortality, which can lead to surviving patients experiencing various forms of physical and psychological stress ^[2–4]. Post-traumatic stress disorder (PTSD) refers to an individual's experiencing traumatic events, heightened arousal, and persistent avoidance or numbing after experiencing a significant physiological or psychological stimulus, which is a potential traumatic event ^[5]. Its main harm lies in the patient's psychological disorder and reduced adherence to treatment, which seriously affects the patient's prognosis ^[6]. There is increasing evidence of a bidirectional relationship between PTSD and CVD ^[7,8]. Great psychological stimulation usually leads to PTSD in patients, affecting their physical and mental health, increasing the risk of adverse cardiovascular events ^[9], hospitalization rates, and mortality rates in affected patients, resulting in a significant public health burden ^[10]. Currently, more cross-sectional studies have been conducted at home and abroad to explore the prevalence and risk factors of PTSD in patients with MI, but the limitations of the sample size, study area and diagnostic criteria have led to large differences between the findings. Jacquet-Smailovic et al. ^[11] showed that the incidence of PTSD symptoms in patients with MI within 12 months after discharge from the hospital ranged from 3.00 to 19.00%. Cao et al. ^[12] showed that the prevalence of PTSD symptoms in Chinese MI patients from the acute phase to 3 months after discharge was 20.40–33.10%. A meta-analysis found that the incidence of PTSD symptoms due to heart disease ranged from 0% to 38.00% ^[13]. Previous studies have shown that PTSD symptoms in patients with MI may be related to patients' age, gender, and personality traits ^[14]. Related studies have found that hippocampal damage, serum cortisol, and C-reactive protein are predictors of PTSD symptoms ^[15–17]. However, there is a lack of comprehensive reports on the prevalence and influencing factors of PTSD in MI patients. Based on this, this study investigated the prevalence and risk factors of PTSD in patients with MI by meta-analysis, aiming to provide a reference basis for effective clinical intervention and preventive management.

2. Methods

2.1. Study registration

This study was registered in the International Prospective Register of Systematic Reviews (PROSPERO Registration No.: CRD42024577243) and was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. This article reports the results of a literature search and does not involve any animal, cell, or human experimental research. This study did not require ethics approval in China.

2.2. Search strategy

Computerized searches of PubMed, the Cochrane Library, Embase, Web of Science, PsycINFO, China Knowledge Network (CNKI), WanFang Data, Wipo Chinese Scientific and Technical Journal Database (VIP) and China Biomedical Literature Database (CBM) for MI Literature related to the factors affecting PTSD in patients was searched with the time limit of building the database to August 01, 2024. The search was conducted using a combination of subject terms and free terms, and the Chinese search terms included “myocardial infarction,” “post-traumatic stress disorder, post-traumatic stress symptoms, traumatic stress disorder, post-traumatic neurosis, post-traumatic stress reaction,” “influencing factors, risk factors, associated factors, predictors, related,” etc. English search terms include “Myocardial Infarction*, Infarction*, Myocardial, Heart Attack*, Myocardial Infarct*, Infarct*, Myocardial *OR* Cardiovascular Stroke* *OR* Stroke*, Cardiovascular,” “Stress Disorder*, Post-Traumatic, Post-Traumatic Stress Disorder*, Post Traumatic Stress Disorder*, Neuroses, Post Traumatic, PTSD, Stress Disorder*, Post Traumatic, Posttraumatic Stress Disorder* *OR* Stress Disorder*, Posttraumatic,” “Risk Factors, Associated Factor, Relevant Factor*, Predicted Factor*, Influencing Factor*, Correlation,” etc. In addition, the references of the included literature were traced. Using PubMed as an example, the specific search strategy is shown in **Table 1**.

2.3. Eligibility and exclusion criteria

Inclusion criteria: (1) The subjects were clinically diagnosed as MI patients; (2) Types of studies include observational studies, including cohort studies, case-control studies, and cross-sectional studies; (3) The study focused on the prevalence and influencing factors of PTSD in MI patients; (4) The outcome measure was PTSD in MI patients; (5) The literature is in Chinese and English.

The exclusion criteria were as follows: (1) The subjects had PTSD before they were diagnosed with MI; (2) Unable to extract valid data or incomplete data literature; (3) The literature types were reviews, case reports, conference abstracts or book chapters; (4) Repeated publications and non-availability of full texts.

2.4. Data extraction

Literature screening, extraction of information and cross-checking were carried out independently by 2 researchers. Disagreements, if any, were resolved by mutual agreement or consultation with the third researcher until the results were consistent. Literature screening was performed in strict accordance with the inclusion and exclusion criteria; after eliminating duplicates, irrelevant literature was excluded by reading the title and abstract, and the rest of the literature was read in its entirety to determine inclusion. Relevant information was extracted and literature related to this study was obtained through the literature tracking method. For articles where available data could not be obtained directly, emails were sent to authors requesting relevant data. Data extraction included: first author, year of publication, type of study, study area, total sample size, number of PTSD cases, PTSD assessment tool, time of PTSD assessment, PTSD incidence and influencing factors.

Table 1. Search strategies of PubMed

Number	Search strategy
#1	("Myocardial Infarction" [Mesh]) OR (Infarction*, Myocardial [Title/Abstract] OR Myocardial Infarction*[Title/Abstract] OR Heart Attack*[Title/Abstract] OR Myocardial Infarct*[Title/Abstract] OR Infarct*, Myocardial [Title/Abstract] OR Cardiovascular Stroke*[Title/Abstract] OR Stroke*, Cardiovascular [Title/Abstract])
#2	("Stress Disorders, Post-Traumatic"[Mesh]) OR (Post-Traumatic Stress Disorder*[Title/Abstract] OR Stress Disorder*, Post-Traumatic[Title/Abstract] OR Post Traumatic Stress Disorder*[Title/Abstract] OR Neuroses, Post-Traumatic[Title/Abstract] OR Neuroses, Post Traumatic[Title/Abstract] OR Post-Traumatic Neuroses[Title/Abstract] OR PTSD[Title/Abstract] OR Stress Disorder*, Post Traumatic[Title/Abstract] OR Posttraumatic Stress Disorder*[Title/Abstract] OR Stress Disorder*, Posttraumatic[Title/Abstract] OR Neuroses, Posttraumatic[Title/Abstract] OR Posttraumatic Neuroses[Title/Abstract] OR Delayed Onset Post-Traumatic Stress Disorder[Title/Abstract] OR Delayed Onset Post Traumatic Stress Disorder[Title/Abstract] OR Post-Traumatic Stress Symptom*[Title/Abstract] OR Posttraumatic Stress Symptom*[Title/Abstract] OR PTSS[Title/Abstract])
#3	("Risk Factors" [Mesh]) OR (influence factor*[Title/Abstract] OR associated factor*[Title/Abstract] OR relevant factor*[Title/Abstract] OR risk factor*[Title/Abstract] OR predicted factor*[Title/Abstract] OR Influencing Factor*[Title/Abstract] OR Correlation [Title/Abstract])
#4	#1 AND #2 AND #3

2.5. Quality assessment

Literature quality was independently evaluated by 2 researchers and cross-validated, and if there were disagreements between the two parties, a 3rd party intervened to discuss and resolve the issue. The quality of literature included in the cohort and case-control studies was rated using The Newcastle-Ottawa Quality Assessment Scale (NOS), with a score of 9 out of 9, with 1 to 3 being low quality, 4 to 6 being moderate quality, and 7 to 9 being high quality^[18]. Cross-sectional studies were scored using the Agency for Health Care Quality and Research (AHRQ), which has a total of 11 entries, with each entry receiving a score of 1 if it was rated as "yes," "no" or "high"^[19]. If each entry is rated as "yes," it will be scored as 1 point, and if it is rated as "no" or "unclear," it will be scored as 0 points out of a total of 11 points, with 0–3 points as low quality, 4–7 points as medium quality, and 8–11 points as high quality.

2.6. Statistical analysis

Meta-analysis of the extracted data was performed using Stata 16.0 software. Effect sizes were expressed using the combined rate and its 95% Confidence Interval (CI), and influence factors were expressed using Odds Ratio (OR) and its 95% CI combined effect size. The included literature was tested for heterogeneity, and the size of heterogeneity was quantified using the I^2 test; if there was no statistically significant heterogeneity between the results of the studies ($P > 0.1$, $I^2 < 50\%$), Meta-analysis was performed using the fixed-effects model; if there was statistically significant heterogeneity between the results of the studies ($P < 0.1$, $I^2 \geq 50\%$), Meta-analysis was performed using the random-effects model. Obvious clinical heterogeneity was dealt with by methods such as sensitivity analysis or subgroup analysis; sensitivity analysis was performed using the one-by-one exclusion method and changing the merger model to determine the stability of the study results. Impact factors for inclusion of ≥ 10 papers were used to detect publication bias in the literature. Differences were considered statistically significant at $P < 0.05$.

3. Results

3.1. Overview of included studies for the systematic review

A total of 16 studies were included^[12,16,20–33]. Among them, 8 were in Chinese^[20,22–26,28,29], and 8 were in

English^[12,16,21,27,30–33]. The database search yielded 736 articles; 169 duplicate publications were excluded, 460 articles were excluded after reading the titles and abstracts, 93 articles were excluded after full-text re-screening, 14 articles were finally included, and 2 articles were included in the manual search. The literature screening process and results are shown in **Figure 1**.

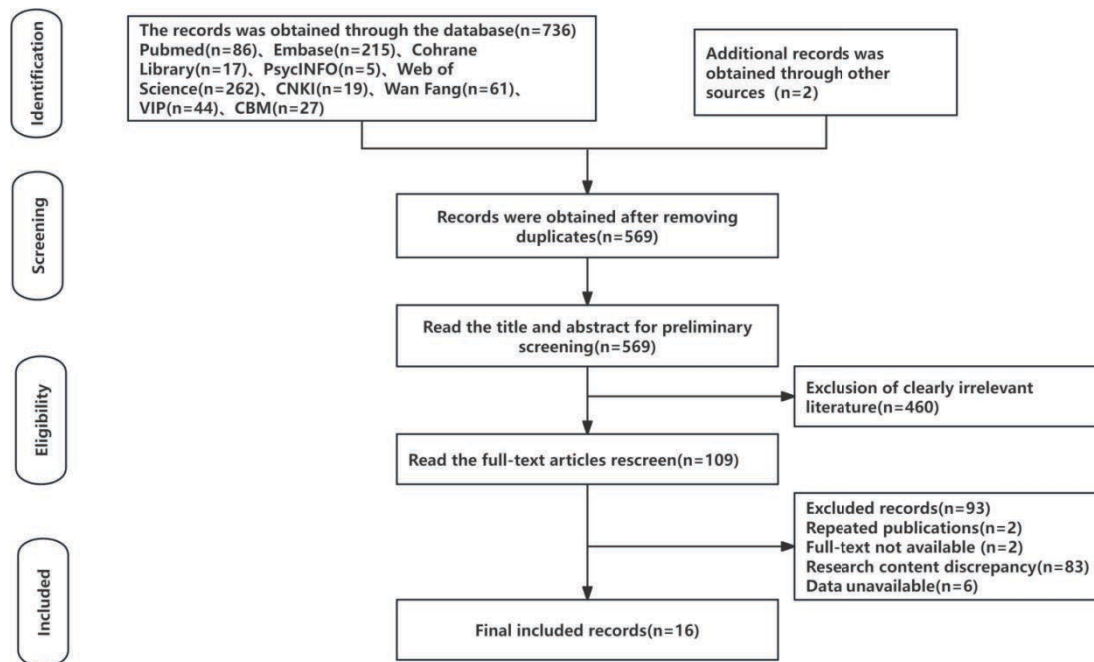


Figure 1. Literature screening flow chart and results.

3.2. Basic characteristics and quality evaluation of the included documents

The basic characteristics of the included studies and the methodological quality evaluation of the literature are shown in **Table 2**, 16 studies were included, with a total sample size of 3768 cases. The 16 articles included 12 cross-sectional studies^[12,16,20,21,23–29,31], 3 cohort studies^[30,32,33], and 1 case-control study^[22]. According to the literature quality evaluation criteria, the quality evaluation of 10 studies was ≥ 6 points, and the quality of the included studies was relatively reliable.

3.3. Meta-analysis of PTSD prevalence in patients with myocardial infarction

3.3.1. Overall prevalence

A meta-analysis was performed on the prevalence of 15 included papers^[12,16,20,21,23–33]. There was significant heterogeneity among the studies ($I^2 = 94.748\%$, $P < 0.001$), so the random-effects model was used for the combination. The results showed that the prevalence of PTSD in MI patients was 20.4% (95% $CI = 15.0–26.5\%$), as shown in the forest diagram (**Figure 2**).

Table 2. Basic characteristics of included literature

Author	Year	Country	Study types	Sample sizes	Case	Prevalence	PTSD assessment tools	PTSD assessment time	Influencing factors	quality score
Wang ^[20]	2024	China	A	200	56	28.00%	PCL-C	60 days after the onset of MI	1、2、3、4	9
Cui ^[21]	2022	China	A	287	92	32.06%	PCL-C	30 days after discharge	5、6、7、8、9	8
Feng ^[22]	2022	China	B	72	32	—	PCL-S	—	10、11、12、13	7
Peng ^[23]	2021	China	A	243	83	34.00%	PCL-C	—	—	9
Cao ^[12]	2021	China	A	113	23	20.40%	PCL-C	3 months after the onset of MI	14、15	9
Gao ^[24]	2019	China	A	266	85	32.00%	PCL-C	60 days after the onset of MI	1、3、4	9
Ni ^[25]	2019	China	A	300	86	28.70%	PCL-C	—	1、7、16、17	8
Li ^[26]	2018	China	A	193	56	29.02%	PCL-C	2 to 3 months after discharge	—	7
Bielas ^[16]	2018	Switzerland	A	183	14	7.70%	PDS	3 months after the onset of MI	10、18、19	8
Lima ^[27]	2018	America	A	271	32	11.80%	PCL-C	—	—	8
Liang ^[28]	2016	China	A	178	41	23.03%	PCL-C	More than 1 month after the onset of MI	1、4、20、21	7
Xiong ^[29]	2014	China	A	240	68	28.30%	PCL-C	It has been more than 1 month since the first onset of MI	2、5、13	8
Dinenberg ^[30]	2014	America	C	579	37	6.40%	CDIS	5 years after the onset of MI	22、23、24	8
Wiedemar ^[31]	2008	Switzerland	A	190	18	9.50%	PDS	—	—	6
Pedersen(1) ^[32]	2004	Denmark	C	226	34	—	PDS	4 to 6 weeks after onset of MI	4、25、26	7
Pedersen(2) ^[33]	2003	Denmark	C	227	33	—	PDS	4 to 6 weeks after onset of MI	4、27、28	7

Abbreviations: A: Cross-sectional study, B: Case-control study, C: Cohort study. PCL-C: Civilian version of post-traumatic stress disorder scale, PCL-S: Post-traumatic Stress Disorder Rating Scale, PDS: 17-item post-traumatic diagnostic scale, CDIS: DSM-IV Computerized Diagnostic Interview Scale. Influencing factors: 1 = age, 2 = social support score, 3 = invasive rumination score, 4 = neuroticism score, 5 = sex, 6 = diabetes, 7 = CK-MB, 8 = Insomnia score, 9 = disease progression fear score, 10 = educational level, 11 = number of interventions, 12 = economic income, 13 = Killip, 14 = smoke, 15 = LVEF, 16 = cTnI, 17 = total cholesterol, 18 = Symptoms of acute stress disorder, 19 = CRP risk, 20 = degree of despair, 21 = fear of death, 22 = ISEL, 23 = ISEL domain score, 24 = ISEL Tangible domain score, 25 = type D personality, 26 = MI, 27 = anxiety, 28 = depression, —: this item does not exist.

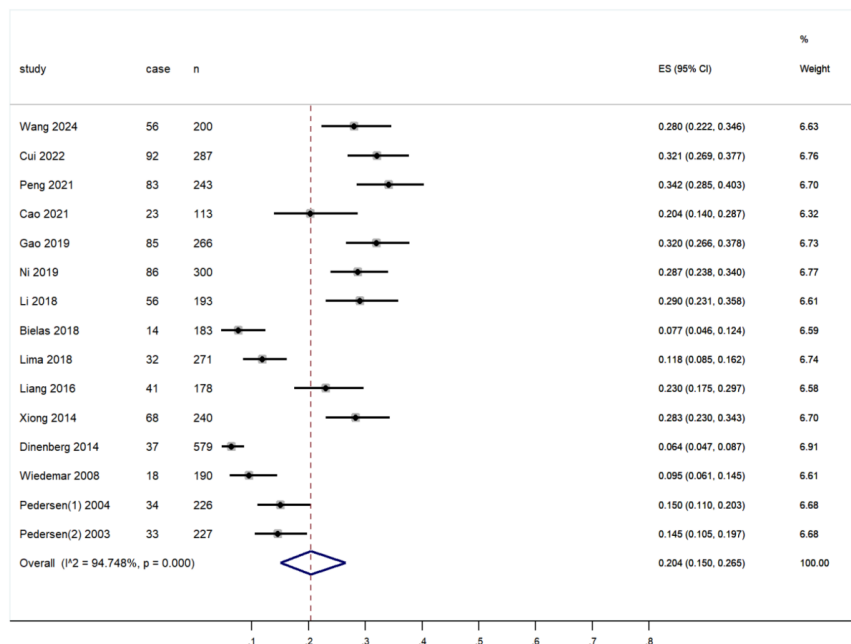


Figure 2. Forest plots for the prevalence of PTSD in myocardial infarction patients.

3.3.2. Subgroup analysis

Subgroup analysis was conducted for the included literatures according to study location and diagnostic criteria, and the results were shown in Table 3. (1) Grouped by study site: Prevalence of MI patients in China and other countries are respectively 28.9% [95% *CI* (26.4%, 31.5%)] and 10.5% [95% *CI* (7.5%, 13.9%)]. (2) According to the evaluation tools used for grouping, the prevalence rates of PTSD among MI patients as assessed by the PTSD Checklist-Civilian Version (PCL-C), the Post-Traumatic Stress Diagnostic Scale (PDS), and the DSM-IV Computerized Diagnostic Interview Schedule (CDIS) are 26.5% [95% *CI* (22.0%, 31.3%)], 11.6% [95% *CI* (8.2%, 15.4%)] and 6.4% [95% *CI* (4.7%, 8.7%)].

Table 3. Results of subgroup analysis of prevalence

Subgroup	Number of articles	Prevalence rate (%)			<i>P</i>
		<i>I</i> ² (%)	Model selection	95% <i>CI</i>	
China	9 [12,20,21,23–26,28,29]	38.776	Fix	28.9 (26.4,31.5)	0.110
Other countries	6 [16,27,30–33]	77.324	Random	10.5 (7.5,13.9)	0.001
PCL-C	10 [12,20,21,23–29]	84.666	Random	26.5 (22.0,31.3)	< 0.001
PDS	4 [16,31–33]	62.427	Random	11.6 (8.2,15.4)	0.046
CDIS	1 [30]	—	—	6.4 (4.7,8.7)	—

—: This item does not exist.

3.3.3. Sensitivity analysis

In the study of prevalence, a one-by-one exclusion method was used to eliminate individual studies, followed by a meta-analysis of the remaining literature to obtain a forest plot for sensitivity analysis. The vertical line indicates that the overall combined effect size is 0.21, with all studies evenly distributed on either side of the vertical line, suggesting that the results are relatively stable, as shown in **Figure 3**.

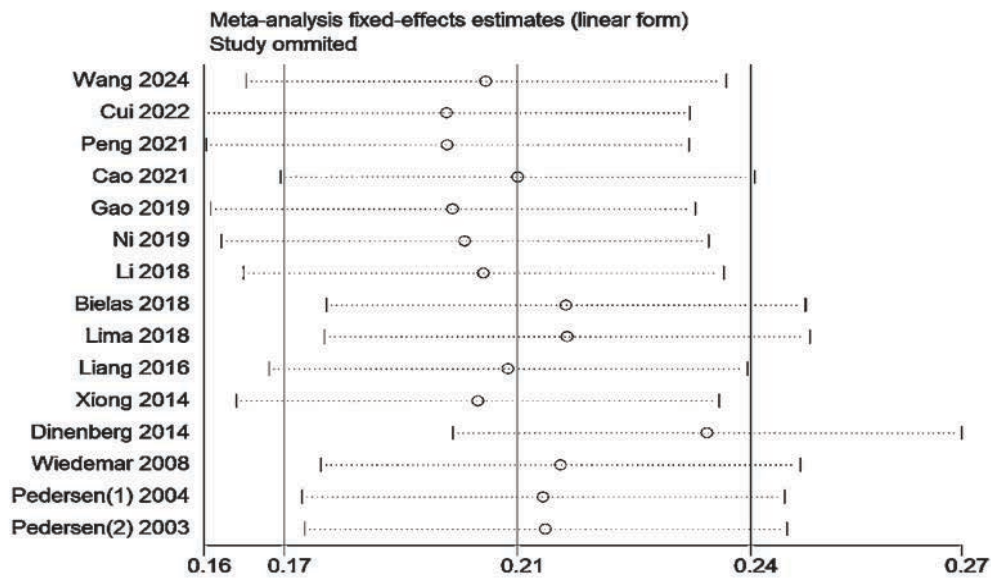


Figure 3. Sensitivity analysis for the prevalence of PTSD in myocardial infarction patients.

3.3.4. Publication bias

Egger's test was used to assess publication bias for studies with a sample size of at least 10. The test results showed $P = 0.267 > 0.05$, indicating that there is no publication bias or that the publication bias is not significant. The funnel plot is shown in **Figure 4**.

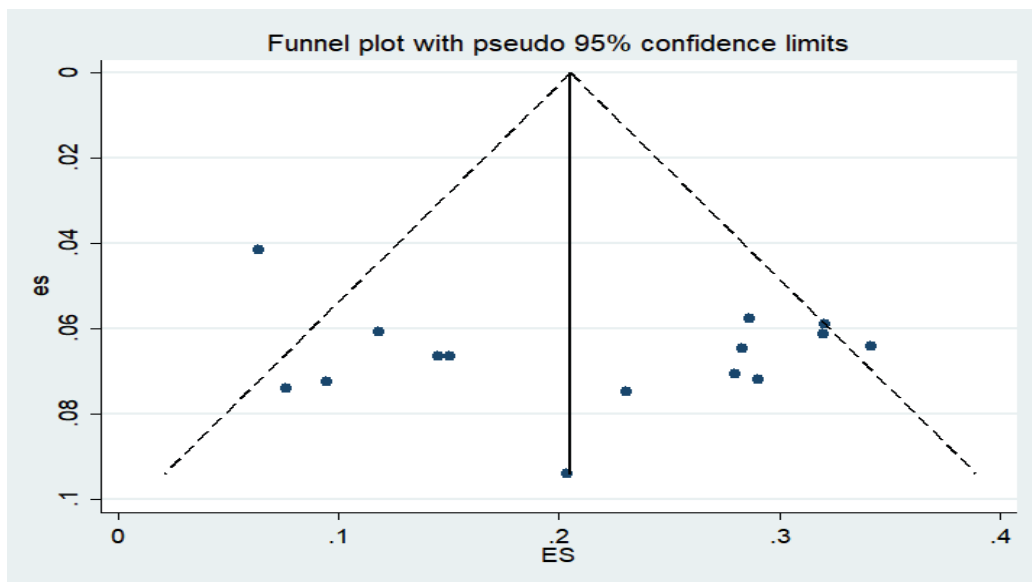


Figure 4. Funnel diagram.

3.4. Results of meta-analysis of influencing factors of PTSD in patients with myocardial infarction

3.4.1. Influencing factors

Influencing factors are shown in **Table 4**.

(1) General Factors

Four studies ^[20,24,25,28] analyzed the impact of age on the occurrence of PTSD in MI patients, showing heterogeneity between studies ($P < 0.001$, $I^2 = 92.0\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that older age is not a risk factor for PTSD in MI patients ($OR = 1.01$, $95\% CI = 0.98-1.04$, $P = 0.440$). Two studies ^[21,29] analyzed the impact of gender on the occurrence of PTSD in MI patients, showing no heterogeneity between studies ($P = 0.842$, $I^2 = 0\%$), the fixed-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that being female is a risk factor for PTSD in MI patients ($OR = 3.12$, $95\% CI = 1.97-4.97$, $P < 0.001$). Two studies ^[16,22] analyzed the impact of education level on the occurrence of PTSD in MI patients, showing heterogeneity between studies ($P = 0.014$, $I^2 = 83.4\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that higher education level is not a risk factor for PTSD in MI patients ($OR = 0.55$, $95\% CI = 0.07-4.48$, $P = 0.574$).

(2) Overall Assessment

Two studies ^[20,29] analyzed the impact of the Social Support Rating Scale (SSRS) scores on the occurrence of PTSD in MI patients, showing heterogeneity between studies ($P = 0.053$, $I^2 = 73.3\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that low SSRS scores are not a risk factor for PTSD in MI patients ($OR = 0.81$, $95\% CI = 0.52-1.26$, $P = 0.346$). Five studies ^[20,24,28,32,33] analyzed the impact of neuroticism on the occurrence of PTSD in MI patients, showing significant heterogeneity between studies ($P < 0.001$, $I^2 = 97.6\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that neuroticism is a risk factor for PTSD in MI patient ($OR=2.21$, $95\%CI=1.20\sim4.07$, $P=0.011$). Two studies ^[20,24] analyzed the impact of intrusive rumination scores on the occurrence of PTSD in MI patients, showing no heterogeneity between studies ($P = 0.980$, $I^2 = 0\%$), the fixed-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that intrusive rumination scores are a risk factor for PTSD in MI patients ($OR = 2.95$, $95\% CI = 1.50-5.83$, $P = 0.002$). Two studies ^[22,29] analyzed the impact of Killip classification on the occurrence of PTSD in MI patients, showing heterogeneity between studies ($P = 0.005$, $I^2 = 87.1\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that Killip classification is not a risk factor for PTSD in MI patients ($OR = 2.29$, $95\% CI = 0.91-5.80$, $P = 0.080$).

(3) Laboratory Indicators

Two studies ^[21,25] analyzed the impact of creatine kinase isoenzyme-MB (CK-MB) on the occurrence of PTSD in MI patients, showing heterogeneity between studies ($P = 0.006$, $I^2 = 86.9\%$), the random-effects model was used to combine effect sizes in a meta-analysis, and the results indicated that CK-MB is not a risk factor for PTSD in MI patients ($OR = 1.03$, $95\% CI = 0.99-1.05$, $P = 0.124$).

3.4.2. Sensitivity analysis

A sensitivity analysis was conducted using a modified combination model to examine the stability of results for four factors: education level, SSRS scores, Killip classification, and CK-MB. The results showed that changing the combination model for the education level factor did not lead to a directional change in the meta-analysis results, indicating stable results. For the SSRS scores, Killip classification, and CK-MB factors, when the fixed-effects model was used to combine effect sizes, the results indicated that SSRS scores ($OR = 0.96$, $95\% CI = 0.94-0.98$,

$P < 0.001$), Killip classification ($OR = 2.60$, 95% $CI = 1.89-3.57$, $P < 0.001$), and CK-MB ($OR = 1.01$, 95% $CI = 1.01-1.02$, $P < 0.001$) are risk factors for PTSD in MI patients, suggesting that these results are unstable.

Another sensitivity analysis was conducted using a leave-one-out method for the factors of age and neuroticism scores to assess result stability. The results indicated that the study by Ni^[25] was the main source of heterogeneity for the “age” factor; after removing it, heterogeneity significantly decreased ($P = 0.766$, $I^2 = 0\%$), without affecting result stability. The study by Liang et al.^[28] was identified as the main source of heterogeneity for the “neuroticism score” factor; after removing it, heterogeneity noticeably decreased ($P = 0.050$, $I^2 = 61.6\%$), again without affecting result stability.

Table 4. Results of Meta-analysis of influencing factors

Influencing factors	Number of articles	Heterogeneity			Combined effect size		<i>P</i>
		<i>I</i> ² (%)	<i>P</i>	Model selection	<i>OR</i> value	95% <i>CI</i>	
General factors							
Age	4 ^[20,24,25,28]	92.0	< 0.001	Random	1.01	(0.98,1.04)	0.440
Sex	2 ^[21,29]	0	0.842	Fix	3.12	(1.97,4.97)	< 0.001
Educational level	2 ^[16,22]	83.4	0.014	Random	0.55	(0.07,4.48)	0.574
Overall assessment							
SSRS score	2 ^[20,29]	73.3	0.053	Random	0.81	(0.52,1.26)	0.346
Neuroticism score	5 ^[20,24,28,32,33]	97.6	< 0.001	Random	2.21	(1.20,4.07)	0.011
Invasive rumination score	2 ^[20,24]	0	0.980	Fix	2.95	(1.50,5.83)	0.002
Killip grading	2 ^[22,29]	87.1	0.005	Random	2.29	(0.91,5.80)	0.080
Laboratory indicators							
CK-MB	2 ^[21,25]	86.9	0.006	Random	1.03	(0.99,1.05)	0.124

3.4.3. Publication bias

Due to the inclusion of fewer than 10 studies for each individual risk factor, the validity of the funnel plot analysis is low; therefore, a funnel plot analysis will not be conducted.

3.4.4. Descriptive analysis

A descriptive analysis was conducted on the results of the studies included in the 16-factor influence analysis for which effect sizes could not be combined. The study by Cui et al.^[12] showed that a history of diabetes ($OR = 2.292$, 95% $CI = 1.022-5.138$), insomnia scores ($OR = 2.045$, 95% $CI = 1.483-2.820$), and fear of disease progression score ($OR = 1.126$, 95% $CI = 1.076-1.179$) are risk factors for PTSD in MI patients ($P < 0.05$). The study by Feng et al.^[22] indicated that the number of interventions ($OR = 1.381$, 95% $CI = 1.034-3.027$) and economic income ($OR = 1.388$, 95% $CI = 1.067-3.271$) are risk factors for PTSD in MI patients ($P < 0.05$). The research conducted by Cao et al.^[12] found that smoking ($OR = 5.12$, 95% $CI = 1.30-20.16$) and left ventricular ejection fraction (LVEF < 50%) ($OR = 0.08$, 95% $CI = 0.02-0.28$) are risk factors for PTSD in MI patients ($P < 0.05$). The study by Ni^[25] showed that cardiac troponin I ($OR = 1.068$, 95% $CI = 1.032-1.106$) and total cholesterol ($OR = 11.393$, 95% $CI = 5.355-24.239$) are risk factors for PTSD in MI patients ($P < 0.05$). The research by Bielas et al.^[16] indicated that acute stress disorder symptoms ($OR = 1.14$, 95% $CI = 1.04-1.25$) and CRP risk categories (OR

= 4.69, 95% *CI* = 1.92–11.45) are risk factors for PTSD in MI patients ($P < 0.05$). The study by Liang et al. [28] found that levels of despair ($OR = 2.01$, 95% *CI* = 1.35–2.67) and fear of death ($OR = 2.94$, 95% *CI* = 2.35–3.26) are risk factors for PTSD in MI patients ($P < 0.05$). Dinenberg et al. [30] reported that scores on the Interpersonal Support Evaluation List (ISEL) ($OR = 0.69$, 95% *CI* = 0.49–0.99), domain scores from ISEL ($OR = 0.69$, 95% *CI* = 0.49–0.98), and tangible support domain scores from ISEL ($OR = 0.67$, 95% *CI* = 0.47–0.96) are risk factors for PTSD in MI patients ($P < 0.05$). Pedersen et al. [32] found that type D personality ($OR = 4.46$, 95% *CI* = 1.36–14.64) and myocardial infarction ($OR = 4.03$, 95% *CI* = 1.43–11.35) are risk factors for PTSD in MI patients ($P < 0.05$). Lastly, Pedersen et al. [33] indicated that anxiety ($OR = 1.75$, 95% *CI* = 1.31–2.33) and depression ($OR = 1.39$, 95% *CI* = 1.18–1.64) are risk factors for PTSD in MI patients ($P < 0.05$).

4. Discussion

4.1. Prevalence rate

The results of this study indicate that the combined prevalence of PTSD in MI patients is 20.4% (95% *CI* = 15.0–26.5%), which is similar to previously reported rates of PTSD incidence in MI patients (21.2%) [34]. There are differences in results among different studies, potentially due to confounding factors such as varying study locations, different hospitals, and different PTSD assessment tools impacting the study outcomes. The subgroup analysis of this study found:

- (1) Study Location: The prevalence of PTSD among MI patients in China (28.9%) is higher than that in other countries (10.5%). This may be related to differences in socioeconomic development levels, lifestyle habits, and the population's access to health information among different countries.
- (2) Assessment Tools: The prevalence of PTSD in MI patients using the PCL-C scale (26.5%) is higher than that using the PDS scale (11.6%) and the CDIS scale (6.4%), with significant differences among the three. The reason for this discrepancy may be due to the lack of a unified standard for the diagnostic threshold for PTSD in MI patients, both domestically and internationally. Although some studies originated from the same research area and used the same assessment tool, they employed different diagnostic criteria. For example, the study by Cao et al. [12] defined a positive PTSD symptom as a PCL-L score ≥ 44 , while the study by Cui et al. [21] defined a positive PTSD symptom as a PCL-L score ≥ 38 .

4.2. Influencing factors

This study found that femininity, neuroticism, and invasive rumination scores were risk factors for PTSD in MI patients.

- (1) There are gender-based differences in PTSD and cardiovascular diseases. Studies have shown that the lifetime prevalence of PTSD in women is twice that of men [35,36]. Female patients are more likely than male patients to exhibit PTSD symptoms in the face of disease stress, which is consistent with the findings of scholars such as Fonkoue and Kobayashi et al. [37,38]. This may be because there is a significant correlation between the size of the amygdala and PTSD symptoms when individuals are under stress [39]. The amygdala in women tends to respond more persistently and sensitively to ongoing negative stimuli, leading to the emergence of intense emotions such as fear [40]. Additionally, due to the interaction between sex hormones and stress peptides [41], women are more sensitive to painful stimuli and more readily perceive the physical and psychological harm caused by illness. Therefore, it is recommended that clinical

healthcare providers pay special attention to the psychological issues of female MI patients, actively communicate with them to reduce negative emotions, and thus lower the risk of PTSD symptoms.

- (2) Neuroticism is positively correlated with PTSD symptoms, indicating that individuals with neurotic personality traits are more likely to develop stress disorders, which is similar to findings from domestic and international studies ^[28,42,43]. Anxiety and tension are significant manifestations of neurotic personality traits ^[44]. When faced with severe physical illnesses, these individuals often experience intense unease and anxiety and may misinterpret their condition as a “terminal illness” or something difficult to cure. They often misconstrue common post-treatment discomforts and physical changes as pathological or abnormal and attempt to eliminate them. However, the more they focus on these physical and psychological changes and strive to get rid of them, the worse their symptoms may become, creating a vicious cycle that could ultimately lead to PTSD. Thus, it is recommended that clinical medical staff screen the personality traits of patients exhibiting significant anxiety and tension, if conditions allow, and provide timely targeted psychological counseling and humanistic care to reduce the risk of PTSD.
- (3) Intrusive rumination refers to negative and passive thinking following traumatic events ^[45], and is associated with the occurrence of PTSD. In this study, the scores for intrusive rumination were positively correlated with PTSD symptoms, with higher scores indicating an increased risk of PTSD. This may be because patients with predominant intrusive thoughts tend to focus on the negative aspects of the acute myocardial infarction stress event, making it difficult for them to shift their focus to positive aspects, which can easily trigger depressive emotions. Therefore, it is recommended that clinical healthcare providers pay attention to patients’ attitudes towards recovery from illness, guiding them to view their illness and treatment process correctly. By re-evaluating and contemplating the occurrence of their illness, patients can be encouraged to actively face future challenges.

4.3. Limitations

This study has certain limitations: (1) The included literature primarily focuses on populations in China, which may introduce selection bias; (2) The insufficient number of included studies prevents bias assessment, and there may be publication bias; (3) For certain influencing factors, such as a history of diabetes, smoking, and type D personality, fewer than two studies were included, making it impossible to conduct a meta-analysis; (4) Most of the included studies are cross-sectional, lacking prospective research. Therefore, future efforts should involve large sample sizes, multi-center, high-quality prospective studies to discuss and validate the prevalence and influencing factors of PTSD in MI patients.

5. Conclusion

In summary, this study reveals that the prevalence of PTSD among MI patients is 20.4%. Gender, neuroticism, and intrusive rumination scores are identified as risk factors for the occurrence of PTSD in MI patients. Healthcare professionals should pay attention to humanistic care in clinical practice, provide appropriate guidance to alleviate patients’ negative emotions, and enhance communication with patients. This is of great significance for reducing and improving the occurrence of PTSD symptoms in MI patients.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Roth G, Mensah G, Johnson C, et al., 2020, Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. *J Am Coll Cardiol*, 76(25): 2982–3021.
- [2] Xu X, Jiang H, et al. 2024, Development of Pathogenesis and Intervention Strategies of Post-Myocardial Infarction Depression. *Chinese Journal of Senile Cardio Cerebrovascular Diseases*, 26(8): 968–970.
- [3] Krantz D, Shank L, Goodie J, 2022, Post-Traumatic Stress Disorder (PTSD) as a Systemic Disorder: Pathways to Cardiovascular Disease. *Health Psychol*, 41(10): 651–662.
- [4] Hao X, Song Q, Chen C, et al., 2016, Current Status and Influencing Factors of Acute Stress Disorder in Patients With Acute Myocardial Infarction. *Modern Preventive Medicine*, 43(11): 2093–2097.
- [5] Ressler K, Berretta S, Bolshakov V, et al., 2022, Post-Traumatic Stress Disorder: Clinical and Translational Neuroscience From Cells to Circuits. *Nat Rev Neurol*, 18(5): 273–288.
- [6] Nachshol M, Lurie I, Benyamini Y, et al., 2020, Role of Psychosocial Factors in Long-Term Adherence to Secondary Prevention Measures After Myocardial Infarction: A Longitudinal Analysis. *Ann Epidemiol*, 52: 35–41.
- [7] Khan N, Iqra T, Joti S, et al., 2023, Association of Cardiovascular Diseases With Post-Traumatic Stress Disorder: An Updated Review. *Cardiol Rev*, November 15, 2023.
- [8] Princip M, Ledermann K, Altwegg R, et al., 2024, Cardiac Disease-Induced Trauma and Stress-Related Disorders. *Herz*, 49(4): 254–260.
- [9] Sumner J, Kubzansky L, Elkind M, et al., 2015, Trauma Exposure and Posttraumatic Stress Disorder Symptoms Predict Onset of Cardiovascular Events in Women. *Circulation*, 132(4): 251–259.
- [10] Lima B, Hammadah M, Pearce B, et al., 2020, Association of Posttraumatic Stress Disorder With Mental Stress-Induced Myocardial Ischemia in Adults After Myocardial Infarction. *JAMA Netw Open*, 3(4): e202734.
- [11] Jacquet-Smailovic M, Tarquinio C, Alla F, et al., 2021, Posttraumatic Stress Disorder Following Myocardial Infarction: A Systematic Review. *J Trauma Stress*, 34(1): 190–199.
- [12] Cao X, Wu J, Gu Y, et al., 2021, Post-Traumatic Stress Disorder and Risk Factors in Patients With Acute Myocardial Infarction After Emergency Percutaneous Coronary Intervention: A Longitudinal Study. *Frontiers in Psychology*, 12: 694974.
- [13] Vilchinsky N, Ginzburg K, Fait K, et al., 2017, Cardiac-Disease-Induced PTSD (CDI-PTSD): A Systematic Review. *Clin Psychol Rev*, 55: 92–106.
- [14] Jiang S, Wang R, et al. 2021, Characteristic Analysis of Symptoms of Post-Traumatic Stress Disorder and Fear of Disease Progression in 126 Patients With Acute Myocardial Infarction. *Integrated Nursing (Chinese and Western Medicine)*, 7(3): 13–17.
- [15] Tanriverdi B, Gregory D, Olino T, et al., 2022, Hippocampal Threat Reactivity Interacts With Physiological Arousal to Predict PTSD Symptoms. *J Neurosci*, 42(34): 6593–6604.
- [16] Bielas H, Meister-Langraf R, Schmid J, et al., 2018, C-Reactive Protein as a Predictor of Posttraumatic Stress Induced by Acute Myocardial Infarction. *Gen Hosp Psychiatry*, 53: 125–130.
- [17] Schaffter N, Ledermann K, Pazhenkottil A, et al., 2021, Serum Cortisol as a Predictor for Posttraumatic Stress Disorder Symptoms in Post-Myocardial Infarction Patients. *J Affect Disord*, 292: 687–694.

- [18] Stang A, 2010, Critical Evaluation of the Newcastle-Ottawa Scale for the Assessment of the Quality of Nonrandomized Studies in Meta-Analyses. *Eur J Epidemiol*, 25(9): 603–605.
- [19] Chou R, Baker W, Banez L, et al., 2018, Agency for Healthcare Research and Quality Evidence-Based Practice Center Methods Provide Guidance on Prioritization and Selection of Harms in Systematic Reviews. *J Clin Epidemiol*, 98: 98–104.
- [20] Wang H, Geng M, Zhang Q, et al., 2024, Influence Factors of Post-Traumatic Stress Disorder in Patients With Acute Myocardial Infarction After Percutaneous Coronary Intervention. *Journal of Cardiovascular Rehabilitation Medicine*, 33(1): 25–30.
- [21] Cui K, Sui P, Zang X, et al., 2022, Development and Validation of a Risk Prediction Model for Post-Traumatic Stress Disorder Symptoms in Patients With Acute Myocardial Infarction in China. *Ann Palliat Med*, 11(9): 2897–2905.
- [22] Feng Q, Xu L, Zheng G, et al., 2022, Study on Symptom Groups of Stress Disorder in Young and Middle-Aged Patients With Acute Myocardial Infarction After Coronary Intervention and Intervention Strategies. *Journal of Bengbu Medical College*, 47(5): 672–674 + 679.
- [23] Peng Q, Yanf Z, Shen Y, et al., 2021, Correlation Between Self-Compassion and Post-Traumatic Stress Disorder in Young and Middle-Aged Patients With Acute Myocardial Infarction. *Henan Medical Research*, 30(8): 1356–1360.
- [24] Gao J, Li J, Xia C, et al., 2019, Status and Risk Factors of Post-Traumatic Stress Disorder in Patients With Primary Acute Myocardial Infarction. *Chinese Medical Frontiers Journal (Electronic Edition)*, 11(6): 52–56.
- [25] Ni F, 2019, Study on Post-Traumatic Stress Disorder and Its Related Factors in Patients With Acute Myocardial Infarction, thesis, Xi'an Medical College.
- [26] Li J, Liu P, Lu Q, et al., 2018, Effects of Attachment and Rumination on Post-Traumatic Stress Disorder in Female Patients With Myocardial Infarction. *Journal of Rehabilitation*, 28(1): 49–54.
- [27] Lima B, Hammadah M, Sullivan S, et al., 2018, Posttraumatic Stress Disorder Is Associated With Enhanced Interleukin-6 Response to Mental Stress in Subjects With a Recent Myocardial Infarction. *Psychosomatic Medicine*, 80(3): A126–A127.
- [28] Liang B, Liang J, Xing Z, et al., 2016, The Influence of Personality Characteristics on Post-Traumatic Stress Disorder Caused by Acute Myocardial Infarction. *Hainan Medicine*, 27(19): 3146–3149.
- [29] Xiong D, Chen L, Deng G, et al., 2014, Incidence of Post-Traumatic Stress Disorder and Its Influencing Factors in Patients With Acute Myocardial Infarction. *Medical Clinical Research*, 31(9): 1805–1807.
- [30] Dinenberg R, McCaslin S, Bates M, et al., 2014, Social Support May Protect Against Development of Posttraumatic Stress Disorder: Findings From the Heart and Soul Study. *Am J Health Promot*, 28(5): 294–297.
- [31] Wiedemar L, Schmid J, Muller J, et al., 2008, Prevalence and Predictors of Posttraumatic Stress Disorder in Patients With Acute Myocardial Infarction. *Heart Lung*, 37(2): 113–121.
- [32] Pedersen S, Denollet J, 2004, Validity of the Type D Personality Construct in Danish Post-MI Patients and Healthy Controls. *J Psychosom Res*, 57(3): 265–272.
- [33] Pedersen S, Middel B, Larsen M, 2003, Posttraumatic Stress Disorder in First-Time Myocardial Infarction Patients. *Heart Lung*, 32(5): 300–307.
- [34] Liu J, Wang L, Wang Y, et al., 2024, Meta-Analysis of Risk Factors for Posttraumatic Stress Disorder in Myocardial Infarction. *Medicine (Baltimore)*, 103(3): e36601.
- [35] Kessler R, Sonnega A, Bromet E, et al., 1995, Posttraumatic Stress Disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*, 52(12): 1048–1060.
- [36] Tolin D, Foa E, 2006, Sex Differences in Trauma and Posttraumatic Stress Disorder: A Quantitative Review of 25 Years

of Research. *Psychol Bull*, 132(6): 959–992.

- [37] Fonkoue I, Michopoulos V, Park J, 2020, Sex Differences in Post-Traumatic Stress Disorder Risk: Autonomic Control and Inflammation. *Clin Auton Res*, 30(5): 409–421.
- [38] Kobayashi I, Sledjeski E, Delahanty D, 2019, Gender and Age Interact to Predict the Development of Posttraumatic Stress Disorder Symptoms Following a Motor Vehicle Accident. *Psychol Trauma*, 11(3): 328–336.
- [39] Morey R, Gold A, LaBar K, et al., 2012, Amygdala Volume Changes in Posttraumatic Stress Disorder in a Large Case-Controlled Veterans Group. *Arch Gen Psychiatry*, 69(11): 1169–1178.
- [40] Andreano J, Dickerson B, Barrett L, 2014, Sex Differences in the Persistence of the Amygdala Response to Negative Material. *Soc Cogn Affect Neurosci*, 9(9): 1388–1394.
- [41] Lehner M, Skorzevska A, Wislowska-Stanek A, 2021, Sex-Related Predisposition to Post-Traumatic Stress Disorder Development – The Role of Neuropeptides. *Int J Environ Res Public Health*, 19(1): 314.
- [42] Chung M, Berger Z, Rudd H, 2007, Comorbidity and Personality Traits in Patients With Different Levels of Posttraumatic Stress Disorder Following Myocardial Infarction. *Psychiatry Res*, 152(2–3): 243–252.
- [43] Stevanovic A, Franciskovic T, Vermetten E, 2016, Relationship of Early-Life Trauma, War-Related Trauma, Personality Traits, and PTSD Symptom Severity: A Retrospective Study on Female Civilian Victims of War. *Eur J Psychotraumatol*, 7: 30964.
- [44] Aidman E, Kollaras-Mitsinikos L, 2006, Personality Dispositions in the Prediction of Posttraumatic Stress Reactions. *Psychol Rep*, 99(2): 569–580.
- [45] Zhang Y, Fu G, Jiang H, et al., 2019, The Impact of Mindfulness in Professional Rescue Workers on Post-Traumatic Stress Disorder: The Role of Intrusive Rumination and Social Support. *Chinese Journal of Clinical Psychology*, 27(2): 311–315.

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Scope of Nursing Practice as Perceived by Nurses Working in China: A Multicenter Cross-Sectional Survey

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Abstract: *Purpose:* To examine variations in Chinese nurses' Actual Scope of Practice (ASCOP) by educational qualifications and professional titles, and to identify regulatory gaps in competency-based role assignments within China's evolving healthcare system. *Method:* A nationwide cross-sectional study using the validated Chinese Nurses' ASCOP Questionnaire is used. Data from 1,540 nurses were analyzed through descriptive statistics, independent t-tests, one-way ANOVA, and Bonferroni correction. ASCOP scores (1–5 scale) were compared across education levels (diploma, bachelor's, postgraduate) and titles (junior/senior). *Results:* The overall ASCOP score was 3.95, with significant disparities in high-complexity tasks: postgraduate nurses (4.25) and senior nurses outperformed diploma holders (3.71) and juniors ($p < 0.01$). Low-complexity tasks showed no educational differences ($p > 0.05$), though bachelor's or postgraduate nurses reported higher frequencies (4.12 vs. 3.89). Alarming, 37.6% of junior nurses routinely performed high-risk procedures beyond their competency. *Conclusion:* A systemic mismatch exists between nurses' qualifications and assigned responsibilities, reflecting inadequate regulatory oversight. To address this, this study recommends: (1) competency-based tiered authorization systems, (2) legal framework updates aligning with China's healthcare reforms, and (3) dynamic monitoring mechanisms. These measures could standardize practice boundaries, mitigate occupational risks, and optimize nursing workforce utilization, particularly in resource-constrained settings.

Keywords: Education; Nursing; Health Workforce; Scope of practice

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1. Background

The shortage of nurses has become a prominent problem globally; specifically, the World Health Organization expects the global shortage of nurses to reach 9 million by 2030 ^[1, 2]. By the end of 2020, the number of nurses per 1000 population in China was 2.97, which is still a large gap compared with that in developed countries ^[3].

The shortage of nurses directly affects the quality of nursing services and patient safety. Whether the allocation of human resources is reasonable and the ratio is appropriate directly affects nursing efficiency, service level, and cost consumption, thereby affecting nursing quality and patient safety ^[4, 5].

Amid an existing shortage of nursing personnel, it is essential to optimize the utilization of available nursing manpower to improve overall efficiency. In numerous clinical settings, nurses are often unable to fully apply the breadth of competencies gained through their education and training ^[6, 7]. A survey conducted in Italy in 2017 showed that almost all nurses performed some non-nursing tasks during the workday ^[8]. A survey conducted between 2014 and 2018 among 1,530 nurses in Guangdong Province, China, revealed that one-third of respondents reported spending a substantial portion of their working hours on non-nursing tasks. This finding underscores the necessity of examining the actual scope of nursing practice to ensure that nursing competencies are effectively utilized ^[9].

The scope of nursing practice is determined by the professional education attained by nurses, relevant legal frameworks, and standards established by the nursing profession. It serves as a comprehensive description of the roles, functions, and activities that nurses are authorized and expected to perform within their professional capacity ^[10]. When nurses operate beyond their defined scope of practice, patient safety may be compromised ^[11]. Moreover, engaging in tasks outside their professional boundaries can lead to heightened feelings of challenge, decreased motivation, or a sense of exploitation in the workplace ^[12]. Ideally, nurses should practice within their optimal scope, leveraging their full educational background and competencies, to deliver high-quality, safe patient care while also enhancing their own job satisfaction ^[13, 14].

Nurses demonstrate an optimal ASCOP when effectively executing the essential duties of their profession, which serves as a hallmark of delivering superior care quality ^[5, 15, 16]. Given the critical role of nursing in ensuring patient safety and enhancing nurse productivity, additional investigation is warranted to examine nurses' scope of practice across various clinical levels. This study pursues a dual *objective*: first, to address the critical need for defining the scope of nursing practice within the Chinese public healthcare system by evaluating the actual scope of practice among nurses in China; and second, to identify the specific tasks undertaken by nurses across varying educational backgrounds and clinical roles.

2. Methods

2.1. Design

This study is a descriptive cross-sectional study designed to measure the actual scope of practice of nurses working in China.

2.2. Setting and participants

The research encompassed 30 medical facilities in China, comprising general, specialty, and community hospitals, while excluding private hospitals. Frontline nurses are selected using a non-random purposive sampling technique. Data collection took place from May 11 to June 15, 2022.

2.3. Instrument

The research utilized the ASCOP questionnaire in China, which was electronically administered. The questionnaire underwent translation into Chinese with approval from the original authors and demonstrated robust reliability

and validity. Comprising two parts, the instrument includes a self-constructed sociodemographic profile in the first part and 26 items in the second part, evaluating nursing activities across six dimensions. These dimensions are as follows: “Assessment and care planning” (5 items), “Teaching of patients and families” (4 items), “Communication and care coordination” (5 items), “Integration and supervision” (4 items), “Quality of care and patient safety” (5 items), and “Knowledge updating and utilization” (3 items). Responses are rated on a 6-point Likert scale ranging from never (1 point) to always (6 points), with higher scores indicating greater clinical practice proficiency among nurses. The questionnaire is structured to align with varying levels of complexity in practice activities, categorized as low (level 1), moderate (level 2), and high (level 3) complexity. Specifically, items 4, 7, 10, 16, 17, 21, and 25 were classified as level 1 activities; items 1, 2, 5, 9, 12, 18, 19, 20, 24, and 26 as level 2 activities; and items 3, 6, 8, 11, 13, 14, 15, 22, and 23 as level 3 activities ^[15].

2.4. Data collection

Upon consultation with the nursing department personnel and upon obtaining consent, either the nursing department director or the head nurse disseminated the Chinese version of the ASCOP QR code using the “Questionnaire Star” platform, facilitated through the WeChat group dedicated to hospital or department nurses. Nurses are instructed to scan the QR code to access the questionnaire and complete the introductory section, which was highlighted in bold black font for emphasis. The questionnaire is completed via WeChat, with each user permitted to respond only once. Furthermore, all questions had to be answered for successful submission, and there was no time limit for responses.

2.5. Data analysis

Data analysis is performed using SPSS 27.0. Participant general information was analyzed descriptively using means (M), counts (n), percentages, and standard deviations (SDs). The independent samples t-test and one-way ANOVA are used to test the ability of ASCOP scores to distinguish the actual scope of practice dimensions and the level of complexity among participants. The multiple comparison “post hoc test” is performed using the Bonferroni method. All tests are two-tailed, and a *p*-value less than 0.05 was considered significant.

The data are presented in two stages. First, the characteristics of participants in each group and the corresponding mean ASCOP scores are determined. Second, the means and standard deviations of the ASCOP scale dimensions are explored, as well as their correlation with participant education levels and current nursing titles.

2.6. Ethical considerations

On the page containing the questionnaire, the background, purpose, and significance of the study are explained to the participants in black boldface font, and any personal information about the person completing the questionnaire is guaranteed to be kept strictly confidential; the contents are used for research purposes only. Answering the questionnaire is considered consent and acceptance to participate in the study.

3. Results

A total of 1695 questionnaires were collected, of which 10 were excluded due to response times less than 60 seconds, and 145 were deemed illogical. The final analysis included 1540 valid questionnaires, resulting in a valid

return rate of 90.86%. Participant characteristics are detailed in the table, revealing a predominantly female (97%), married (66%) cohort, primarily consisting of general hospital staff (92%). Bachelor's degree nurses comprised 52% of the sample, with junior nurses accounting for 68%. The majority of participants were front-line clinical nurses (88%) aged between 25–44 years (73%).

Table 1. Participant characteristics and corresponding overall ASCOP scores ($n=1540$)

Characteristics		n	Percentage	Overall mean M (SD)	Statistical test; <i>P</i> -value
Gender	Male	49	3.20%	3.89 (1.25)	$t=-0.357$; $P=0.723$
	Female	1491	96.80%	3.95 (0.99)	
Age (years)	18–24*	230	14.90%	3.90 (1.03)	$F=7.530$; $P=0.001$
	25–44*	1126	73.10%	3.91 (0.98)	
	$\geq 45^{**}$	184	11.90%	4.21 (1.01)	
Marital status	Married*	1018	66.10%	4.02 (0.99)	$F=9.305$; $P < 0.001$
	Unmarried *	501	32.50%	3.81 (1.00)	
	Other	21	1.40%	3.55 (0.68)	
Working experience (years)	0–3 *	303	19.70%	3.77 (1.02)	$F=13.018$; $P < 0.001$
	4–20 *	581	37.70%	3.88 (0.97)	
	$\geq 21^{**}$	656	42.60%	4.09 (0.98)	
Current nursing position	Junior**	1044	67.80%	3.81 (0.98)	$F=38.920$; $P < 0.001$
	Intermediate**	388	25.20%	4.12 (0.95)	
	Senior **	108	7.01%	4.51 (0.90)	
Current nursing function	Staff	1361	88.38%	3.87 (0.98)	$t=-9.041$; $P < 0.001$
	Admin	179	11.62%	4.56 (0.87)	
Education level	Diploma**	709	46.00%	3.85 (1.01)	$F=7.998$; $P < 0.001$
	BSN*	801	52.00%	4.02 (0.97)	
	Postgraduate*	30	1.90%	4.30 (1.07)	
Hospital class	Tertiary*	752	48.80%	4.01 (0.97)	$F=5.294$; $P=0.005$
	Grade II	695	45.10%	3.91 (1.01)	
	Grade I *	93	6.00%	3.69 (0.98)	
Type of hospital	General *	1414	91.80%	3.96 (1.00)	$F=3.127$; $P=0.044$
	Specialty*	109	7.10%	3.72 (0.92)	
	Community	17	1.10%	(1.20)	

(1)SD=standard deviation.

(2) *represents a statistical difference from one group of data, **represents a statistically significant difference from two groups of data.

(3) BSN represents Bachelor of Science in Nursing.

Table 1 reveals substantial variations in mean ASCOP scores across sociodemographic characteristics. Nurse leaders exhibited the highest ASCOP scores ($M=4.56$, $SD=0.87$), significantly exceeding those of staff members

($M=3.87$, $SD=0.98$; $t=-9.041$, $p < 0.001$). Divorced nurses or those with “other” marital status had the lowest scores ($M=3.55$, $SD=0.68$), and a statistically significant difference was observed between the scores of married and unmarried nurses ($F=9.305$, $p < 0.001$). Gender did not significantly influence the total ASCOP scores of male and female nurses ($t=-0.357$, $p=0.49992$). Interestingly, nurses working in community hospitals reported higher scores ($M=4.02$, $SD=1.20$) than those in general ($M=3.96$, $SD=1.00$) and specialized ($M=3.72$, $SD=0.92$) hospital settings.

Table 2 displays the mean scores for the analysis of study dimensions, ranging from 3.39 to 4.25 ($M=3.95$; $SD=0.99$). The predominant activities conducted by nurses included “Quality of care and patient safety” ($M=4.25$), “Teaching of patients and families” ($M=4.20$), “Assessment and care planning” ($M=4.14$), and “Knowledge updating and utilization” ($M=3.94$). Conversely, activities associated with “Communication and care coordination” ($M=3.70$) and “Integration and supervision of staff” ($M=3.39$) were less frequently performed.

An investigation into the influence of educational attainment and professional titles among nurses indicated that senior nurses ($M=4.91$; $SD=0.94$) were more engaged in activities related to quality of care and patient safety compared to intermediate ($M=4.48$; $SD=1.02$) and junior ($M=4.09$; $SD=1.08$) nurses. Statistical analysis revealed significant differences among senior, intermediate, and junior nurses ($F=42.925$; $P < 0.001$). Furthermore, nurses holding a Bachelor’s degree in nursing demonstrated a higher level of engagement in quality of care and patient safety practices ($M=4.32$; $SD=1.05$) in comparison to their counterparts with a diploma education ($M=4.15$; $SD=1.10$; $F=5.639$; $P=0.004$).

Table 2. Mean (SD) scores on ASCOP scale dimensions by nurse education level and position type ($n=1540$)

Dimension	Overall M (SD)	Education level			Title		
		Diploma M (SD)	BSN M (SD)	Postgraduate M (SD)	Junior M (SD)	Intermediate M (SD)	Senior M (SD)
Assessment and care planning	4.14 (1.04)	4.05* (1.08)	4.21* (0.99)	4.23 (1.09)	4.05** (1.04)	4.32* (1.02)	4.44* (0.93)
		$F=4.504$; $P = 0.011$				$F=14.496$; $P < 0.001$	
Teaching of patients and families	4.20 (1.04)	4.16 (1.07)	4.24 (1.01)	4.28 (1.24)	4.12** (1.07)	4.22* (0.96)	4.55* (0.99)
		$F=1.119$; $P = 0.327$				$F=12.029$; $p < 0.001$	
Communication and care coordination	3.70 (1.11)	3.59** (1.11)	3.77** (1.10)	4.33** (1.22)	3.56** (1.10)	3.87** (1.07)	4.32** (1.06)
		$F=10.086$; $P < 0.001$				$F=30.131$; $P < 0.001$	
Integration and supervision of staff	3.39 (1.17)	3.19** (1.13)	3.55* (1.17)	4.00* (1.26)	3.12** (1.08)	3.86** (1.12)	4.33** (1.17)
		$F=22.946$; $P < 0.001$				$F=106.772$; $P < 0.001$	
Quality of care and patient safety	4.25 (1.08)	4.15* (1.10)	4.32* (1.05)	4.54 (1.19)	4.09** (1.08)	4.48** (1.02)	4.91** (0.94)
		$F=5.639$; $P=0.004$				$F=42.925$; $P < 0.001$	
Knowledge updating and utilization	3.94 (1.11)	3.87* (1.13)	3.98 (1.09)	4.38* (1.13)	3.83** (1.12)	4.07** (1.05)	4.48** (1.05)
		$F=4.291$; $P = 0.014$				$F=20.361$; $P < 0.001$	

The ASCOP complexity levels of the participants' practices (**Table 3**) yielded notable findings. Nurse education did not significantly impact the performance of low-complexity tasks ($F=1.820$; $P=0.162$). However, advanced and mid-level nurses engaged in low-complexity tasks more frequently than junior nurses ($F=18.481$; $P < 0.001$). In contrast, high-complexity ASCOP tasks were significantly more common among graduate and undergraduate nurses compared to diploma-educated nurses ($F=17.749$; $P < 0.001$). Senior nurses predominantly carried out high-complexity ASCOP tasks ($M=4.43$; $SD=0.99$) ($F=72.760$; $P < 0.001$).

Table 3. Mean (SD) scores on ASCOP complexity subscale dimensions by nurse education level and position type ($n=1540$)

Dimension	Overall M(SD)	Education level			Title		
		Diploma M (SD)	BSN M (SD)	Postgraduate M (SD)	Junior M (SD)	Intermediate M (SD)	Senior M (SD)
Low complexity	4.26 (1.01)	4.21 (1.03)	4.30 (0.97)	4.40 (1.12)	4.16** (1.02)	4.42* (0.95)	4.65* (0.91)
		$F=1.820$; $P=0.162$			$F=18.481$; $P < 0.001$		
Moderate complexity	3.99 (1.02)	3.91* (1.05)	4.05* (0.98)	4.30 (1.08)	3.88** (1.03)	4.15** (0.97)	4.48** (0.89)
		$F=5.149$; $P=0.006$			$F=23.679$; $P < 0.001$		
High complexity	3.65 (1.08)	3.49** (1.07)	3.77* (1.06)	4.23* (1.12)	3.45** (1.03)	3.99** (1.02)	4.43** (0.99)
		$F=17.749$; $P < 0.001$			$F=72.760$; $P < 0.001$		

4. Discussion

This study offers a preliminary assessment of the scope of nursing practice within Chinese hospitals. The results indicate that the level of nursing practice was moderate ($M=3.95$; $SD=0.99$), higher than that reported in a previous international study in Canada ($M=3.21$), but lower than those reported in studies from Lebanon ($M=4.42$) and Saudi Arabia ($M=4.59$)^[17–19]. These findings suggest a lack of clearly defined role boundaries for nurses, regardless of their educational background or certification^[20]. Specifically, the data imply that diploma-qualified nurses, who may be inadequately prepared for advanced nursing practice, could potentially compromise patient safety^[21, 22].

Nurses' educational attainment is positively associated with their nursing practice competencies, as evidenced by their ASCOP scores. Across all dimensions, nurses with postgraduate degrees exhibited the highest ASCOP scores, followed by those with bachelor's degrees, and those with diplomas had the lowest scores^[17]. This finding aligns with the results of previous national and international studies, which have consistently demonstrated a positive correlation between higher nursing education and enhanced nursing practice competencies^[18,23]. These results underscore the importance of leveraging the nursing workforce's diverse educational backgrounds to deliver the highest quality of patient care.

The findings of this study corroborate previous international research, which has consistently demonstrated that nurses' status and role within the healthcare team significantly influence the expansion of their scope of practice^[17–19, 22–24]. Furthermore, the demographic characteristics of the participants in the current study also had a broad effect on their scope of practice ($p < 0.05$). However, there was no strong evidence of widespread differences in the participants' daily scope of practice.

The observed variations in ASCOP scores among nurses employed in different hospital settings can be

attributed to a range of organizational factors, including institutional policies, accreditation status, and level of care provided ^[25–27]. For instance, nurses working in tertiary hospitals exhibited higher ASCOP scores compared to those in secondary or primary care facilities, while community hospital nurses scored higher than their counterparts in general or specialty hospitals. However, these differences had a limited impact on nurses' day-to-day work practices.

The study also aimed to discern the activities in which nurses with varying educational credentials and positions predominantly engaged. The findings revealed that nurses holding graduate degrees exhibited higher proficiency across all dimensions of the ASCOP questionnaire compared to their counterparts. This was followed by nurses with bachelor's degrees and diploma qualifications, respectively. Likewise, nurses in charge-level positions and above demonstrated a broader scope of ASCOP activities. These results can be attributed to the tendency for nurses with graduate and undergraduate qualifications to occupy leadership roles.

This study found that "Quality of care and patient safety" was the most frequently performed ASCOP (Acute Situation Care of Patients) dimension. This contrasts with previous international studies, which identified different predominant dimensions: "Assessment and care planning" in the USA, "Communication and care coordination" in Saudi Arabia, and "Teaching of patients and families" in Lebanon ^[17–19]. Assessing patients is a crucial step in recognizing and responding to patient deterioration, and advanced physical assessment is key to diagnosing and managing complex patient conditions ^[28, 29]. However, the least reported ASCOP dimension in this study and previous international studies was "Integration and supervision of staff," which may be attributed to the fact that the majority of study participants were staff nurses (88.4%), who were rarely involved in the integration and supervision of staff in their daily work ^[24]. Consistent with earlier international studies, the present study found that high-complexity ASCOP activities were frequently performed by graduate and charge nurses ^[30]. Interestingly, at lower levels of complexity, the mean ASCOP score also increased with higher nurse education level and title, suggesting that nurses with higher education and positions perform a broader range of nursing practices.

5. Study limitations

This study employed a cross-sectional design, which inherently limits the ability to establish causality or track changes in ASCOP over time. Additionally, the study did not encompass all regions of China, potentially compromising the generalizability of the findings. Subsequent research is warranted to elucidate the present state of ASCOP.

6. Implications for Nursing Practice

The study's results should prompt nursing directors in China to reassess job descriptions and specify the nursing tasks suitable for each educational level or job position. This measure is crucial to prevent nurses from exceeding their skill levels. Tasks involving quality of care, patient safety, and complex nursing care should be assigned to nurses with advanced education or higher job titles. Additionally, the significance of accurate care assessment and planning in ensuring patient safety and quality of care cannot be overstated.

7. Conclusions

Evaluating nurses' scope of practice is crucial for optimizing nursing workforce utilization, enhancing nursing care

quality, and ensuring patient safety. Deviations from nurses' educational boundaries or underutilization of their skills can significantly impact patient safety, care quality, and staff motivation. Amid healthcare system reforms in China, nursing managers face the critical task of efficiently allocating nurses and maximizing the expertise of frontline clinical staff. The Nursing ASCOP guidelines offer a valuable framework for Chinese nursing managers to govern and safeguard nursing practice within legal parameters.

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References

- [1] Aiken LH, Sloane D, Griffiths P, et al., 2017, Nursing Skill Mix in European Hospitals: Cross-Sectional Study of the Association With Mortality, Patient Ratings, and Quality of Care. *BMJ Qual Saf*, 26(7): 559–568. <https://doi.org/10.1136/bmjqs-2016-005567>
- [2] Aldossary A, 2013, The Role Legitimacy of Nurses in Saudi Arabia. *Journal of Health Specialties*, 1(1): 28–28.
- [3] Aljohani KA, Alamri MS, Al-Dossary R, et al., 2022, Scope of Nursing Practice as Perceived by Nurses Working in Saudi Arabia. *Int J Environ Res Public Health*, 19(7): 4220. <https://doi.org/10.3390/ijerph19074220>
- [4] Bettencourt AP, McHugh MD, Sloane DM, et al., 2020, Nurse Staffing, the Clinical Work Environment, and Burn Patient Mortality. *J Burn Care Res*, 41(4): 796–802. <https://doi.org/10.1093/jbcr/iraa061>
- [5] Cho E, Sloane DM, Kim EY, et al., 2015, Effects of Nurse Staffing, Work Environments, and Education on Patient Mortality: An Observational Study. *Int J Nurs Stud*, 52(2): 535–542. <https://doi.org/10.1016/j.ijnurstu.2014.08.006>
- [6] Copanitsanou P, Fotos N, Brokalaki H, 2017, Effects of Work Environment on Patient and Nurse Outcomes. *Br J Nurs*, 26(3): 172–176. <https://doi.org/10.12968/bjon.2017.26.3.172>
- [7] D'Amour D, Dubois CA, Dery J, et al., 2012, Measuring Actual Scope of Nursing Practice: A New Tool for Nurse Leaders. *J Nurs Adm*, 42(5): 248–255. <https://doi.org/10.1097/NNA.0b013e31824337f4>
- [8] Dehghani K, Nasiriani K, Salimi T, 2016, Requirements for Nurse Supervisor Training: A Qualitative Content Analysis. *Iran J Nurs Midwifery Res*, 21(1): 63–70. <https://doi.org/10.4103/1735-9066.174760>
- [9] Dery J, 2014, L'Etendue Effective de la Pratique d'Infirmieres en Pediatrie: Ses Determinants et Son Influence sur la Satisfaction Professionnelle, thesis, Universite de Montreal.
- [10] Dery J, Clarke SP, D'Amour D, et al., 2016, Education and Role Title as Predictors of Enacted Scope of Practice in Generalist Nurses in a Pediatric Academic Health Sciences Center. *Journal of Nursing Administration*, 46(5): 265–270. <https://doi.org/10.1097/nna.0000000000000341>
- [11] Dubois CA, D'Amour D, Pomey MP, et al., 2013, Conceptualizing Performance of Nursing Care as a Prerequisite for Better Measurement: A Systematic and Interpretive Review. *BMC Nurs*, 12: 7. <https://doi.org/10.1186/1472-6955-12-7>
- [12] Fares S, Clinton M, Younan L, 2018, The First Arabic Version of the Actual Scope of Nursing Practice Scale: Psychometric

- Evaluation. *J Nurs Manag*, 26(8): 1059–1065. <https://doi.org/10.1111/jonm.12635>
- [13] Grosso S, Longhini J, Tonet S, et al., 2021, Prevalence and Reasons for Non-Nursing Tasks as Perceived by Nurses: Findings From a Large Cross-Sectional Study. *J Nurs Manag*, 29(8): 2658–2673. <https://doi.org/10.1111/jonm.13451>
- [14] Hickey PA, Pasquali SK, Gaynor JW, et al., 2016, Critical Care Nursing's Impact on Pediatric Patient Outcomes. *Ann Thorac Surg*, 102(4): 1375–1380. <https://doi.org/10.1016/j.athoracsur.2016.03.019>
- [15] Iwu EN, Holzemer WL, 2017, HIV Task Sharing Between Nurses and Physicians in Nigeria: Examining the Correlates of Nurse Self-Efficacy and Job Satisfaction. *J Assoc Nurses AIDS Care*, 28(3): 395–407. <https://doi.org/10.1016/j.jana.2017.02.005>
- [16] Lee E, 2016, Safety Climate and Attitude Toward Medication Error Reporting After Hospital Accreditation in South Korea. *Int J Qual Health Care*, 28(4): 508–514. <https://doi.org/10.1093/intqhc/mzw058>
- [17] Li X, Zhang Y, Yan D, et al., 2020, Nurses' Intention to Stay: The Impact of Perceived Organizational Support, Job Control and Job Satisfaction. *J Adv Nurs*, 76(5): 1141–1150. <https://doi.org/10.1111/jan.14305>
- [18] Liming Y, 2008, A Discussion on the Scope of Nursing Practice. *Chinese Nursing Management*, 2008(03): 12–15.
- [19] Liu H, Ye Z, 2020, *China Statistical Yearbook*, China Statistical Press.
- [20] Liu X, Liu J, Liu K, et al., 2021, Association of Changes in Nursing Work Environment, Non-Professional Tasks, and Nursing Care Left Undone With Nurse Job Outcomes and Quality of Care: A Panel Study. *International Journal of Nursing Study*, 115: 103860. <https://doi.org/10.1016/j.ijnurstu.2020.103860>
- [21] Massey D, Chaboyer W, Anderson V, 2017, What Factors Influence Ward Nurses' Recognition of and Response to Patient Deterioration? An Integrative Review of the Literature. *Nurs Open*, 4(1): 6–23. <https://doi.org/10.1002/nop.2.53>
- [22] McCorkle R, Engelking C, Lazenby M, et al., 2012, Perceptions of Roles, Practice Patterns, and Professional Growth Opportunities: Broadening the Scope of Advanced Practice in Oncology. *Clin J Oncol Nurs*, 16(4): 382–387. <https://doi.org/10.1188/12.Cjon.382-387>
- [23] Michel O, Garcia Manjon AJ, Pasquier J, et al., 2021, How Do Nurses Spend Their Time? A Time and Motion Analysis of Nursing Activities in an Internal Medicine Unit. *J Adv Nurs*, 77(11): 4459–4470. <https://doi.org/10.1111/jan.14935>
- [24] Mijovic H, McKnight J, English M, 2016, What Does the Literature Tell Us About Health Workers' Experiences of Task-Shifting Projects in Sub-Saharan Africa? A Systematic, Qualitative Review. *J Clin Nurs*, 25(15–16): 2083–2100. <https://doi.org/10.1111/jocn.13349>
- [25] Muller R, Cohen C, Delmas P, et al., 2021, Scope of Nursing Practice on a Surgery Ward: A Time-Motion Study. *J Nurs Manag*, 29(6): 1785–1800. <https://doi.org/10.1111/jonm.13318>
- [26] Nomura AT, Silva MB, Almeida MA, 2016, Quality of Nursing Documentation Before and After the Hospital Accreditation in a University Hospital. *Rev Lat Am Enfermagem*, 24: e2813. <https://doi.org/10.1590/1518-8345.0686.2813>
- [27] Organization WH, 2016, *Global Strategy on Human Resources for Health: Workforce 2030*, Geneva.
- [28] Powers J, 2013, Are You Practicing to Your Full Potential? *Nursing Made Incredibly Easy*, 11(3): 4.
- [29] Younan L, Clinton M, Fares S, et al., 2019, A Descriptive Study of the Composition and Scope of Practice of Nursing Staff in Acute Care Hospitals of Lebanon. *Journal of Nursing Regulation*, 9(4): 34–41.
- [30] Zambas SI, Smythe EA, Koziol-McLain J, 2016, The Consequences of Using Advanced Physical Assessment Skills in Medical and Surgical Nursing: A Hermeneutic Pragmatic Study. *Int J Qual Stud Health Well-being*, 11: 32090. <https://doi.org/10.3402/qhw.v11.32090>

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Perioperative Nursing Gamification Course Design Based on Immersive Virtual Reality Technology Under the Concept of Medical and Educational Collaboration

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Abstract: This paper mainly discusses the perioperative nursing course teaching model suitable for higher vocational education. The core content of “perioperative nursing” course is set according to surgical nursing posts, and gamified course objectives are designed according to learners’ cognitive rules. Typical nursing tasks are used as the carrier, teaching case base is formed based on the concept of medical and educational collaboration, and gamified teaching situations are created based on VR technology to optimize the teaching process and enable students to experience the learning process immersive. Enhance students’ job competency and professional competence. In the course design, modular teaching, project teaching, team cooperation teaching, gamification teaching, VR immersive teaching, medical teaching collaborative evaluation and other modes are aggregated, and the course design of perioperative nursing is re-carried out.

Keywords: Medical education collaboration; Virtual reality technology; Perioperative nursing; Gamification; Course design

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1. Introduction

To address the practical needs of China’s healthcare development and to enhance the advancement of medical education, the State Council, the Ministry of Education, the National Health Commission, and other relevant departments have repeatedly issued policy directives emphasizing the importance of “coordination in medical education.” These policies explicitly call for the integration of undergraduate medical education, postgraduate training, and continuing professional development. The goal is to improve the overall medical education system by fostering deeper collaboration between medical colleges and healthcare institutions, thereby jointly cultivating medical professionals who are well-prepared to meet job-specific requirements.

Due to the gap between the theoretical knowledge of the classroom and the hands-on clinical practice of students in medical colleges and universities, the medical and health talents that have been cultivated cannot meet the needs of actual employers. As an important link between hospital practice and classroom learning, actively developing clinical case resources has become a key way to train medical talents. Perioperative nursing is an important part of surgical nursing curriculum, which is closely combined with clinical practice. Students need to develop strong clinical thinking skills, and the immersive features of virtual reality can provide them with more diverse and engaging learning experiences. The continuous emergence of immersive technology has injected new vitality into educational innovation. Virtual Reality (VR) technology can not only enable learners to directly experience objects and events that are inaccessible on the physical level, but also enhance learners' participation and motivation, and extend the scope of learning ^[1]. The core of virtual reality (VR) is the creation of an Immersive Virtual Environment (IVE), which can visualize three-dimensional data, offer an interactive setting, and enhance the sense of presence in a computer-generated world. At the same time, it allows learners to safely simulate real-world tasks in a controlled environment ^[2].

Immersive learning refers to providing a learning environment close to the real world through virtual reality technology, and learners improve their technical level by participating in interaction and practice. Immersion is a new teaching concept. "Immersion teaching" is the embodiment of immersion theory, with the characteristics of immersion, interaction, and flexible mode ^[3]. High-quality games offer a stronger sense of immersion for players, and similarly, well-designed gamified learning experiences can provide learners with a deeper and more engaging immersive learning environment ^[4]. Gamified course design based on immersive learning begins with a focus on course structure, taking into account the learner's sense of immersion. It involves reflecting on current challenges in gamified course design from the perspective of immersion, and rethinking the components and approaches to enhance the overall learning experience.

2. Design of course objectives

To carry out immersive gamification course learning under the concept of medical and teaching collaboration, the learning objective is redesigned. The course design comprehensively considers the goals of cultural foundation, independent development, and social participation, aiming to achieve the "five frameworks"; goal integrity, stage-based progression, hierarchical structure, progressive development, and sustainability. It also adheres to the "seven principles" of immersive instructional design: alignment with learners' cognitive levels; a sense of reasonable substitution; clearly defined boundaries with internal freedom; cross-border experiences simulating real work scenarios; provision of diverse perspectives and references; "pressure valve" mechanisms tailored to learner characteristics; and the replacement of "rule pressure" with "peer pressure" ^[5,6].

Based on these principles, the perioperative nursing content was categorized into three main sections: preoperative nursing, intraoperative nursing, and postoperative nursing, totaling 16 instructional hours.

2.1. "Perioperative Nursing" course objectives

2.1.1. Social participation objectives

- (1) Be able to judge group behavior and individual behavior according to the course design operation instructions.
- (2) Ability to regulate the behavior of others and improve personal behavior.

- (3) Understand the role of communication in learning through sharing and presentation.
- (4) Cooperation, understanding and respect through interaction with other medical staff and patients.

2.1.2. Cultural base objectives

- (1) As a ward nurse, it is important to understand the concept of the perioperative period, provide targeted preoperative health education based on the type of surgery, perform standard preoperative preparations, and ensure proper morning care on the day of surgery. (2 periods)
- (2) As a ward nurse, it is important to be familiar with the classification and indications of various types of anesthesia, to prepare appropriately for each type prior to administration, and to monitor patients post-anesthesia while providing care for potential complications. (2 periods)
- (3) As an operating room nurse, it is essential to correctly navigate from the non-restricted area through the semi-restricted area to the restricted area, and to perform surgical hand-washing, don sterile surgical attire, and wear sterile gloves in accordance with standard protocols. (6 periods)
- (4) As an operating room nurse, it is important to be familiar with the layout and management of the operating room, perform appropriate skin disinfection for different types of surgical areas, differentiate the roles and responsibilities of scrub nurses and circulating nurses, and have a thorough understanding of the principles and precautions of aseptic technique in the operating room. (2 periods)
- (5) As an operating room nurse, it is essential to assist surgeons by effectively preparing and handling surgical instruments throughout the procedure, ensuring a smooth and sterile operating environment. (2 periods)
- (6) As a ward nurse, the ability to assess and manage common postoperative discomforts and complications is essential for ensuring patient safety and promoting recovery. (2 periods)

2.1.3. Independent development goals

- (1) Able to reasonably plan class time management.
- (2) Develop a sense of teamwork and competition.
- (3) Recognize the advantages of teamwork.
- (4) Can optimize the shortcomings in perioperative nursing process.
- (5) Understand the differences between patients in different care scenarios according to the pre-organizer of the course.
- (6) Appreciate the difference between “my care” and “the care of others.”

3. Design of teaching implementation process

Currently, surgical education at the institution primarily follows a blended approach combining modular teaching, project-based learning, and clinical internships. To enhance the integration of VR technology into the perioperative nursing curriculum and promote course gamification, the implementation process has been redesigned. This new course model is structured around group-based division of labor, task-oriented learning, task execution, and outcome evaluation.

3.1. Build clinical case nursing teaching process based on VR technology

The “teacher-led, student-centered” task teaching is carried out in the three stages before, during and after

class, and the blended teaching method combining online self-study, statistical feedback, group cooperation and classroom teaching is used. According to the online learning situation, teachers carry out targeted classroom teaching, match teaching objectives to real work situations, construct VR scenes, design typical work tasks, guide students to discuss in class, propose solutions and implement them in VR scenes. The implementation process requires the cooperation of team members to play corresponding roles. Improper operation or no clear division of labor will lead to adverse consequences for patients. When team members perform tasks correctly and work in close coordination with patients, the outcomes can vary significantly. This process is simulated through VR scenarios, allowing students to engage in an immersive and realistic experience of perioperative patient care. The final stage involves presenting the results, engaging in discussion and refinement of the care plans, and reinforcing the learning outcomes. The teaching flow chart for perioperative nursing tasks is illustrated in **Figure 1**.

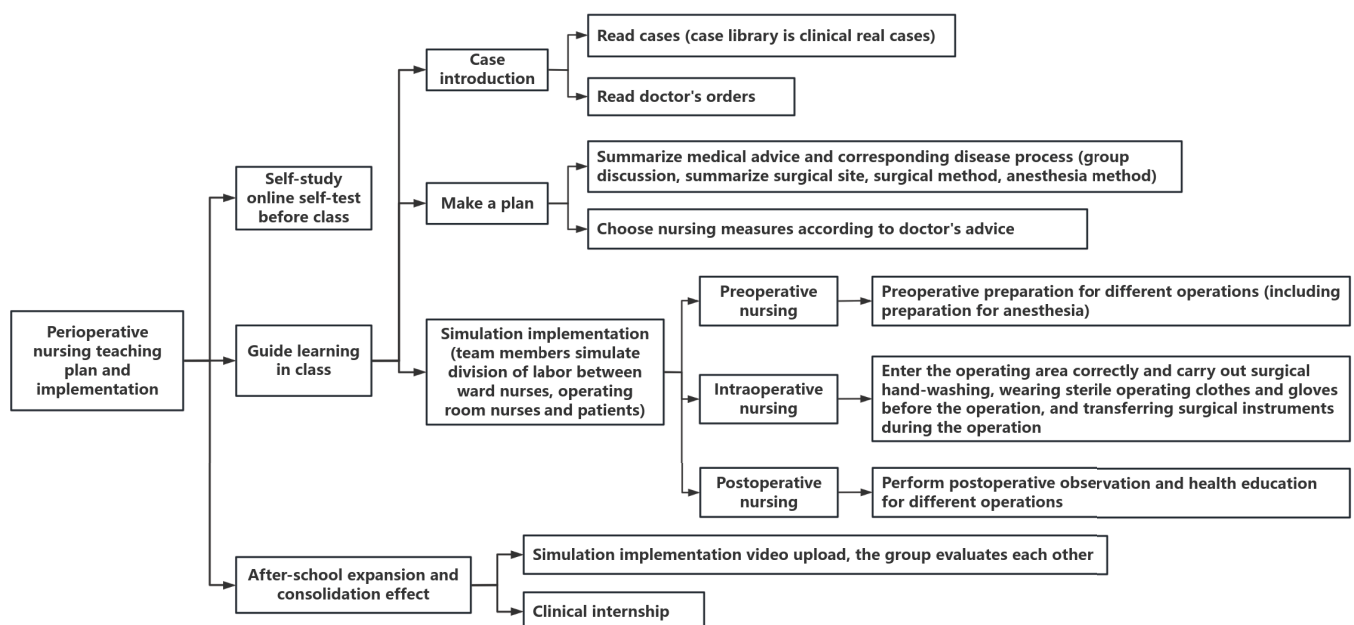


Figure 1. Perioperative nursing teaching plan and implementation

3.2. Construction of gamified clinical case database based on medical and educational collaboration

Case writing in nursing education should be based on real and typical clinical situations. Each case should have a clear and standard format to make it easy to organize and manage. Cases should start simple and gradually become more complex, helping students learn step by step, think critically, and stay interested. All cases must match the teaching goals and syllabus, focusing on key points and common challenges. It is best to choose cases with a single disease and revise them into clear, standard teaching cases [7, 8].

“Surgical nursing” encompasses over 100 common diseases, with perioperative nursing being a key focus. It involves thousands of theoretical knowledge points and corresponding practical skills. The challenge in teaching lies in training students to apply this comprehensive knowledge to solve nursing problems. To address this, the original “surgical nursing” content, covering hundreds of diseases, will be reorganized into five major learning modules: general surgery, brain surgery, chest surgery, exotics, and orthopedics. A total of 15 typical cases of

surgical care were summarized, including 3 gastrointestinal diseases, 1 abdominal injury, 2 biliary tract diseases, 1 esophageal cancer, 1 breast cancer, 2 urinary system cases, 1 nervous system case, 2 fractures, and 1 thyroid disease. For example, the case of appendicitis among gastrointestinal diseases is shown in **Table 1**.

Table 1. Teaching case demonstration

Perioperative nursing of a patient with appendicitis	
[Case No.] 01	[Chapter]19
[Case source] Collection of clinical real cases [Specialty area, direction] General surgical nursing [Type of surgery] Emergency surgery	
[Case details] Mr. Zhang, male, 30 years old, was admitted to hospital due to sudden metastatic right lower abdominal pain accompanied by nausea and vomiting for 4 hours. Physical examination after admission was as follows: T: 39.2°C, P: 85 times/min, R: 21 times/min, BP 120/75mmHg; In general, the abdomen is flat and soft, the tenderness of McGregor's point is obvious, and there is no rebound pain. Blood routine: White blood cell count 8.5*10 ⁹ /L, neutrophil 0.87. B ultrasonography indicated appendicitis. Clinical diagnosis: acute appendicitis. Laparoscopic appendectomy under general anesthesia was recommended for emergency treatment.	
Task 1: As a ward nurse, please prepare the patients for preoperative nursing. Task 2: As a traveling nurse in the operating area, please do a good job of intraoperative care for patients. Task 3: As a surgical instrument nurse, please provide intraoperative care to the patient. Task 4: The patient successfully returned to the ward, as a ward nurse, please do postoperative care for the patient.	
[Scenario hypothesis] Scenario 1: The patient was not told to fast before surgery, and the patient developed aspiration pneumonia after surgery. Scenario 2: The traveling nurse did not count the items together with the instrument nurse after the operation, resulting in the stitches being left in the patient's abdominal cavity. Scenario 3: The instrument nurse did not follow the aseptic principle in the process of washing hands, wearing surgical clothes and gloves, and the patient had an incision infection after surgery. Scenario 4: The patient did not turn to one side before anesthesia and vomiting asphyxiated; The patient did not change to semi-seated position after anesthesia, and subphrenic abscess appeared after surgery. After 24h, the patient was not informed to get out of bed, and the postoperative intestinal adhesion occurred. The patient was not informed of the feeding time, and the patient ate after being anesthetized and awake, and the appendiceal stump ruptured.	

3.3. School-enterprise co-construction teaching evaluation system

Traditional teaching assessment mainly has the following shortcomings^[9, 10]:

- (1) Focusing solely on professional knowledge and individual skills, the examination format is limited and cannot fully assess the overall abilities of students.
- (2) Most assessments are final exams, which do not provide timely feedback on the quality of the teaching process. As a result, teachers are unable to identify issues in teaching and make necessary adjustments to their strategies and methods in a timely manner.
- (3) The assessment does not offer sufficient guidance for the development of students' abilities.

The current design adopts diversified assessment forms, process assessment and stage assessment, knowledge, skill assessment and ability assessment, and adopts the model of combining internal evaluation and social evaluation, so as to reflect students' ability and teaching results more comprehensively.

3.3.1. In-school evaluation

- (1) Group implementation accounts for 40%. According to the effect of the implementation of the students' situation and the work tasks undertaken in it, the assessment and evaluation are mainly conducted to

examine the students' comprehensive application and teamwork ability.

- (2) Theoretical assessment accounts for 40% of the total evaluation and is conducted through a closed-book examination, primarily focusing on assessing students' understanding of basic professional knowledge.
- (3) Internship case analysis and report account for 20%. The students' written language expression, oral communication and health education ability are mainly examined by the probation group.

3.3.2. Social evaluation

Social evaluation is introduced at various levels, mainly through the following mechanisms:

- (1) In gamification teaching, frontline clinical nursing cadres are invited to participate in teaching, jointly develop gamification cases, implementation plans, evaluation standards, etc., and participate in the situational implementation assessment.
- (2) Selected operation pacesetters will participate in an operation skills competition, where their performance will be evaluated by clinical nursing experts.

3.3.3. Student evaluation

The teaching department investigates the students through questionnaires and evaluates them from the aspects of teaching satisfaction, teaching participation, modern teaching methods, and so on.

4. Conclusion

Based on the concept of medical and educational collaboration, this study designed a gamified perioperative nursing course based on VR technology to enable students to carry out immersive learning. It not only contains the essential features of the gamified curriculum goal design, but also pays special attention to the generation of learners' immersion experience. Teaching design should consider not only the construction of a complex and realistic learning environment, but also support the advanced development of students' personalized learning needs. The integration of immersive learning and gamification learning is a concrete attempt to practice personalized wisdom education. This approach aims to accelerate the shift in curriculum objective design under the vision of a learning-oriented society, moving the focus from the course itself to individual students, and from traditional teaching to enriched learning experiences. It serves as an effective strategy for creating challenging and engaging courses in the era of intelligent education, transforming "water lessons" into "gold lessons." Moreover, it represents a meaningful attempt to practice and implement high-quality, student-centered learning that truly prioritizes the learner.

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Disclosure statement

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References

- [1] Chatzea VE, Logothetis I, Kalogiannakis M, et al., 2024, Digital Educational Tools for Undergraduate Nursing Education: A Review of Serious Games, Gamified Applications and Non-Gamified Virtual Reality Simulations/Tools for Nursing Students. *Information*, 15(7): 410.
- [2] Cascella M, Cascella A, Monaco F, et al., 2023, Envisioning Gamification in Anesthesia, Pain Management, and Critical Care: Basic Principles, Integration of Artificial Intelligence, and Simulation Strategies. *J Anesth Analg Crit Care*, 3: 33.
- [3] Wong JYH, Ko J, Nam S, et al., 2022, Virtual ER, a Serious Game for Interprofessional Education to Enhance Teamwork in Medical and Nursing Undergraduates: Development and Evaluation Study. *JMIR Serious Games*, 10(3): e35269.
- [4] Nasiri M, Amirmohseni L, Mofidi A, et al., 2019, Educational Games Developed for Students in Perioperative Nursing: A Systematic Review and Appraisal of the Evidence. *Nurse Education in Practice*, 37: 88–96.
- [5] Stathakarou N, Kononowicz A, Mattsson E, et al., 2024, Gamification in the Design of Virtual Patients for Swedish Military Medics to Support Trauma Training: Interaction Analysis and Semistructured Interview Study. *JMIR Serious Games*, 12: e63390.
- [6] Barteit S, Lanfermann L, Barnighausen T, et al., 2021, Augmented, Mixed, and Virtual Reality-Based Head-Mounted Devices for Medical Education: Systematic Review. *JMIR Serious Games*, 9(3): e29080.
- [7] Shahrezaei A, Sohani M, Taherkhani S, et al., 2024, The Impact of Surgical Simulation and Training Technologies on General Surgery Education. *BMC Med Educ*, 24: 1297.
- [8] Bai S, Zeng H, Zhong Q, et al., 2024, Application of Gamification Teaching in Disaster Education: Scoping Review. *JMIR Serious Games*, 12: e64939.
- [9] Simonetti V, Tomietto M, Comparcini D, et al., 2022, Effectiveness of Virtual Reality in the Management of Paediatric Anxiety During the Peri-Operative Period: A Systematic Review and Meta-Analysis. *International Journal of Nursing Studies*, 125: 104–115.
- [10] Berton A, Longo UG, Candela V, et al., 2020, Virtual Reality, Augmented Reality, Gamification, and Telerehabilitation: Psychological Impact on Orthopedic Patients' Rehabilitation. *Journal of Clinical Medicine*, 9(8): 2567.

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Research on the Impact of Conception Vessel Dredging Therapy Based on the Theory of Shifting Essence and Changing Qi in Inner Canon of Huangdi on Physical and Mental Health

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Abstract: This study, based on the theory of shifting essence and changing Qi in Inner Canon of Huangdi, deeply explores the theoretical basis, operation method of Conception Vessel Dredging Therapy and its influence on human health. Through case analysis and the statistical analysis of medical records during the pandemic, it reveals the remarkable effects of this method in regulating the endocrine system, improving metabolism, and relieving physical and mental diseases. It provides a theoretical and practical basis for the application of traditional Chinese medicine anti-aging therapy in the modern health field, and helps to explore new ways to delay aging and improve physical and mental health.

Keywords: Shifting essence and changing Qi; Conception vessel dredging therapy; Inner canon of Huangdi; Endocrine regulation; Metabolic improvement; Anti-aging; Mental health

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1. Introduction

In today's society, with the acceleration of the pace of life and the increase of environmental pressure, people's aging speed has significantly accelerated. Various cliff-like aging symptoms appear around the age of 30, which forms a huge contrast with the situation recorded in Inner Canon of Huangdi that the ancients only showed normal aging at the age of 50^[1]. How to effectively delay aging and improve physical and mental health has become an important research topic in the fields of medicine and health preservation. As a classic work of traditional Chinese medicine, Inner Canon of Huangdi contains rich health preservation wisdom. Among them, the theory of shifting essence and changing Qi provides a new idea for solving modern health problems^[2]. The purpose of this study is to deeply explore the conception of vessel dredging therapy based on the theory of shifting essence and changing Qi, analyze its influence on human health, and excavate the modern anti-aging value of traditional Chinese

medicine health preservation therapy.

2. The traditional Chinese medicine basis of the theory of shifting essence and changing Qi

2.1. The relationship between meridians and metabolism, emotions

Traditional Chinese medicine believes that meridians are the channels for the circulation of Qi and blood in the human body, and whether they are unobstructed directly affects human health. When the meridians are blocked, it will lead to poor metabolism, premature aging of the body, and unstable emotions. This view is consistent with the theory of systemic circulation in Western medicine. Western medicine believes that poor circulation will block the channels for cells to obtain nutrients and expel toxins, which will lead to metabolic imbalance, premature aging, and diseases, and at the same time affect emotional regulation. Inner canon of Huangdi clearly states that “the meridians can determine life and death, treat all diseases, adjust deficiency and excess, and must be unobstructed”, emphasizing the importance of unobstructed meridians for human health ^[3].

The circulation of Qi and blood in the meridians is driven by Yang Qi. If the kinetic energy of Yang Qi is higher than the flow resistance in the meridians, the flow rate of the meridians can be accelerated, to achieve improved metabolism and keep people in a young and happy state. Just as Suwen on the Vitality Connecting with Heaven says, “Yang Qi is like the sun. If it loses its place, one’s lifespan will be shortened and one’s health will be impaired”, which fully illustrates the key role of Yang Qi in maintaining human health ^[4].

2.2. The connotation and mechanism of action of shifting essence and changing Qi

Shifting essence and changing Qi is an ancient therapy of the ancient physicians recorded in Inner Canon of Huangdi. This therapy does not use medicine or needles and stones. It directly injects Yang Qi into people through a special way, to rapidly improve metabolism. In modern health maintenance, whether people are undergoing other physical and mental therapies or not, first using the method of shifting essence and changing Qi to expel the accumulated metabolic toxins on the Conception Vessel can reverse the atrophy of endocrine glands, restore the body to a young state, bring peace to the heart, and significantly enhance the efficacy of subsequent other therapies. Its mechanism of action is mainly based on the close connection between the Conception Vessel and the human endocrine system. The acupoints on the Conception Vessel correspond to important endocrine glands. By dredging the Conception Vessel, it can regulate the endocrine system, and then affect the physical and mental state of the human body.

3. The specific content of Conception Vessel Dredging Therapy

3.1. The corresponding relationship between the Conception Vessel and endocrine glands

The positions of the three dantians on the Conception Vessel closely correspond to the important endocrine glands of the human body, and the endocrine system controls the aging speed of the human body ^[5]. When the endocrine glands are blocked, the hormone levels will be imbalanced, triggering a series of chain reactions related to aging and emotions. For example, a decline in estrogen levels can result in dry and rough skin, the formation of wrinkles and pigmentation, and may also contribute to psychological issues such as depression and anxiety. Similarly, abnormal thyroid hormone levels can lead to symptoms including weight fluctuations, fatigue, nervousness, mood

instability, irritability, and heightened emotional reactivity. Ancient traditional Chinese medicine found that the three major acupoints of Yintang, Shanzhong, and Guanyuan on the Conception Vessel correspond to the three dantians. By regulating these three major acupoints, it can have a positive impact on the endocrine glands, slow down or even reverse their atrophy, and make people return to a young state and maintain emotional stability.

3.2. The levels and methods of Conception Vessel dredging therapy

The Conception Vessel Dredging Therapy by shifting essence and changing qi is divided into 7 levels, corresponding to the skin, tendons, muscles, internal organs, bones, mind, and spirit respectively, and can be dredged from different depths of the meridians. At the same time, according to the distance between the doctor and the person seeking help, this method also derives 49 dredging methods, which can gradually open the 24 acupoints on the circulation of the Conception Vessel from different distances. In actual operation, taking the “draping” method as an example, after the person seeking help receives the “Yang Qi” of the doctor from the high-dimensional space with the Laogong acupoint of the palm, the palm is slightly in contact with the skin at the dredging point, and the Yang Qi will be transmitted into the body from the “skin” layer. During this process, the person seeking help needs to keep the mouth slightly open to avoid the upward movement of pathogenic Qi to the head, which may cause discomfort such as dizziness. When the Qi is injected into the dredging point, the person seeking help will gradually feel a sense of heat, numbness, and swelling, as well as the feeling and sound of the flow of Qi and blood in the Conception Vessel. Some lesion points will also have a transient phenomenon of Qi attacking the lesion, and then trigger disease-expelling reactions such as hiccups, yawns, tears, flatulence, and increased urine and stool volume. These sensations of Qi and disease-expelling reactions are important criteria for judging whether the toxins are expelled and whether the metabolism is improved. The details are shown in **Table 1**.

Table 1. Disease-expelling reaction triggered by “Yang Qi”

Disease-expelling channel	Disease-expelling reaction
Mouth	Hiccups, yawns, nausea, vomiting, white foam
Skin	Expelling cold, sweating, skin itching, rashes, acne, hot and cold alternation
Urethra	Increased urine volume, foamy urine
Nostrils	The exhaled breath has a sour and rotten smell, expelling turbid Qi
Eyes	Shedding tears
Anterior Yin	Abnormal vaginal secretions, abnormal color and texture of menstrual blood
Anus	Flatulence, increased stool volume, abnormal color and texture of stool

4. Case analysis

4.1. Case 1: Conditioning insomnia, decreased immunity, and anxiety (dredging the Yintang acupoint)

A 53-year-old woman has long suffered from insomnia, has low immunity, and catches a cold almost every month. She is also always inexplicably emotionally anxious. Through inspection, it was found that her pineal gland was severely calcified and atrophied, and most of it was in a grayish connective tissue state. The melatonin secreted by the pineal gland behind the Yintang acupoint is responsible for regulating the human sleep-wake cycle. Ancient

traditional Chinese medicine believes that this place is the “house of storing the spirit” and controls people’s emotions ^[6]. As people age, the pineal gland begins to calcify and atrophy around the age of seven, and the circulation gradually becomes blocked, which will have a serious impact on sleep, immunity, and emotions, and may even lead to diseases such as schizophrenia.

When using the method of shifting essence and changing qi to dredge her Yintang acupoint, after the Yang Qi entered the pineal gland, the woman first felt numbness and swelling between her eyebrows, and then her entire face felt numb. At the moment of dredging the surface layer, she involuntarily shed tears, which was a manifestation of the release of the pent-up emotions in the pineal gland. After dredging, she was no longer anxious and irritable, felt relaxed, and was able to sleep soundly until dawn that night. And her sleep quality has remained good for some time. The problems of decreased immunity and anxiety caused by the disorder of pineal gland secretion have also been cured.

In addition, dredging the Yintang acupoint can also effectively improve physical discomforts such as dizziness, headache, insomnia, amnesia, cranial nerve injury, low vision, cerebral palsy, syringomyelia, and psychological discomforts such as stress, anxiety, and schizophrenia.

4.2. Case 2: Conditioning adolescent depression and low concentration (dredging the Shanzhong acupoint)

A 15-year-old Taiwanese girl suffered from severe depression, had social phobia since childhood, had very few friends at school, would scratch her arms with a cutter whenever she was a little unhappy, and had tried to commit suicide by cutting her wrists and taking sleeping pills several times. Although her mother took her to try many psychological consultations and treatments of traditional Chinese and Western medicine, her condition continued to deteriorate. The girl’s depressive symptoms were closely related to the blockage of the Shanzhong acupoint. Under the Shanzhong acupoint lies the thymus gland that controls happiness. The secretion of thymosin affects the synthesis and release of neurotransmitters, and then regulates emotions. When the neurotransmitters are in balance, people have positive and happy emotions; conversely, pessimism and depression will occur. Due to the influence of long-term negative emotions, the Shanzhong acupoint of the girl was blocked, the thymosin could not be synthesized normally, and the neurotransmitters were imbalanced, leading to the aggravation of depressive symptoms.

After using Conception Vessel Dredging Therapy by shifting essence and changing Qi to inject Qi into her Shanzhong acupoint, at first she did not have obvious feelings. As the dredging progressed, she began to feel the energy of Yang Qi, her chest was warm, and the heat sensation descended to her abdomen. There was a sound from the deep layer of the Shanzhong acupoint, and then she began to hiccup to expel pathogenic Qi, and the atrophy of the thymus gland gradually reversed. After dredging, her chest tightness was greatly reduced, her face became pink, the corners of her mouth turned up, she felt comfortable, and her stress resistance and concentration were significantly improved.

In addition, dredging the Shanzhong acupoint can also quickly relieve physical discomforts such as chest tightness, weak resistance, chest pain, hypertension, coronary heart disease, and palpitations, as well as psychological discomforts such as depression, sullenness, restlessness, and palpitations. At the same time, it can improve concentration and intuition, and help control emotions.

4.3. Case 3: Improving energy and achieving a younger facial appearance (dredging the Guanyuan acupoint)

A 38-year-old Asian American woman has been insisting on physical exercise all year round to maintain abundant energy. However, in recent years, she has experienced post-exercise symptoms of low energy, fatigue, and drowsiness. Additionally, her facial skin quality and complexion have noticeably deteriorated, appearing dull, shriveled, and grayish-yellow, making her look significantly older than her actual age. For sub-healthy people, strenuous exercise may consume a large amount of Yang Qi, and Yang Qi is the key to maintaining a youthful appearance. The facial aging of this woman is due to the lack of nourishment of Yang Qi. Under the Guanyuan acupoint are the adrenal glands and gonads that control energy, and the adrenaline and sex hormones they secrete are in charge of the energy conversion and reproductive function of the whole body. Ancient traditional Chinese medicine calls it the “house of storing essence” [7].

After using Conception Vessel Dredging Therapy by shifting essence and changing Qi to open the blockage of her Guanyuan acupoint, the woman’s fatigue disappeared, her body became strong, she was no longer sleepy, a strong heat sensation appeared in her lower abdomen, her originally grayish and yellowish complexion became shiny, and a pinkish color appeared on her cheeks, returning to a young state. After that, she was full of energy, and her skin condition was like that of a girl in her early twenties.

In addition, dredging the Guanyuan acupoint can also regulate physical discomforts such as fatigue, drowsiness, premature aging, weakness, dizziness, slow development, low back pain, neck pain, rheumatoid arthritis, irregular menstruation, dysmenorrhea, decreased sexual function, impotence and premature ejaculation, as well as psychological discomforts such as fatigue, drowsiness, lack of ambition, fear, worry, mental decadence, depression and world-weariness.

5. Statistical analysis of medical records during the pandemic

During the global pandemic, the “Taosit Qi Healing the World” project used Conception Vessel Dredging Therapy by shifting essence and changing Qi to help more than a hundred thousand people open the blocked points on the Conception Vessel within three years, effectively eliminating their physical and mental illnesses and enhancing the positive Qi of heaven and earth. Through the statistical analysis of the cases shared by 1,178 beneficiaries around the world, it was found that as the Yang Qi was injected, these patients all showed varying degrees of rejuvenation while their illnesses were eliminated. These real feedbacks provide important modern practical evidence for this ancient physical and mental therapy of shifting essence and changing Qi, and fully prove the effectiveness and wide applicability of this therapy in improving human health.

6. Discussion

6.1. The modern medical significance of Conception Vessel Dredging Therapy

From the perspective of modern medicine, Conception Vessel Dredging Therapy has a positive impact on multiple systems of the human body, such as metabolism, immunity, and nerves, by regulating the endocrine system. The hormones secreted by endocrine glands participate in various physiological processes of the human body. When there is an endocrine disorder, a series of diseases and aging symptoms will be triggered. Conception Vessel Dredging Therapy can improve metabolic function, enhance immunity, and stabilize emotions by slowing down

or even reversing the atrophy of endocrine glands and regulating hormone levels. At the same time, this method may regulate the overall function of the human body by affecting the neuro-endocrine-immune network, which is consistent with the theory in modern medicine that the human body systems are interconnected and mutually influential.

6.2. The complementarity with modern medical therapies

As a traditional Chinese medicine health preservation therapy, Conception Vessel Dredging Therapy has obvious complementarity with modern medical therapies. Modern medicine has precision and high efficiency in the diagnosis and treatment of diseases, but it has certain limitations in preventing diseases, improving the overall health status, and regulating psychological emotions. Conception Vessel Dredging Therapy focuses on the overall conditioning of the human body, emphasizes the harmony and unity of the body and mind, and can play a unique role in preventing diseases, delaying aging, and regulating emotions. Combining the two can provide patients with more comprehensive and personalized health solutions, improve the treatment effect, and promote human health.

6.3. The limitations and prospects of the research

Although this study has achieved certain results, there are still some limitations. Firstly, the research is mainly based on case analysis and the statistical analysis of medical records, and lacks strict control experiments, making it difficult to completely rule out the influence of other factors on the results. Secondly, regarding the mechanism of action of Conception Vessel Dredging Therapy, the current research still stays at the level of traditional Chinese medicine theory, and lacks in-depth modern medical experimental research. Future research can further design rigorous control experiments, use modern medical detection means, deeply explore the mechanism of action of Conception Vessel Dredging Therapy, and clarify its specific influence on human physiological and psychological indicators.

At the same time, expanding the sample size and conducting multi-center, large-scale studies can enhance the reliability and generalizability of the research findings. In addition, the combined application of Conception Vessel Dredging Therapy and other modern medical therapies can also be explored to provide more choices and support for human health undertakings.

7. Conclusion

Conception Vessel Dredging Therapy based on the theory of shifting essence and changing Qi in Inner Canon of Huangdi can have a positive impact on the human endocrine system by regulating the acupoints on the Conception Vessel. It can effectively improve metabolic function, relieve physical and mental diseases, delay aging, and improve physical and mental health. Case analysis and the statistical analysis of medical records during the pandemic provide strong evidence in support for the effectiveness of this method. Although this study has certain limitations, Conception Vessel Dredging Therapy has shown great application potential in the modern health field. In the future, more research and exploration on this method should be strengthened to promote the integration of traditional Chinese medicine health preservation therapy and modern medicine, and make greater contributions to human health undertakings.

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Disclosure statement

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References

- [1] Zhang F, 2015, The Inner Canon of Huangdi (Essence of Chinese Sinology Classics). Beijing United Publishing, 2015(1): 7.
- [2] Zhang F, 2015, The Inner Canon of Huangdi (Essence of Chinese Sinology Classics). Beijing United Publishing, 2015(1): 158.
- [3] Guo A, 2012, Miraculous Pivot of Huangdi Neijing. Jiangsu Phoenix Science and Technology Publishing House, 2012(1): 223.
- [4] Zhang F, 2015, The Inner Canon of Huangdi (Essence of Chinese Sinology Classics). Beijing United Publishing, 2015(1): 32.
- [5] Liu F, 2012, Re-Read The Inner Canon of Huangdi. Shanghai Science and Technology Publishing House, 2012(1): 276–280.
- [6] Zhang F, 2015, The Inner Canon of Huangdi (Essence of Chinese Sinology Classics). Beijing United Publishing, 2015(1): 218.
- [7] Zhang F, 2015, The Inner Canon of Huangdi (Essence of Chinese Sinology Classics). Beijing United Publishing, 2015(1): 219.

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The Impact of Continuous Care on Independent Living Skills and Psychosocial Adaptation of Patients with Hypertensive Intracerebral Hemorrhage After Discharge

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Abstract: *Objective:* To analyze the value of continuous care for patients with hypertensive intracerebral hemorrhage (HICH). *Methods:* A total of 80 patients with HICH who visited our hospital from January 2024 to December 2024 were selected as samples and randomly divided into two groups. The observation group received continuous care, while the control group received routine care. The Functional Independence Measure (FIM), Symptom Checklist-90 (SCL-90), and complications were compared between the two groups. *Results:* The FIM score of the observation group was higher than that of the control group ($P < 0.05$). The SCL-90 score of the observation group was lower than that of the control group ($P < 0.05$). The incidence of HICH complications in the observation group was lower than that in the control group ($P < 0.05$). *Conclusion:* The application of continuous care in HICH nursing can enhance patients' independent living skills outside the hospital, optimize their psychosocial adaptation, and is safe and efficient.

Keywords: Hypertensive intracerebral hemorrhage; Continuous care; Psychosocial adaptation; Independent living

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1. Introduction

HICH refers to a type of disease caused by abnormal blood pressure leading to intracerebral hemorrhage, which is the rupture and bleeding of intracranial small arteries induced by excessive blood pressure and atherosclerosis. It poses risks of disability and fatality. The recovery process of HICH is slow, and the damage to brain tissue is irreversible. After onset, patients are prone to psychological and physical impairments, requiring nursing intervention to optimize psychological and physical functions and shorten the recovery time of HICH. Routine care, which focuses on the management and control of HICH symptoms, has limitations^[1]. Continuous care extends inpatient HICH nursing to the home, ensuring the quality of home care as much as possible, optimizing

patients’ independent living skills outside the hospital, and facilitating their return to society. Based on this, this study explores the value of continuous care using 80 HICH patients who visited the hospital from January 2024 to December 2024 as samples.

2. Materials and methods

2.1. Materials

Eighty patients with HICH who visited our hospital from January 2024 to December 2024 are selected as samples and randomly divided into groups. The baseline data of HICH patients in the observation group were compared with those in the control group ($P > 0.05$), as shown in **Table 1**.

Table 1. Analysis of baseline data of HICH

Group	n	Gender(%)		Age (years)		History of hypertension (years)		Bleeding volume(ml)	
		Male	Female	Range	Mean	Range	Mean	Range	Mean
Group A	40	23(57.50)	17(42.50)	41–72	56.88 ± 2.43	2–6	4.21 ± 0.88	22–52	40.02 ± 1.48
Group B	40	24(60.00)	16(40.00)	42–71	56.91 ± 2.41	2–7	4.19 ± 0.91	22–53	40.11 ± 1.51
X ² /t	-	0.0516		0.0554		0.0999		0.2692	
P	-	0.8203		0.9559		0.9207		0.7885	

2.2. Inclusion and exclusion criteria

The inclusion criteria are: (1) Meet the criteria for HICH in the “Guidelines for the Prevention and Treatment of Hypertension in China”^[21]; (2) Signed informed consent; (3) No severe cardiovascular and cerebrovascular diseases.

Meanwhile, the exclusion criteria are: (1) Organ function impairment; (2) Incomplete case information; (3) Death.

2.3. Methods

2.3.1. Control group

(1) File creation

For HICH patients who meet discharge criteria, healthcare providers should offer a thorough explanation of discharge precautions, create a HICH file to record basic information, diagnosis and treatment information, medication information, and contact details, as well as provide patients with departmental consultation phone numbers.

(2) Education

Patients should be encouraged to adopt regular and healthy lifestyle habits, to extend sleep time, pay attention to slowly changing body positions, and avoid getting up immediately after waking up. It is recommended to maintain a supine position for 30 seconds after waking up, then slowly turn to a sitting position, maintain the sitting position for 30 seconds before turning to a standing position, and stand at the bedside for 30 seconds before walking. Additionally, healthcare providers should guide patients in performing proper home rehabilitation exercises. These include bed exercises in different positions, such as active and passive movements of the joints and body, rolling over, and turning the body forward,

backward, and side to side. Patients should also practice sitting balance exercises to help them maintain a stable and comfortable sitting position. Standing exercises should be included as well, such as standing while eating, dressing themselves, using the toilet, and climbing stairs.

2.3.2. Research group

(1) Telephone follow-up

After discharge from HICH, complete a telephone follow-up every 15 days to evaluate patients' home exercise status, diet planning, lifestyle habits, recovery status, and emotional changes. Simultaneously, inquire about medication adherence and comprehensively analyze the physical health status of HICH patients. Correct bad habits promptly, urge regular exercise and a balanced diet, and remind patients to take medication as prescribed. Deepen the popularization of HICH knowledge, including risk factors and pathogenesis of cerebral hemorrhage, explain daily precautions in detail, and stabilize anxiety and tension to reduce the recurrence of cerebral hemorrhage.

(2) Home visits

After discharge from HICH, healthcare providers should complete a home visit every month to evaluate patients' medication adherence, blood pressure monitoring cooperation, analyze changes in body mass, and assess their cognition. Home education for patients with HICH should focus on promoting a healthy lifestyle and preventing complications. Patients are advised to follow a low-fat diet, ensure adequate intake of vitamins and high-quality protein, avoid greasy foods, and increase consumption of fruits and vegetables to prevent constipation. Foods rich in iodine, such as seaweed and kelp, are recommended to help reduce cholesterol buildup in the arteries. For patients with facial paralysis, it is important to prevent choking and aspiration by limiting talking during meals and choosing soft or liquid foods. Patients should be taught to monitor and record their blood pressure independently using an arm-type monitor, and seek timely medical attention if they experience symptoms such as fatigue, chest tightness, or high blood pressure. Harmful habits like smoking and alcohol use should be avoided, and attention should be given to cold prevention, warmth preservation, and blood lipid regulation to reduce the risk of increased blood viscosity and rebleeding. For those with hyperlipidemia, regular aerobic exercise should be encouraged to promote metabolism and stabilize lipid levels. Patients with significant anxiety or depression should be supported through emotional expression and provided with positive examples of successful HICH recovery to enhance confidence and reduce psychological stress.

(3) WeChat follow-up

Invite HICH patients to join the home care management WeChat group. The nurse in charge should share health knowledge daily, including emotion regulation methods, blood pressure monitoring methods, etc., and guide patients to ask questions in the group. The nurse should professionally answer their questions and inspire patients' confidence in recovery.

2.4. Observation indicators

- (1) Independent living ability: Twelve weeks after discharge, the independent living ability of HICH patients is evaluated using the FIM scale, which consists of 18 items (ranging from 18-126 points). The score is positively correlated with independent living ability.
- (2) Psychosocial adaptation: Twelve weeks after discharge, the psychosocial adaptation ability of HICH

patients is evaluated using the SCL-90 scale, which consists of 9 items (ranging from 1–5 points based on asymptomatic to severe symptoms). The score is negatively correlated with psychosocial adaptation ability.

(3) Complications: Record cases of pulmonary infection, electrolyte imbalance, and negative nitrogen balance.

2.5. Statistical analysis

The data is processed using SPSS 23.0 software. Count data are recorded as percentages and analyzed using the chi-square test. Measurement data are recorded as mean \pm standard deviation and analyzed using the t-test. Statistical differences are considered significant at $P < 0.05$.

3. Results

3.1. FIM scores of HICH patients

The observation group had higher FIM scores compared to the control group, with $P < 0.05$, which is shown in Table 2.

Table 2. Comparison of FIM scores in HICH patients ($\bar{x} \pm s$)

Group	Self-care	Sphincter control	Transfer	Mobility	Communication	Social cognition	Total score
Observation group ($n=40$)	26.61 \pm 0.41	8.61 \pm 0.33	11.96 \pm 0.36	8.89 \pm 0.38	15.31 \pm 0.58	17.21 \pm 0.62	88.38 \pm 1.73
Control group ($n=40$)	25.11 \pm 0.36	5.42 \pm 0.22	11.01 \pm 0.32	5.87 \pm 0.31	11.05 \pm 0.39	16.08 \pm 0.51	77.36 \pm 1.28
<i>t</i>	17.3873	50.8694	12.4741	38.9475	38.5485	8.9022	32.3862
<i>P</i>	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

3.2. SCL-90 scores of HICH patients

The SCL-90 scores of the observation group were lower than those of the control group ($P < 0.05$), as shown in Table 3.

Table 3. Comparison of SCL-90 scores for HICH patients ($\bar{x} \pm s$)

Group	Obsessive symptoms	Somatization	Depression	Anxiety	Interpersonal sensitivity
Observation group ($n=40$)	1.25 \pm 0.25	1.75 \pm 0.25	1.32 \pm 0.26	1.21 \pm 0.27	1.54 \pm 0.21
Control group ($n=40$)	1.59 \pm 0.33	1.91 \pm 0.33	1.91 \pm 0.44	1.87 \pm 0.46	1.59 \pm 0.28
<i>t</i>	5.1940	2.4442	7.3012	7.8259	0.9035
<i>P</i>	0.0000	0.0168	0.0000	0.0000	0.3690

Group	Horror	Hostility	Psychosis	Paranoid
Observation group ($n=40$)	1.25 \pm 0.19	1.05 \pm 0.33	1.35 \pm 0.43	1.78 \pm 0.33
Control group ($n=40$)	1.92 \pm 0.42	1.62 \pm 0.42	1.69 \pm 0.68	1.95 \pm 0.39
<i>t</i>	9.1923	6.7492	2.6727	2.1045
<i>P</i>	0.0000	0.0000	0.0092	0.0386

3.3. Complications in HICH patients

The complication rate of HICH in the observation group was lower than that in the control group ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of complication rates in HICH (n,%)

Group	Pulmonary infection	Electrolyte disturbance	Negative nitrogen balance	Incidence rate
Observation group (n=40)	0(0.00)	1(2.50)	0(0.00)	1(2.50)
Control group (n=40)	1(2.50)	4(10.00)	1(2.50)	6(15.00)
X^2	-	-	-	3.9139
P	-	-	-	0.0479

4. Discussion

HICH refers to cerebral parenchymal hemorrhage lesions induced by abnormal elevations in blood pressure. Its pathological features include the rupture of intracranial small arteries, which is characterized by high risks of disability and fatality, and can induce physical dysfunction and psychological stress responses^[3]. Additionally, the recovery process of HICH is slow, and nursing intervention is necessary to accelerate patients' rehabilitation. Conventional nursing focuses on the management and control of HICH symptoms within the hospital, with inadequate attention to out-of-hospital management, resulting in poor quality of out-of-hospital rehabilitation. The extended care model extends in-hospital HICH services to out-of-hospital settings, urging patients to engage in home-based rehabilitation exercises and correcting their maladaptive behaviors, which is beneficial for the prognosis of HICH^[4]. During the actual extended care service, follow-up is conducted through various forms such as phone calls, home visits, and WeChat groups, covering multiple aspects including exercise, diet, and psychological adaptability, which can meet the needs of different HICH patients and is comprehensive and scientific^[5].

Whether HICH patients have independent living abilities refers to their ability to take care of themselves. In this paper, the FIM scale is selected for evaluation, which can not only provide a detailed assessment of HICH patients' physical function but also comprehensively evaluate their cognitive function and social communication abilities, thereby accurately reflecting their recovery of social activity abilities. The focus of out-of-hospital care for HICH patients should include managing disease etiology and consolidating treatment effects. Implementing extended care strategies provides regular and continuous out-of-hospital services for HICH patients, utilizing phone calls and home visits to understand their psychological and physiological states, correct their maladaptive behaviors, cultivate their self-care skills, and urge them to engage in rehabilitation exercises, which can accelerate the recovery of their physiological functions^[6]. Furthermore, the restoration of self-care abilities in HICH patients can positively impact their psychosocial adaptability. Based on the data analysis in this paper, the FIM scores of the observation group are higher than those of the control group, with $P < 0.05$. This suggests that extended care can alleviate the condition of HICH patients, optimize their independent living abilities outside the hospital, and facilitate their return to society.

Conventional HICH care focuses only on inpatient care, and rehabilitation services are discontinued after discharge, leading to some patients not properly monitoring their blood pressure or taking medications regularly, and even developing secondary HICH complications that require readmission for treatment. The extended

care model provides regular education services to HICH patients and their families, explaining in detail the precautions for outpatient care, which can urge patients to adhere to long-term treatment. Combined with follow-up information, it adjusts patients' medication and dietary therapy methods and develops exercise strategies, which can optimize patients' awareness of self-prevention and control of blood pressure fluctuations and stimulate their subjective initiative^[7]. Based on the data analysis in this article, the SCL-90 score of the observation group was lower than that of the control group, with $P < 0.05$. The reason for this is that during the extended care service, patients' physiological status is comprehensively evaluated through telephone follow-ups, their unhealthy behaviors are corrected, and HICH knowledge is disseminated targeting patients' cognitive weaknesses. This allows patients to understand the risk factors and precautions related to cerebral hemorrhage, which can reduce the risk of HICH recurrence. Through home visits, patients are guided to correctly monitor their blood pressure and take medications reasonably. Education is provided on diet, cough prevention, unhealthy behavior management, and emotional counseling, which can enhance the quality of home care for patients. Answering patients' questions and sharing HICH-related knowledge through WeChat follow-ups can urge patients to actively fight against HICH^[8].

In addition, extended care services can compensate for the deficiencies in community management of HICH patients in China, improve patients' own awareness of HICH, and have the advantage of initiative, which can continuously enhance patients' health care abilities and optimize their physical and mental states in practice. Therefore, patients' psychosocial adaptability improves. The final set of data shows that the complication rate of HICH in the observation group was lower than that in the control group, with $P < 0.05$. The reason for this is that extended care can meet the needs of modern HICH patients, allowing them to continue to enjoy nursing services after discharge, which can shorten their recovery period and avoid the deterioration of HICH condition due to insufficient nursing professionalism during outpatient rehabilitation^[9].

Furthermore, nurses' deepened supervision and management of HICH patients can enhance the quality of care and meet the outpatient care needs of different HICH patients. Emphasizing patient education before discharge and follow-up education can ensure smooth continuity between inpatient and outpatient care, thereby correcting unreasonable behaviors of HICH patients and reducing complications^[10]. However, this study includes a small sample of HICH patients, and there may be deviations in the impact of extended care on their independent living abilities and psychosocial adaptability. Further exploration of the value of extended care with a larger sample of HICH patients is needed in the future.

5. Conclusion

In summary, the application of extended care in the nursing of HICH patients can reduce HICH-related complications, optimize patients' psychosocial adaptability and independent living abilities after discharge, and is worthy of promotion.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Qiu Y, Liang H, Wang F, 2024, Investigation on the Demand for Continuous Nursing Services Among Patients with Hypertensive Cerebral Hemorrhage. *Integrated Traditional Chinese and Western Medicine Nursing*, 10(7): 49–53.
- [2] Wang Z, 2024, Interpretation of the Updated Points of the “Guidelines for the Prevention and Treatment of Hypertension in China (2024 Revised Edition)”. *Chinese Journal of Cardiology*, 29(5): 391–395.
- [3] Liu L, 2024, Application of Personalized Continuous Nursing in the Care of Patients with Hypertensive Cerebral Hemorrhage. *Weekly Digest – Pension Weekly*, 2024(3): 245–247.
- [4] Zhao L, Wang X, Wang L, et al., 2024, The Influence of Standardized Continuous Nursing on the Rehabilitation of Patients After Cerebral Hemorrhage Surgery. *China Standardization*, 2024(12): 277–280.
- [5] Wei J, Liu H, Lu H, et al., 2021, Application of Continuous Nursing Based on Siebens Domain Management Mode in Severe Cerebral Hemorrhage Patients. *Chinese Journal of Modern Nursing*, 27(22): 3055–3059.
- [6] Yang H, Jiang S, Cui Y, 2020, Clinical Observation of Multi-Mode Refined and Continuous Nursing Based on the Cooperation of Patients’ Families Applied to Elderly Cerebral Hemorrhage Surgery. *Geriatrics & Healthcare*, 26(4): 629–632.
- [7] Zhou X, Zhang X, Feng J, et al., 2023, Systematic Evaluation of the Effect of Continuous Nursing Based on the Omaha System Framework on the Rehabilitation of Patients After Hypertensive Cerebral Hemorrhage Surgery. *Evidence-Based Nursing*, 9(3): 394–401.
- [8] Wang Z, Xu J, 2019, The Influence of Personalized Guidance Scheme Combined with Hyperbaric Oxygen Intervention on the Living Ability and Limb Function of Patients with Hypertensive Cerebral Hemorrhage. *Modern Journal of Integrated Traditional Chinese and Western Medicine*, 28(31): 3519–3522.
- [9] Cai R, Deng J, Wei C, et al., 2023, The Application Effect of Targeted Nursing Intervention on Improving Postoperative Complications and Prognosis of Patients with Hypertensive Cerebral Hemorrhage Complicated with Diabetes. *Diabetes New World*, 26(7): 107–110.
- [10] Huang Y, Liang W, Liang J, et al., 2021, The Influence of Continuous Nursing Under the Framework of the Medical Community on the Self-Management Ability and Quality of Life of Stroke Patients After Discharge. *Chinese Medical Innovation*, 18(23): 109–113.

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Study on the Effect of Drug Therapy Combined with Psychological Intervention on Adolescent Patients with Depression

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Abstract: Research on the effects of drug therapy combined with psychological intervention in adolescent patients with depression represents a critical focus in contemporary psychiatric medicine. This study aims to explore the synergistic therapeutic approach of integrating pharmacological treatment with psychological interventions, focusing on its positive impacts on symptom alleviation, quality-of-life enhancement, and clinical recovery in adolescent depression. A cohort of 62 adolescents was selected as research participants, with randomized allocation into either monotherapy (drug-only) or combination therapy (drugs + psychological intervention) groups. Key evaluation metrics included anxiety levels, clinical efficacy, and incidence of adverse reactions

Keywords: Drug combination; Psychological intervention; Adolescents with depression

Online publication: June 3, 2025

1. Introduction

The “Notice on Exploring Specialized Services for Depression and Alzheimer’s Disease Prevention and Treatment” issued by the General Office of the National Health Commission explicitly mandates that healthcare institutions at all levels should standardize and consistently conduct training on depression prevention and treatment. Emphasis is placed on enhancing training for non-psychiatric physicians to improve their ability to identify depression and facilitate timely referrals. The notice advocates for collaborative practices, such as establishing joint clinics or telemedicine consultations between general hospitals and psychiatric institutions. Maternal and child health centers and traditional Chinese medicine hospitals are required to set up psychiatric (psychological) departments. Primary healthcare institutions are urged to build robust collaborative mechanisms with psychiatric hospitals through models like medical consortia. Additionally, depression prevention and treatment knowledge must be integrated into mandatory continuing education programs for community

physicians, ensuring that general practitioners at community health stations (township hospitals) acquire screening and diagnostic competencies. Psychiatric institutions are tasked with extending expert services to grassroots levels via medical consortia, providing scientific diagnoses and tailored treatment plans for community-based depression patients. Special “green channels” for diagnosing and treating complex depression cases should be established to ensure prompt admission of severe cases ^[1]. This policy underscores the national prioritization of adolescent depression management. Universities and colleges should align with such national directives to foster talent development in ways that support societal progress.

2. Materials and methods

2.1. Clinical data

A total of 62 adolescent depression patients treated at our hospital from July 2023 to July 2024 were enrolled and randomly assigned to two groups with 31 patients in each group. In the monotherapy group, there were 16 females and 15 males, and the average age was (16.78 ± 1.08) years old. There were 4 severe patients, 12 moderate patients, and 15 mild patients with major problems. In the combination therapy group, there were 13 females and 18 males with an average age of (16.78 ± 1.08) years old, and there were 5 severe patients, 13 moderate patients, and 13 mild patients with major problems. The mean years of disease were (2.08 ± 1.48) . It can be seen that the comparison of clinical patient data between the two groups was not statistically significant and had a certain comparability. This study has been approved by the hospital committee ^[2].

Inclusion criteria: Participants were in the age range of 12 to 17 years with depression at their first visit and had to exhibit core symptoms (e.g., low mood, loss of interest, etc.) according to the International Classification of Diseases 10th Edition (ICD-10) diagnostic criteria for depression; Parents of all participants should be fully aware of the content of this study, and voluntarily sign informed consent to ensure the rationality and legality of the study; Participants should be able to receive drug treatment and psychological intervention in accordance with the research protocol to ensure the accuracy and reliability of the research data ^[3].

Exclusion criteria: Participants had serious physical diseases such as heart, liver and kidney, or suffered from mental diseases such as schizophrenia and bipolar disorder; Participants may have serious language disorders, intellectual disabilities; The participants had not received antidepressant medication or psychotherapy; They had a severe allergic reaction to the antidepressants used in the study ^[4].

2.2. Methods

The monotherapy group could take drug therapy, fluoxetine preparation (fluoxetine hydrochloride tablets or capsules), Paxil preparation (Paxetine hydrochloride tablets), sertraline preparation (sertraline hydrochloride tablets or capsules), etc. for mild depression patients to increase the concentration of serotonin in the brain to improve depressive symptoms. Patients with moderate depression can use paroxetine hydrochloride tablets, fluvoxamine maleate tablets, Citalopram hydrobromide tablets, Venlafaxine hydrochloride capsules, duloxetine hydrochloride capsules, and other drugs. To alleviate the situation of adolescent depression, SSRI drugs can be used for patients with severe depression, which can not only regulate emotions but also regulate the level of neurotransmitters in the brain and improve the emotional state and sleep quality of patients. In the combination therapy group, the following interventions were required along with the medication ^[5]:

(1) Family therapy

By introducing the whole family system as the treatment object, family therapy aims to improve the communication mode among family members and solve the potential problems in the process, to enhance the family support function. In this process, the doctor will pay attention to the individual symptoms of the patient by adjusting the family structure. If the patient's symptoms have improved to a certain extent, the doctor will continue to use this method. If the patient's symptoms have certain problems, the doctor will adjust the model of getting along with the family until the family finally becomes a whole balanced state. In addition, family therapy also emphasizes mutual understanding and support among family members, and ultimately makes the family form a more harmonious and supportive family environment ^[6].

(2) Physical therapy

On the one hand, electroconvulsive therapy (ECT) can be used, in which is that the patient will receive a certain amount of electrical stimulation for a short period of time to induce a brief systemic convulsion, so that the brain can "reset" and improve depressive symptoms ^[7]. Although ECT may be accompanied by some short-term and long-term side effects, such as short-term memory impairment, headache, etc., but under the operation of an experienced medical team, its safety and effectiveness have been widely recognized. Especially in emergency situations, ECT may become a key means of saving lives. On the other hand, repetitive transcranial magnetic stimulation (rTMS) can be used to generate a weak current in the brain to stimulate the neuronal activity in a specific area, to better regulate the activity pattern of the brain, but there may still be certain side effects such as headache and scalp discomfort ^[8].

(3) Cognitive behavioral therapy (CBT)

Cognitive behavioral therapy (CBT) refers to a series of carefully designed cognitive and behavioral skills training to help patients identify and change those negative, distorted thinking patterns and the resulting bad behavior habits, to better enable patients to establish a more positive and rational cognitive framework, and better manage their emotions. Through a series of structured sessions, CBT helps patients learn to identify these automated negative thoughts, known as "cognitive distortions", such as all-or-nothing thinking, overgeneralization, personalization, etc. Once the patient is able to identify these distorted thoughts, treatment moves to the next stage -- challenging and reframing them ^[9].

(4) Supportive psychotherapy

The doctor's patient listening and unconditional support and companionship can not only improve patients' treatment compliance, but also promote their active participation in the treatment program, to better help patients through difficulties. Supportive psychotherapy not only helps patients overcome psychological difficulties, but also paves the way for them to gradually return to normal social and academic life. Therapists help patients rebuild their social skills and enhance their self-confidence in interpersonal communication through role-playing, scenario simulation, and other techniques. In addition, doctors will guide family members to recognize the pressure and challenges the patient is under through family interviews and family therapy, and encourage family members to treat the patient with a more open, understanding, and supportive attitude. This kind of family support not only provides a more harmonious and inclusive rehabilitation environment for the patient, but also provides an opportunity for the emotional connection between the family members to repair, jointly creating a good

family atmosphere for the patient's comprehensive recovery ^[10].

(5) Psychoanalytic therapy

Psychoanalytic therapy holds that people's behavior and emotions are often driven by impulses, desires, and fears that lie beneath our consciousness. These deep psychological contents, although not directly perceptible, affect our thinking and emotional responses all the time ^[11]. Through the method of free association, doctors will encourage patients to freely express their thoughts, feelings, dreams and any thoughts that come into their minds during the treatment, no matter how insignificant or illogical these thoughts may seem, they can unconsciously express those repressed emotions and wishes in the bottom of their hearts, to enhance patients' subconscious cognition ^[12]. To better transform the negative emotions into an acceptable perspective for adolescents with depression.

2.3. Observational indicators and evaluation criteria

- (1) Doctors compared the anxiety degree and depression degree of the monotherapy group and the combination therapy group, using the self-rating depression scale (SDS) greater than 73 for severe depression patients, 63 to 72 for moderate depression patients, 53 to 62 for mild depression patients; The self-rating Anxiety Scale (SAS) was used, in which more than 70 points were classified as severe anxiety, between 60 and 69 points were moderate anxiety, and between 50 and 59 points were mild anxiety ^[13].
- (2) The clinical efficacy of the two groups of patients was compared, and the results showed that the SAS and SDS scores of the patients were reduced by > 75% after intervention; Effective: the SAS and SDS scores were reduced by 50%–75% after intervention; Ineffective: patients' SAS and SDS scores decreased by < 50% after intervention. Total response rate = (obvious + effective)/total cases × 100%.
- (3) Adverse conditions caused by headache, scalp discomfort, nausea, etc.

3. Results

(1) Anxiety and depression in the two groups

The scores of anxiety and depression in the two groups were 57.23 ± 4.02 after intervention in the monotherapy group ($n = 31$), 62.32 ± 4.23 before intervention, and 46.93 ± 5.33 after intervention in the SDS group. In the combination therapy group ($n = 31$), SAS score was 57.17 ± 5.11 before intervention and 37.66 ± 4.34 after intervention, SDS score was 62.25 ± 4.34 before intervention and 37.82 ± 5.12 after intervention.

(2) Comparison of clinical efficacy between the two groups

The reciprocal number of patients in the monotherapy group was 31, the obvious effect was 8, the effective effect was 13, the ineffective was 10, and the total effective rate was 21 (67.74). The reciprocal number of patients in the combination therapy group was 31, the obvious effect was 10, the effective rate was 19, the ineffective rate was 2, and the total effective rate was 29 (93.55). The value was 6.613, and the P value was 0.010.

4. Discussion

With the rapid development of information technology, there are increasing cases of depression among teenagers. The specific reasons are as follows:

(1) Psychological vulnerability

Teenagers are in the critical period of transition from children to adults, but some parents may think that they are busy with work and neglect to care for their teenagers. As a result, some teenagers are affected by internal and external factors in psychological and physiological aspects, and it is difficult to adjust their emotions and cognition, thus falling into a state of depression ^[14].

(2) Emotional problems

Teenagers are people in adolescence and they will have a desire for intimate relationships at this stage, but due to a lack of social skills, peer competition pressure, family tension, or romantic relationship twists and turns, it may lead to emotional problems. When it is accumulated to a certain degree, it may lead to depression phenomenon ^[15].

(3) Virtual network

With the rapid development of information technology, many parents may have no way to control teenagers' addiction to online games, which leads to a disconnect between teenagers and the real world, reduces face-to-face social interaction, and exacerbates loneliness and social anxiety. In addition, the negative information and comparative culture on the Internet may also deal a blow to the sense of self-worth of teenagers. Teenagers have been immersed in the Internet space, looking for pleasure in the Internet space, so that they rarely speak in real life, forming a distorted psychology.

(4) Study pressure

Because some parents only focus on their children's grades, they will not communicate and exchange with their children. As a result, the child can not communicate for a long time under the high-pressure environment consumes too much energy and physical strength, resulting in a sense of remorse and helplessness, which leads to depression. There are also some students and teenagers who do not want to live up to their parents' hopes, give themselves a lot of pressure, just immersed in learning every day, will not communicate and exchange with others, resulting in a tendency of depression.

(5) Economic pressure

Although adolescents themselves may not directly bear the financial burden, the economic status of their families directly affects their quality of life, their access to educational resources, as well as their access to mental health services. Family economic difficulties may lead to adolescents' limited educational resources, interest cultivation, social activities, etc., and increase their sense of inferiority and social isolation. In addition, financial stress may increase tensions among family members and further affect adolescents' mental health.

Psychological intervention for depression should pay attention to the following issues:

- (1) Medical staff should meet with adolescents constantly, to observe their unique psychological development characteristics, such as self-identity exploration, lack of emotional regulation, and strong need for social relationships.
- (2) The approach the health care provider takes after identifying each patient's situation (root causes of depression, family background, social support status)
- (3) The health care provider should also communicate with the youth, to clearly know the method that

adolescents do not want to take

(4) The medical staff can verify the implementation after determining the treatment goals of adolescents

(5) The medical staff can regularly observe the emotional state and quality of life of adolescents after treatment to ensure that they have been treated well.

Depressed adolescents are in an autistic environment for a long time, so the medical staff should carry out their own therapy, so that they can be treated in the case of ensuring their own safety. The medical staff may have a flexible recovery period for the treatment of adolescent depression and the adolescent can not be cured immediately, so the adolescent should be treated with drugs and through regular checks to determine the final recovery of the adolescent, to ensure the healthy growth of the adolescent.

5. Conclusion

Health care workers use antidepressants Escitalopram, fluoxetine, sertraline, etc. to regulate the function of neurotransmitters in the brain to achieve antidepressant effects. These drugs are able to block the reabsorption of serotonin and norepinephrine or activate their receptors, thereby alleviating depressive symptoms in patients. However, drug treatment can only control the symptoms and cannot fundamentally solve the psychological problems of patients. Therefore, cognitive behavioral therapy, psychoeducation, and family therapy can also be used to help patients identify and change negative thinking patterns and behavior habits, improve their self-cognition and self-regulation ability, better cope with the pressure and challenges in life, and reduce the recurrence of depressive emotions. This comprehensive treatment approach can not only effectively control symptoms but also improve patients' quality of life and promote their full recovery. In the future, the research in this field should be deepened and more optimized treatment plans should be explored to further improve the treatment effect of adolescent depression.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Yu Y, Yi T, Liu P, et al., 2025, Analysis of Influencing Factors of Combined Treatment of Traditional Chinese and Western Medicine in Inpatients With Depression. *Anhui Medical and Pharmaceutical Journal*, 29(03): 512–518.
- [2] Wang X, Chen M, Teng Y, et al., 2025, Analysis of Self-Harm and Suicidal Behavior and Non-Enzymatic Antioxidants and Thyroid Hormone Levels in Adolescents With Depression. *China Modern Doctor*, 63(05): 15–18.
- [3] Wei Y, 2025, Scientific Understanding of Senile Depression. *Family Medicine (Second Half of the Month)*, 2025(02): 36–37.
- [4] Zhang A, An J, 2025, Research Progress of Mental Complications After Traumatic Brain Injury. *Physician Online*, 15(02): 87–91.
- [5] Di J, Cheng G, 2025, Study on the Mechanism of Xiaoyao Tablets in the Treatment of Depression Based on Network Pharmacology and Molecular Docking. *Chinese Journal of Pharmaceutics (Online Edition)*, 23(01): 22–35.
- [6] Xu H, Song L, 2025, Effects of Amisulpride Combined With Escitalopram on Depressive Symptoms and Cognitive Function in Patients With Depression. *Chinese and Foreign Medical Research*, 23(05): 35–38.

- [7] Shi Y, Yin J, 2025, Differences in Clinical Effects of Fluvoxamine and Other SSRIs Antidepressants in the Treatment of Patients With Depression With Anxiety and Distress Characteristics. *Journal of Shandong Second Medical University*, 47(01): 6–11, 82.
- [8] Ailifeire A, Ailaiti T, 2025, Research Progress of Esketamine in Perioperative Depressive Symptoms in Cancer Patients. *Anesthesia Safety and Quality Control*, 7(01): 82–86.
- [9] Su J, Shi C, Li B, et al., 2025, Exploring the Differential Correlation Between Gray Matter Volume and Body Mass Index in Depression Based on MRI. *Chinese Journal of CT and MRI*, 23(02): 16–18, 49.
- [10] Yang X, Rui C, Zhou C, 2025, The Influence of SFBT Combined With Escitalopram Oxalate in the Treatment of Patients With Unipolar Depression on Depressive Symptoms and Serum Neurotransmitter Levels. *Heilongjiang Medicine and Science*, 48(02): 189–190, 193.
- [11] Qi B, Zheng Q, Yang S, 2025, Analysis of the Effect of Mindfulness-Based Cognitive Therapy Combined With Drug Treatment on the Psychological Status and Cognitive Function of Adolescent Patients With Depression. *Psychological Monthly*, 20(03): 158–160.
- [12] Wan G, Shan J, Liu J, 2025, The Effect of Repetitive Transcranial Magnetic Stimulation Combined With Dynamic Group Psychotherapy in Patients With Depression and Suicidal Tendencies. *Psychological Monthly*, 20(03): 164–166.
- [13] Wang L, Yin Y, Liu S, 2025, The Influence of Group Sandplay on the Coping Styles and Depression Degree of Patients With Depression. *Psychological Monthly*, 20(03): 167–169.
- [14] Ren M, Mao J, Wu S, 2025, The Application Research of Cognitive Behavioral Therapy in the Rehabilitation Stage of Patients With Depression. *Psychological Monthly*, 20(03): 146–148, 154.
- [15] Dong H, Ji X, Qin B, 2025, The Influence of Family Member Participation-Based Individualized Nursing Model on the Mental Health Level of Patients With Depression. *Psychological Monthly*, 20(03): 152–154.

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Effects of Standardized Bronchoscopic Interventional Therapy on Efficacy and Degree of Stenosis in Patients with Airway Stenosis

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Abstract: *Objective:* To analyze the treatment effect of standardized bronchoscopic interventional therapy (i.e., interventional therapy) on airway stenosis. *Methods:* Forty patients with airway stenosis admitted to the hospital between September 2022 and September 2024 were selected and randomly divided into two groups using a random number table. The experimental group received interventional therapy, while the reference group received conventional treatment. The total effective rate, degree of airway stenosis, shortness of breath score, and lung function indicators were compared. *Results:* The total effective rate in the experimental group was higher than that in the reference group. The proportion of mild stenosis in the degree of airway stenosis was higher in the experimental group than in the reference group. The shortness of breath score was lower in the experimental group than in the reference group. The lung function indicators were better in the experimental group than in the reference group ($P < 0.05$). *Conclusion:* Interventional therapy is effective for patients with airway stenosis, as it can reduce the degree of stenosis, improve symptoms of shortness of breath, and protect patients' lung function.

Keywords: Standardized bronchoscopic interventional therapy; Airway stenosis; Therapeutic effect; Degree of stenosis

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1. Introduction

The etiology of airway stenosis is complex, including sarcoidosis, long-term endotracheal intubation, airway tuberculosis, or tracheotomy, manifesting as extrinsic airway stenosis or large airway obstruction. Patients with this disease commonly experience symptoms such as dyspnea and shortness of breath and are prone to complications such as atelectasis or obstructive pneumonia^[1]. Bronchoscopic intervention is a novel minimally invasive therapy for this disease that utilizes standardized and normalized interventional treatment processes to accurately locate stenotic lesions, determine the scope of stenosis, and select the optimal treatment plan to improve efficacy. Additionally, interventional therapy can precisely evaluate the intubation angle and depth, understand

catheter position, and provide guidance for catheter placement plans, significantly reducing the degree of stenosis and addressing the disease's etiology ^[2]. This therapy offers diversified treatment approaches that can alleviate disease severity through multiple mechanisms, resulting in significant therapeutic effects. Based on this, the study selected 40 patients with airway stenosis to evaluate the implementation effect of interventional therapy.

2. Materials and methods

2.1. General information

Forty patients with airway stenosis admitted to the hospital between September 2022 and September 2024 are selected and randomly divided into two equal groups using a random number table. The experimental group consisted of 20 patients, including 12 males and 8 females, with an age range of 34–69 years and a mean age of (52.15 ± 4.19) years. The duration of illness ranged from 10–77 days, with a mean of (45.36 ± 7.94) days. The length of airway stenosis ranged from 1.05–3.41 cm, with a mean of (2.04 ± 0.52) cm. The reference group also consisted of 20 patients, including 11 males and 9 females, with an age range of 33–67 years and a mean age of (52.20 ± 4.21) years. The duration of illness ranged from 11–79 days, with a mean of (45.97 ± 7.80) days. The length of airway stenosis ranged from 1.01–3.45 cm, with a mean of (2.08 ± 0.53) cm. There were no statistically significant differences in baseline characteristics between the two groups ($P > 0.05$).

The inclusion criteria of the study are: comprehensive diagnosis of benign airway stenosis based on CT scan, pathological examination, and clinical signs; meeting the indications for bronchoscopic intervention; patient age less than 80 years old; normal cognitive function and consciousness state; complete clinical data; fully informed about the study. Meanwhile, the exclusion criteria of the study are: outpatient treatment; juvenile patients; patients with malignant tumors; presence of contraindications for treatment; participation in other studies.

2.2. Methods

The control group chose conventional treatment: assisting patients to complete relevant examinations such as electrocardiogram, chest CT, and coagulation function. Balloon dilation therapy is performed on the stenotic lesion, with each dilation lasting 2–4 minutes and repeated 2–3 times. Additional dilation treatments are administered on the 8th, 15th, and 22nd days.

The experimental group chose interventional therapy: After assisting the patients to complete relevant examinations and ensuring that they meet the indications for bronchoscopic intervention, patients are required to fast for 8 hours, underwent localized intravenous anesthesia, and had a bronchoscope slowly and accurately inserted through the nasal cavity. A venous channel is established for oxygen therapy with an oxygen flow rate of 2–3L per minute. Patient vital signs were monitored throughout.

Standardized therapies included:

- (1) Cryotherapy: The bronchoscope is guided to the stenotic lesion, inflammatory material and necrotic tissue in the area were removed, and a cryoprobe is inserted through the endoscopic channel directly to the lesion. The cryopreservation system is activated to freeze and thaw the lesion tissue for 5 minutes, turning it into ice. This process is repeated 1–3 times until the lesion was completely frozen, and then the probe was removed. Cryotherapy is performed once every week for 4 weeks.
- (2) Balloon dilation: After anesthesia, a bronchoscope is placed at the stenotic site, a guidewire is inserted, and an appropriately sized balloon catheter is slowly inserted along the guidewire to the lesion site. A suitable

amount of normal saline is injected into the balloon for pressurization therapy, with the pressure level adjusted according to the degree of stenosis. The recommended atmospheric pressure is 3–5 atmospheres. The dilation is maintained for 1–2 minutes and repeated 2–3 times before removing the balloon. Balloon dilation therapy is performed once every week for 4 weeks.

- (3) Argon plasma treatment: An electrode is placed on the distal end of the patient's lower extremity (unilateral), and the argon plasma device is connected. The air velocity is adjusted appropriately, and the electrode is inserted through the original bronchoscope channel. The coagulation treatment power is set at 20–60W, ensuring that the oxygen concentration is less than 35%. The treatment frequency is the same as above.
- (4) High-frequency electric knife treatment: A curved bronchoscope is placed at the stenosis, and an appropriate electric knife is used for multiple treatments on the stenotic lesion.
- (5) Stent implantation: A covered stent is placed in the biopsy hole, and the inserter is slowly placed inside the airway. The stent position is adjusted appropriately to expand the airway.

2.3. Observation indicators

- (1) Degree of airway stenosis: CT scans are performed, and the stenosis range is evaluated using multi-planar reconstruction (MPR) and curved planar reconstruction (CRP) images. The stenosis degree is calculated as follow: (diameter of the proximal end of the stenosis – minimum diameter of the stenotic segment) ÷ diameter of the proximal end of the stenosis * 100%. Mild stenosis refers to a degree not exceeding 25%, moderate stenosis ranges from 26–75%, and severe stenosis exceeds 75%.
- (2) Shortness of breath score: Grade 0 indicates no shortness of breath, scoring 0 points; Grade 1 indicates shortness of breath symptoms during fast walking, scoring 1 point; Grade 2 indicates shortness of breath symptoms during normal walking, scoring 2 points; Grade 3 indicates obvious shortness of breath and difficulty breathing during normal walking, scoring 3 points; Grade 4 indicates severe shortness of breath during mild activity, scoring 4 points.
- (3) Lung function indicators: Lung function tester is used to measure the forced expiratory volume in one second (FEV1), maximum lung capacity (VCmax), and forced vital capacity (FVC).

The above indicators are evaluated both before treatment and one month after treatment.

2.4. Therapeutic effect evaluation criteria

- (1) Complete effectiveness: Normal bronchial function, no airway stenosis
- (2) Partial effectiveness: Significant improvement in bronchial function, stenosis improvement exceeding 50%, significant improvement in subjective symptoms
- (3) Mild effectiveness: Improvement in bronchial function, stenosis improvement less than 50%, improvement in subjective symptoms
- (4) No effect: No change in bronchial function, no improvement in stenosis or subjective symptoms.

2.5. Statistical analysis

Data are processed using SPSS 28.0 software. Measurement data are expressed as $[\bar{x} \pm s]$, and compared and tested using t-values. Count data are expressed as numbers and percentage [n/%], and compared and tested using chi-square (χ^2) values. Statistical significance is set at $P < 0.05$.

3. Results

3.1. Comparison of the total effective rate between the two groups

The total effective rate of the experimental group was higher than that of the reference group ($P < 0.05$), as shown in Table 1.

Table 1. Comparison of the total effective rate between the two groups [n/%]

Group	Number of cases	Completely effective	Partially effective	Mildly effective	No effect	Total effective rate
Experimental group	20	10 (50.00)	5 (25.00)	4 (20.00)	1 (5.00)	95.00 (19/20)
Control group	20	7 (35.00)	4 (20.00)	3 (15.00)	6 (30.00)	70.00 (14/20)
χ^2	-	-	-	-	-	4.329
P	-	-	-	-	-	0.038

3.2. Comparison of the degree of airway stenosis between the two groups

The proportion of mild stenosis in the experimental group was higher than that in the reference group ($P < 0.05$), as illustrated in Table 2.

Table 2. Comparison of the degree of airway stenosis between the two groups [n/%]

Group	Number of cases	Mild stenosis	Moderate stenosis	Severe stenosis
Experimental group	20	14(70.00)	6(30.00)	0
Control group	20	7(35.00)	10(50.00)	3(15.00)
χ^2	-	4.912	1.667	3.243
P	-	0.027	0.197	0.072

3.3. Comparison of shortness of breath scores between the two groups

Before treatment, there was no difference in shortness of breath scores between the two groups ($P > 0.05$). After one month of treatment, the shortness of breath score in the experimental group was lower than that in the reference group ($P < 0.05$). The results are shown in Table 3.

Table 3. Comparison of shortness of breath scores between the two groups [$\bar{x} \pm s$, points]

Group	Number of cases	Before treatment	After treatment
Experimental group	20	3.05 \pm 0.49	0.24 \pm 0.06
Control group	20	3.01 \pm 0.51	0.97 \pm 0.17
t	-	0.253	18.109
P	-	0.802	< 0.001

3.4. Comparison of lung function indicators between the two groups

Before treatment, there was no difference in lung function indicators between the two groups ($P > 0.05$). After one month of treatment, the lung function indicators in the experimental group were better than those in the reference group ($P < 0.05$). The results are shown in Table 4.

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

Group	Number of cases	FEV ₁ (%)		VC _{max} (L)		FVC(%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	20	1.58 ± 0.16	2.08 ± 0.24	1.78 ± 0.11	2.79 ± 0.32	3.05 ± 0.41	2.21 ± 0.27
Control group	20	1.60 ± 0.15	1.79 ± 0.20	1.79 ± 0.15	2.31 ± 0.28	3.08 ± 0.37	2.70 ± 0.34
t	-	0.408	4.151	0.240	5.048	0.243	5.047
P	-	0.686	< 0.001	0.811	< 0.001	0.809	< 0.001

4. Discussion

The pathogenesis of airway stenosis is related to factors such as decreased lung function or significant changes in the anatomical structure of the airways. It continuously affects the body's oxygen supply status and can induce many pathophysiological changes, leading to complications such as lung infections. Among the types of airway stenosis diseases, benign lesions are the main type, requiring early symptomatic treatment to prevent conditions such as respiratory distress syndrome^[3]. Among conventional treatments, airway dilating drugs such as dexamethasone can improve the degree of stenosis and restore lung ventilation function to a certain extent.

However, long-term medication has many side effects and can easily lead to drug resistance, so the feasibility of treatment is limited. Orotracheal intubation ventilation therapy or endoscopic mucosal resection under bronchoscopic guidance are common treatments for this disease, and they have a good effect on improving airway stenosis. However, there are many complications after treatment, so it has limitations. Driven by the development of endoscopic diagnosis and treatment equipment and imaging technology, the placement of stents in the airway has become a newer therapy for this disease^[4]. Based on this premise, standardized bronchoscopy intervention treatment came into being. This therapy reduces the pressure level inside the airway, prevents related symptoms such as bronchial asthma, and reduces the chance of restenosis. For benign tumors and other etiologies, interventional therapy can directly remove tumor tissue, combined with cryotherapy for systematic treatment of residual sites, ultimately achieving ideal treatment results. The operational process of interventional therapy is relatively simplified, efficient, and reliable, and does not cause significant damage to the patient's airway tissue, so the feasibility of treatment is high^[5].

The results showed that the total effective rate of the experimental group was higher than that of the control group, the proportion of mild airway stenosis was higher than that of the control group, the dyspnea score was lower than that of the control group, and the lung function index was better than that of the control group ($P < 0.05$). The reason is that interventional therapy can accurately locate the stenosis site, the whole treatment process is painless, and can be repeated according to the treatment effect, so it has a strong radical cure^[6]. During treatment, cryotherapy uses high-pressure gas that passes through a throttle orifice to rapidly lower pressure and generate extreme cold. This sudden temperature drop causes the targeted lesion tissue to cool quickly, leading to rapid cell necrosis. Additionally, it can result in the formation of microthrombi or induce significant reperfusion injury within the affected tissue^[7].

In addition, cryotherapy can stimulate the immune system and cause a large number of diseased cells to undergo apoptosis. During cryotherapy, granulation tissue, vascular endothelium, or mucosal tissue all contain high water content, so they are more sensitive to cryopreservation. Based on this, this therapy is not easy to cause

local reactions, which can make patients highly tolerant to the treatment process, so the treatment safety is better. Balloon dilation can accurately place the balloon at the site of airway stenosis, and use a high-pressure gun pump to allow the balloon to expand moderately, thereby effectively expanding the airway, which is convenient for treatment and is an ideal treatment for diseases such as tuberculous airway stenosis^[8]. Argon plasma treatment can effectively transmit high-frequency electrical energy, and use ionization reaction to quickly solidify diseased tissue. The stent implantation can accurately place a stent at the location of the airway stenosis, and the expansion effect of the covered stent can be exerted for a long time, and the duration of the treatment effect is longer^[9, 10].

5. Conclusion

In summary, interventional therapy can use bronchoscopy to carry out various treatment interventions such as cryotherapy, balloon dilation or high-frequency electric knife, etc., to reduce the degree of airway stenosis, reduce the accompanying dyspnea symptoms of patients, and can significantly improve the lung function of patients. Its treatment is highly effective and can be used as a standardized therapy for patients with this disease.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Guo J, Luo D, 2023, Effects of Standardized Bronchoscopic Intervention on the Efficacy and Degree of Stenosis in Patients with Benign Airway Stenosis. *Journal of Rare and Uncommon Diseases*, 30(3): 22–24.
- [2] Gong B, Wang K, Li W, et al., 2020, The Value of Rigid Bronchoscopy Combined with Electronic Bronchoscopy in the Treatment of Severe Central Airway Stenosis. *Journal of Xi'an Jiaotong University (Medical Edition)*, 41(2): 268–274.
- [3] Feng Z, 2024, Analysis of the Effect of Standardized Bronchoscopic Intervention on the Efficacy and Degree of Stenosis in Patients with Benign Airway Stenosis. *Medical Forum*, 6(4): 145–147.
- [4] Wu X, Wang T, Wang J, et al., 2022, The Rescue Value of Emergency Bronchoscopic Intervention in Patients with Malignant Airway Stenosis. *Chinese Journal of Respiratory and Critical Care Medicine*, 21(10): 715–719.
- [5] Chen H, Li Y, Yang L, et al., 2023, Complications During Interventional Treatment of Airway Stenosis via Rigid Bronchoscopy. *Shandong Medical Journal*, 63(6): 67–69.
- [6] Wang T, Zhang J, Qiu X, et al., 2020, Effectiveness and Influencing Factors of Interventional Treatment for Cicatricial Airway Stenosis Under Bronchoscopy. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 43(9): 784–790.
- [7] Ding Y, Li F, Huang H, et al., 2020, Analysis of the Efficacy of Bronchoscopic Intervention in the Treatment of Central Airway Stenosis After Lung Transplantation. *Chinese Journal of Respiratory and Critical Care Medicine*, 19(3): 276–280.
- [8] Chen J, Shi J, Sun P, et al., 2022, Application of Extracorporeal Membrane Oxygenation in Bronchoscopic Interventional Surgery for Patients with Severe Airway Stenosis. *Chinese Journal of Respiratory and Critical Care Medicine*, 21(7): 498–504.
- [9] Sun H, Xiang B, Wang B, et al., 2023, Combined Application of Local Cryotherapy and Absolute Ethanol Injection Therapy via Fiberoptic Bronchoscopy in the Treatment of Bronchial Tuberculosis with Scar Stenosis and Airway Obstruction. *Shandong Medical Journal*, 63(33): 40–44.

- [10] Zeng Z, Zhang X, 2020, Progress in the Application of Endoscopic Intervention in Airway Stenosis. China Medical Herald, 17(31): 45–49, 57.

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Evaluation of the Effectiveness and Satisfaction of Nurses' Full Humanistic Care in the Treatment and Nursing of Pediatric Nebulization

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Abstract: *Objective:* To evaluate the value of humanistic nursing care during pediatric nebulization treatment. *Methods:* From January 2024 to June 2024, 250 pediatric patients receiving nebulization treatment were given routine care and included in the control group. From July 2024 to December 2024, 250 pediatric patients receiving nebulization treatment were given full humanistic care by nurses and included in the observation group. The differences in patient compliance, symptom resolution time, parental satisfaction, and emotional scores were compared. *Results:* The compliance of pediatric nebulization patients in the observation group was higher than that in the control group ($P < 0.05$). The disappearance time of inflammation, cough, expectoration, fever, and hospital stay in the observation group were shorter than those in the control group ($P < 0.05$). Parental satisfaction with pediatric nebulization in the observation group was higher than that in the control group ($P < 0.05$). The scores of anxiety (SAS) and depression (SDS) among parents of pediatric nebulization patients in the observation group were lower than those in the control group ($P < 0.05$). *Conclusion:* The application of nurses' full humanistic care in pediatric nebulization treatment can promote the resolution of respiratory system symptoms, optimize patients' lung function, improve patient cooperation, and is highly effective and feasible.

Keywords: Pediatric Nebulization; Humanistic Care; Nursing Effect

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1. Introduction

Due to the incomplete development of children's bodies, they are prone to secondary respiratory diseases after being infected with external pathogens. Nebulization is often used as a treatment method, which utilizes nebulization devices to convert medications into fine mist particles that enter the body through the mouth and nose. This method has multiple effects, such as anti-inflammation, spasmolysis, and expectoration, and has advantages such as precise targeting, rapid onset, and high safety. It has been widely used in the treatment of pediatric diseases^[1]. However, children have low self-awareness and may not cooperate with nebulization

procedures, making it necessary to provide nursing services during treatment. Conventional nursing only follows medical instructions and does not prioritize humanistic care, resulting in poor patient cooperation. Nurses' full humanistic care is a modern nursing strategy that is systematic and scientific, meeting the psychological and physiological needs of patients ^[2]. This study explores the value of humanistic care using 500 pediatric nebulization patients from January 2024 to January 2025 as samples.

2. Materials and methods

2.1. Materials

From January 2024 to June 2024, a total of 250 pediatric patients receiving nebulization treatment are given routine care and included in the control group. Meanwhile, from July 2024 to December 2024, another 250 pediatric patients receiving nebulization treatment are given nurses' full humanistic care and included in the observation group. The data of pediatric nebulization patients in the observation group were compared with those in the control group ($P > 0.05$). See Table 1 for details.

Table 1. Analysis of data on pediatric patients undergoing nebulization inhalation therapy

Group	Gender	Age(years)		Disease duration(d)	
		Male	Female	Range	Mean
Observation group	250	140 (56.00)	110(44.00)	2–6	4.58 ± 0.48
Control group	250	142 (56.80)	108(43.20)	2–7	4.61 ± 0.51
X^2/t	-	0.0325		0.6773	
P	-	0.8569		0.4985	

2.2. Inclusion and exclusion criteria

The inclusion criteria in this study are: (1) Respiratory system symptoms such as cough, expectoration, and fever; (2) Family members signed the informed consent; (3) Nebulization therapy.

Meanwhile, the exclusion criteria in this study are: (1) Hepatic and renal dysfunction; (2) Congenital heart disease; (3) Poor mental state.

2.3. Methods

2.3.1. Observation group

Nurses provided humanistic care throughout the process, including:

- (1) Assessment of the child's condition: Changes in the child's face, respiratory status, and vital signs are observed. It is assessed whether the child has nausea, vomiting, or other adverse reactions to nebulization. Nebulization procedures are gently completed, forced nebulization is avoided, and conditions such as hypoxia are prevented.
- (2) Environmental management: The patient's room is ventilated twice daily and is disinfected once daily. A disinfection machine is used for two hours each day to reduce bacteria in the indoor environment. The temperature and humidity of the environment are adjusted to enhance the child's comfort. A quiet state is maintained in the treatment room, and negative distractions such as noise are avoided. The child's anxiety is alleviated to improve the effectiveness of control. The room is checked for dangerous items to prevent

accidental injuries.

- (3) Psychological counseling: Children undergoing nebulization are often young, and respiratory diseases can affect their psychological and physical health. Psychological counseling is provided due to the child's young age and limited language ability. For children ≤ 1 year old, physical touch such as hugging, stroking, and comforting is used to soothe them. For children > 1 year old, affirmative and encouraging language is communicated to guide cooperation. During nebulization, attention is diverted using cartoons or small toys. The psychological and emotional needs of parents are also addressed, and they are informed of the expected efficacy of nebulization to enhance their confidence in recovery.
- (4) Education: Some parents of children undergoing nebulization may have inadequate knowledge about nebulization. Educational videos and manuals are used to explain the advantages and principles of nebulization to parents. Parents are advised not to apply oily face cream, as it may increase glucocorticoid adherence. Risk factors such as air pollution and smoke are explained, and preventive advice is given to avoid recurrence of the child's condition.
- (5) Position guidance: The child's position is adjusted according to breathing difficulty and individual needs to improve comfort. After repositioning, changes in complexion and respiratory status are observed.
- (6) Nebulization precautions: The nebulization solution is prepared in advance, and a suitable diluent is selected based on the child's condition, with sterile distilled water being recommended. The child's respiratory tract is cleaned before inhalation, and a sitting position is maintained to help the drug reach the targeted area.
- (7) Post-nebulization management: The child's face is cleaned immediately after therapy. For younger children, the mouth is cleaned with a sterile saline swab. Older children are given warm water to gargle. The child's back is gently patted to assist with expectoration.

2.3.2. Control group

Nebulization equipment and medication are prepared according to the doctor's instructions. After receiving the nebulization device, the child is assisted into a supine or seated position, and unnecessary distractions are avoided. The medication is placed in the nebulizer, the mask is secured on the child's face, and the nebulization device is turned on. The child is guided to breathe correctly, and the nebulization inhalation time and medication dosage are adjusted based on the child's actual physiological state.

2.4. Observation indicators

- (1) Child compliance: The child is recorded as compliant if the nebulization procedure is completed without refusal or crying. If mild crying occurs but the child is comforted through body language and encouraging words and is able to cooperate, the case is recorded as partially compliant. If the child cries incessantly and cannot be effectively comforted, the case is recorded as non-compliant.
- (2) Symptom indicators: The disappearance time of inflammation, cough, expectoration, fever, and the length of hospital stay are recorded.
- (3) Satisfaction: Satisfaction is evaluated using a self-made parental satisfaction scale for pediatric nebulization inhalation care. Scores of >70 , $30-70$, and <30 are interpreted as satisfaction, basic satisfaction, and dissatisfaction, respectively.
- (4) Parental emotion scores: SAS (critical value of 50) and SDS (critical value of 53) are positively correlated

with anxiety and depression among parents of children undergoing nebulization inhalation.

2.5. Statistical analysis

Data are processed using SPSS 23.0. Count data (%) are tested using the chi-square test, and measurement data (\pm s) are tested using the t-test. There is a statistically significant difference with $P < 0.05$.

3. Results

3.1. Child compliance indicator

The compliance rate of the observation group undergoing nebulization inhalation was 97.22%, which was higher than the 80.56% of the control group ($P < 0.05$). The results are shown in **Table 2**.

Table 2. Comparison of child compliance indicators (n,%)

Group	Compliance	Basic Compliance	Non-compliance	Compliance Rate
Observation group (n=250)	148(59.20)	100(40.00)	2(0.80)	248(99.20)
Control group (n=250)	100(40.00)	138(55.20)	12(4.80)	238(95.20)
X^2	-	-	-	7.3468
P	-	-	-	0.0067

3.2. Symptoms and indicators of the patients

The observation group showed shorter disappearance times for inflammation, cough, expectoration, fever, and hospital stay compared to the control group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of symptom indicators (d, $\bar{x} \pm s$)

Group	Time for Inflammation to Disappear	Time for Cough to Disappear	Time for Expectoration to Disappear	Time for Fever to Disappear	Length of Hospital Stay
Observation group (n=250)	4.39 \pm 0.42	4.49 \pm 1.09	4.69 \pm 0.69	4.09 \pm 0.42	9.36 \pm 1.06
Control group (n=250)	6.91 \pm 0.59	6.42 \pm 1.72	6.58 \pm 0.83	6.15 \pm 0.58	11.11 \pm 1.42
t	55.0171	14.9860	27.6866	45.4845	15.6150
P	0.0000	0.0000	0.0000	0.0000	0.0000

3.3. Parent satisfaction indicators

The observation group had a higher parent satisfaction rate of 97.22% for nebulized inhalation compared to 83.33% in the control group ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of parent satisfaction indicators (n,%)

Group	Satisfied	Basically satisfied	Dissatisfied	Satisfaction rate
Observation group (n=250)	138(55.20)	110(44.00)	2(0.80)	248(99.20)
Control group (n=250)	110(44.00)	126(50.40)	14(5.60)	236(94.40)
X ²	-	-	-	9.2975
P	-	-	-	0.0023

3.4. Parent emotional scores

After nursing, parents of pediatric nebulized inhalation patients in the observation group had lower anxiety (SAS) and depression (SDS) scores compared to the control group ($P < 0.05$). The results are illustrated in **Table 5**.

Table 5. Comparison of parent emotional scores ($\bar{x} \pm s$)

Group	SAS(score)		SDS(score)	
	Before nursing	After nursing	Before nursing	After nursing
Observation group (n=250)	54.11 \pm 2.36	36.21 \pm 1.21	55.26 \pm 2.41	35.42 \pm 1.28
Control group (n=250)	54.09 \pm 2.37	43.58 \pm 1.45	55.31 \pm 2.39	44.16 \pm 1.39
<i>t</i>	0.0945	61.7036	0.2329	73.1336
<i>P</i>	0.9247	0.0000	0.8159	0.0000

4. Discussion

Respiratory diseases are common inflammatory conditions in pediatrics, often associated with immune system dysfunction. These diseases lead to an increase in inflammatory cells in the airways, such as histamine and interleukin levels, which can induce pathological changes like increased mucus secretion, airway mucosal edema, and airway stenosis. As the disease progresses, symptoms such as paleness, chest tightness, cough, and dyspnea may arise, affecting the child's normal life and necessitating prompt hospitalization for treatment^[3]. Clinically, nebulized inhalation therapy is commonly used to treat pediatric respiratory diseases. The nebulized drug solution is delivered to the lungs in microscopic particles through the respiratory tract, suppressing airway inflammation and relieving bronchial spasms. This approach reduces drug distribution in non-diseased areas, thereby lowering the risk of adverse drug reactions^[4]. However, due to their young age, children often cannot effectively cooperate with nebulization procedures. Therefore, nursing intervention is essential during nebulization therapy. Conventional nursing primarily focuses on completing nebulization procedures and alleviating symptoms, overlooking the individualized needs of patients. As clinical nursing concepts continue to evolve, the nurse-led humanistic care model has gradually matured. This model prioritizes patients receiving nebulized inhalation therapy, providing efficient services that improve patient compliance and reduce nurse-patient disputes^[5].

Based on the data analysis in this article, the compliance rate of the observation group receiving nebulization inhalation was 97.22%, which was higher than the control group's 80.56%, with $P < 0.05$. Analyzing the reasons, children may feel anxious and scared when entering an unfamiliar environment for medical treatment. During the entire process of humanistic nursing care, nurses comfort young children through physical contact and older children through encouraging words and playing cartoons, which can alleviate their negative emotions. Emphasis

on environmental management, such as daily disinfection, ventilation, and adjustment of temperature and humidity in the ward, can reduce children's resistance to the medical environment and further improve their compliance^[6]. Another set of data shows that the disappearance time of inflammation, cough, phlegm, fever, and hospitalization time in the observation group were shorter than those in the control group, with $P < 0.05$. This is because nurses focus on the actual physiological and psychological needs of children during the entire process of humanistic nursing care, which can reduce their struggling and crying, and avoid problems such as interrupted nebulization and wasted medicine due to low treatment compliance, thereby shortening the time for various symptoms to subside^[7].

Another set of data indicates that the satisfaction rate of parents of children receiving nebulization inhalation in the observation group was 97.22%, which was higher than the control group's 83.33%, with $P < 0.05$. This is because nurses provide a comfortable medical environment for children receiving nebulization therapy, reduce their fear and anxiety towards the unfamiliar medical environment, and comfort them in various ways according to their age during the nebulization process, which can shift their attention away from the procedure, eliminate their nervousness, and improve their compliance. Emphasis on ward environment management can also enhance the comfort of children during their visit, resulting in high satisfaction among parents^[8]. The final set of data reveals that the SAS and SDS scores of parents in the observation group were lower than those in the control group, with $P < 0.05$.

Children are special types of patients who may fear unfamiliar environments, be mischievous, shy, sensitive, and have limited understanding of their own illnesses and nebulization therapy. Resistance to treatment during the therapy process can exacerbate negative emotions among parents, which is not conducive to a good doctor-patient relationship^[9]. Implementing a comprehensive humanistic nursing care strategy allows nurses to assess the child's respiratory status, facial changes, monitor vital signs, observe adverse reactions, and perform gentle operations, thereby establishing a good nurse-patient relationship. Nurses fully understand the child's mental and pathological states, comfort them emotionally, and urge them to cooperate with respiratory disease treatment, thus alleviating parents' negative emotions^[10].

5. Conclusion

In summary, the implementation of comprehensive humanistic nursing care for children receiving nebulized inhalation can improve lung function, shorten the duration of illness, increase parental satisfaction, and enhance children's cooperation with nebulization procedures. This approach has significant value for promotion in clinical practice.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] He D, Hou S, Zhao Y, 2024, The Influence of Nursing Based on Feedforward Control Concept on Emotional Expression and Compliance Behavior of Children with Bronchial Pneumonia Treated by Nebulization Inhalation. *Guizhou Medical Journal*, 48(9): 1490–1491.

- [2] Zhang F, Zhang Y, 2020, The Effect of Continuous Nursing Intervention on the Compliance of Home Nebulization Inhalation Therapy for Children with Bronchial Pneumonia. *Anhui Medical Journal*, 41(3): 339–342.
- [3] Du X, Li T, Liu J, 2024, Observation on the Influence of Feedforward Control Method Combined with Family Members' Participation in Situational Games on the Standardization and Compliance of Nebulization Inhalation Therapy for Children with Bronchial Pneumonia. *Heilongjiang Medical Journal*, 48(9): 1136–1139.
- [4] Zhou T, Geng J, Zhang H, et al., 2024, The Influence of Continuous Nursing Measures on Home Nebulization Therapy for Pediatric Bronchial Pneumonia. *Women's and Children's Health Guide*, 3(6): 141–143.
- [5] Wang B, Su G, Zhang Y, 2024, Application of Humanized Nursing Intervention in Nebulization Inhalation Therapy for Children with Bronchial Pneumonia. *Tibet Medical Journal*, 45(1): 132–133.
- [6] Xi X, Yin S, Wu H, 2022, Application Effect of Feedforward Control Nursing in Nebulization Inhalation Therapy for Pediatric Bronchial Pneumonia. *Journal of Clinical and Pathological Research*, 42(7): 1681–1686.
- [7] Long Y, 2024, Application Effect of Feedforward Control Nursing in Nebulization Inhalation Therapy for Pediatric Bronchial Pneumonia. *Frontiers in Medicine*, 14(24): 101–103.
- [8] Ge L, Wang X, 2024, Application Effect of Feedforward Control Nursing in Nebulization Inhalation Therapy for Pediatric Bronchial Pneumonia. *Chinese and Foreign Medical Treatment*, 43(20): 144–147.
- [9] Li Y, Zhang L, Lv Q, et al., 2020, Application Effect of Trust Building in Nebulization Inhalation Therapy for Children with Bronchial Pneumonia. *Chinese Journal of Modern Nursing*, 26(19): 2612–2615.
- [10] Han L, 2020, Application Research of Targeted Nursing in Mucosolvan Nebulization Inhalation Therapy for Pediatric Pneumonia. *Chinese Remedies and Clinics*, 20(23): 4043–4045.

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Clinical Advances in Esophageal Anti-reflux Stents

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Abstract: As an emerging treatment, esophageal anti-reflux stent has gradually become the palliative treatment of choice for many digestive diseases due to its features of low trauma, high safety, and conformity to the physiological and anatomical structure of the esophagus. This study presents a review of the latest clinical progress of esophageal anti-reflux stents to provide theoretical references for subsequent studies.

Keywords: Esophageal anti-reflux stent; Esophageal cancer; Gastroesophageal reflux; Palliative care

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1. Introduction

With the improvement of national living standards, the incidence of digestive diseases is rising, and the esophageal anti-reflux stent has also received widespread attention as an emerging therapeutic means^[1,2]. The stent is mainly used to relieve stenosis and obstruction at the lower esophagus and gastroesophageal conjunction and effectively prevent complications such as reflux, and can be widely used in malignant stenosis of the esophagogastric conjunction, pancreatic achalasia, gastroesophageal reflux disease, esophageal fistula, esophageal perforation, esophageal diverticulum, and esophageal dysfunction and other diseases^[3-5]. It has gradually become the preferred palliative treatment for some gastrointestinal diseases because of its characteristics of low trauma, high safety, and conformity to the physiological anatomy of the esophagus. This study reviews the latest progress of esophageal anti-reflux stents, introducing their mechanism of action, material selection, and clinical application. Meanwhile, it looks forward to the development direction and application value of this field, and provides a reference for further research on esophageal anti-reflux stents.

2. Overview

The esophageal anti-reflux stent is used to reduce the incidence of reflux events by placing a structurally specific stent at the gastroesophageal junction to form a physical barrier that enhances the pressure on the lower esophageal sphincter and prevents gastric contents from refluxing into the esophagus. The principle is similar to that of fundoplication in traditional surgery, but it is minimally invasive and has the clinical advantage of significantly reducing the risk of treatment and shortening the postoperative recovery period ^[6–8].

The structure of esophageal anti-reflux stents is generally consistent, typically consisting of two main components: the stent body and an anti-reflux valve. The valve, added to the distal end of a traditional esophageal stent, helps prevent gastric content reflux while maintaining esophageal patency. Currently, anti-reflux stent structures mainly include windward pocket valve stents, tricuspid valve stents, and cardiac umbrella valve stents ^[9]. Most of the currently available stents are retrievable or adjustable, and they are designed by pulling a lasso cord attached to one or both ends, or by using a dedicated retrieval device before complete endothelialization.

The stent surface can be fully coated, partially coated or bare stent. Uncoated stents are poorly histocompatible, and their long-term placement can stimulate the normal mucosal tissue of the esophagus or tumor tissue proliferation into the stent mesh, leading to restenosis of the stent ^[10]. Commonly used coating materials for coated esophageal stents include polyester, silicone, and polyethylene ^[11]. The surface of partially or fully coated esophageal stents becomes smooth, and they are easily displaced or even dislodged after placement ^[12]. Currently, the most widely used clinical stent is the coated nickel-titanium metal stent, which has the advantages of good histocompatibility, morphologic memory, and moderate elasticity. Coated SEMS is the stent of choice for the treatment of malignant lesions in the esophagus, and its main advantage is that it can avoid inward tumor growth ^[13, 14].

3. Esophageal anti-reflux stents in esophageal cancer

Esophageal cancer (EC) is the eighth most common type of cancer in the world, and its mortality rate is the sixth most common malignant tumor worldwide ^[15]. Progressive dysphagia due to malignant obstruction of the esophagus is the main symptom of advanced esophageal cancer, and more than half of the patients who seek medical attention for dysphagia have already progressed to advanced esophageal cancer, losing the opportunity for radical surgical resection ^[16]. Among the various treatments for middle- and late-stage esophageal cancer, esophageal stent placement has the unique advantage of instantly relieving dysphagia, and it is a safe and effective method to improve the nutritional status of patients and enhance their quality of life ^[17]. In recent years, with the improvement of manufacturing level as well as material science technology, a variety of anti-reflux stents have been developed, and randomized controlled trials have been conducted to evaluate various types of esophageal anti-reflux stents.

Sasso *et al.* included a total of 10 randomized clinical trials involving 467 patients with esophageal cancer, in which self-expanding metallic stents with valve (SEMS-V) were placed in the study group (234 patients) and non-valve self-expanding metallic stents (SEMS-NV) were placed in the control group (233 patients) ^[1]. A self-expanding metallic stent with valve (SEMS-V) was inserted into 234 of these patients. The results showed that both groups had safety and efficacy in esophageal cancer remission, and there was no statistically significant difference in the incidence of GERD, dysphagia remission, technical success, stent displacement, and obstruction after stenting. Dua *et al.* conducted a double-blind controlled study involving 60 patients with malignant dysphagia, in which self-expandable metal stents (SEMS) and SEMS with tricuspid anti-reflux valves

(SEMS-V) were implanted at the gastroesophageal junction. The results showed that both groups demonstrated comparable outcomes in terms of dysphagia scores at 2 weeks and GERD-HRQL scores at 4 weeks ^[18]. After 24 weeks of follow-up, no valve-related complications were observed in the SEMS-V group, and there was no significant difference in GERD symptom scores between the two groups, suggesting that the antireflux valve may have functional limitations, and not ruling out the possibility that the use of proton pump inhibitors may have an interfering effect on GERD assessment. Although antireflux stents theoretically prevent reflux, the studies by Sasso *et al.* and Dua *et al.* failed to confirm the clinical benefits of esophageal antireflux stents.

Shim *et al.* randomly assigned 36 patients with gastroesophageal junction cancer to placement of newly designed self-expanding metal stents with anti-reflux mechanisms or standard open stents ^[19]. Technical success, clinical efficacy, dysphagia scores, reflux symptoms, and complications were assessed one week after the procedure with 24-hour ambulatory esophageal pH monitoring. Studies have shown that newly designed anti-reflux stents are effective in relieving dysphagia caused by malignant cancers at the gastroesophageal junction, as well as being more effective than currently available anti-reflux stents in preventing gastroesophageal reflux. A Belgian study used the Niti-S double-coated anti-reflux stent ^[3]. The study included 29 patients with malignant esophageal stenosis who underwent Niti-S double-coated anti-reflux stent placement (30 stents in total). The results of this study confirmed the significant efficacy of the stents on dysphagia and reflux symptoms, with no stent migration observed, a low incidence of tissue overgrowth, and no serious complications such as perforation, fistula, or food impaction. This study suggests that the Niti-S esophageal dual-coverage anti-reflux stent is a safe and effective treatment option for malignant esophageal strictures. However, the results of this study are small, but larger multicenter studies are needed to further validate its long-term efficacy.

4. Esophageal anti-reflux stents in pancreatic dysplasia

Pancreatic achalasia is a rare primary esophageal dyskinesia characterized by loss of function of the distal esophageal and lower sphincter plexus cells, most commonly seen in the elderly population ^[20]. Its pathogenesis, in addition to histologic abnormalities, may be related to molecular inflammation and genetic factors, and its clinical manifestations include dysphagia, regurgitation, chest pain, and weight loss. Currently, treatment options for cardia dysphagia focus on lowering the resting pressure of the lower esophageal sphincter to help empty the esophagus and relieve symptoms. Therapeutic measures include botulinum toxin injections, endoscopic balloon dilatation or transoral endoscopic myotomy (POEM) as well as performing Heller myotomy and laparoscopic surgery ^[21]. Stent placement has become an important alternative for refractory or inoperable patients. Stent placement has minimally invasive and rapid results, a reversible design, and flexible therapeutic properties, which can effectively relieve dysphagia, reduce reflux, and improve patients' quality of life.

As early as 1996, De Palma *et al.* demonstrated the short-term efficacy and safety of removable self-expanding metal stents for the treatment of cardia laxity ^[22]. In 2009, Tang *et al.* placed a perimetabolic anti-reflux stent in 20 patients with cardia laxity, and all of them showed significant improvement in their dysphagia, with only a few of them experiencing transient chest pain or a foreign-body sensation, and no recurrence after a follow-up period of 8 to 30 months ^[23]. No recurrence was observed after 8–30 months of follow-up, which strongly proved that the treatment of cardia dysphagia with periosteal anti-reflux esophageal stent has the characteristics of convenient operation, few complications, safety, and good near-term therapeutic efficacy. However, because of its unknown pathogenesis and mechanism, the long-term efficacy and stent placement time

need to be further observed.

A retrospective study involving 166 patients with achalasia of the cardia compared the outcomes of fully coated anti-reflux metallic stent (FCARMS) implantation and peroral endoscopic myotomy (POEM) ^[4]. The results showed that FCARMS was comparable to POEM in short-term efficacy (< 6 months) and was more cost-effective. However, POEM demonstrated significant long-term advantages (> 2 years), particularly in patients evaluated with high-resolution manometry. However, long-term (> 2 years) POEM had a significant advantage, especially in high-resolution manometry II (HRM II) patients. This result suggests the need to individualize the choice of stenting according to patient type, economic conditions, and treatment expectations. The results suggest that stenting is a cost-effective and safe therapeutic option for cardia dystrophy.

5. Application of esophageal anti-reflux stents in gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is a common disease of the digestive system in which gastric contents (including gastric acid and digestive enzymes) reflux into the esophagus, causing uncomfortable symptoms or complications ^[24]. GERD is widely prevalent worldwide, and according to the statistics, the global prevalence of GERD ranges from 2.5% to 51.2%, with an average prevalence of 14.8%. According to statistics, the global prevalence of GERD ranges from 2.5% to 51.2%, with an average prevalence of 14.8% ^[25]. The main clinical symptoms are heartburn, reflux, and atypical symptoms such as chest pain, dysphagia, cough, and recurrent pneumonia, as well as common complications such as esophagitis, Barrett's esophagus, and esophageal stricture ^[26]. Its pathogenesis is mainly due to esophageal sphincter (LES) dysfunction, decreased esophageal clearance, delayed gastric emptying, and weakened esophageal mucosal defense mechanism. The current treatment is mainly to reduce gastric acid secretion, promote the healing of esophageal mucosa, enhance the function of the lower esophageal sphincter by minimally invasive means, reduce reflux, and rebuild the anti-reflux barrier through surgery ^[27]. Anti-reflux stents have become a novel option for some patients who are ineffective on medications and lifestyle modifications and cannot tolerate surgery on their own. The use of esophageal anti-reflux stents in GERD has only been reported in case or small-sample studies. Hirdes *et al.* first reported the placement of a self-designed anti-reflux system (RCS) inside the stent in 10 patients with gastroesophageal reflux despite esophageal stenting through the LES and in one patient with severe bile reflux after esophageal jejunostomy and conducted a prospective follow-up study ^[28]. The results showed that placement of the RCS was technically feasible and safe, and that the RCS hardly migrated when the appropriate diameter was selected, while the patients experienced a significant reduction in reflux symptoms. However, the study had a small number of patients, a nonrandomized design, and lacked pH measurements. Its clinical efficacy should be evaluated in a controlled trial. Qiu *et al.* reported a study of symptomatic follow-up of 28 patients with CZES-type anti-reflux esophageal stents who had been followed up for more than two years ^[29]. The results showed that the CZES-type anti-reflux esophageal stent was effective in preventing acid reflux and maintained good physical properties over a long period of time.

6. Conclusion

This study introduces the clinical application of esophageal anti-reflux stents in esophageal cancer, pancreatic achalasia, and gastroesophageal reflux disease by reviewing the relevant literature on esophageal anti-reflux stents. Anti-reflux stents have not yet been applied in large scale in clinical practice. However, as an emerging therapeutic

means, they have shown good anti-reflux effect and clinical application prospect. More prospective clinical trials are needed to validate the anti-reflux stent in terms of material selection, design of anti-reflux structure, exploration of indications, long-term efficacy, complication control, and timing of clinical application. Through the continuous improvement of stent materials and design, as well as the combination of individualized treatment and combined treatment strategies, it is expected that the therapeutic effect of esophageal anti-reflux stents will be further improved in the future, and they may become the first-line treatment modality for the treatment of middle- and late-stage esophageal cancer, pancreatic achalasia, gastroesophageal reflux disease, and other diseases.

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References

- [1] Sasso JGRJ, de Moura DTH, Proenca IM, et al., 2022, Anti-Reflux Versus Conventional Self-Expanding Metal Stents in the Palliation of Esophageal Cancer: A Systematic Review and Meta-Analysis. *Endosc Int Open*, 10(10): E1406–E1416.
- [2] Pandit S, Samant H, Morris J, et al., 2019, Efficacy and Safety of Standard and Anti-Reflux Self-Expanding Metal Stents: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *World J Gastrointest Endosc*, 11(4): 271–280.
- [3] Van Overbeke L, van Dongen J, 2022, Niti-S Esophageal Covered Stent (Double Anti-Reflux Type): An Observational Patient Registry/Post-Market Clinical Follow-Up Study. *Acta Gastroenterol Belg*, 85(3): 493–497.
- [4] Tang YF, Jin P, Tao YR, et al., 2022, Comparison of Fully Coated Anti-Reflux Metal Stenting and Per-Oral Endoscopic Myotomy in Patients With Achalasia: A Propensity Score-Matched Retrospective Study. *BMC Gastroenterol*, 22(1): 253.
- [5] Bi Y, Yi M, Yu Z, et al., 2020, Covered Metallic Stent for the Treatment of Malignant Esophageal Fistula Combined With Stricture. *BMC Gastroenterol*, 20(1): 248. doi:10.1186/s12876-020-01398-6
- [6] Tata MD, Mahazir NQA, Keat OW, et al., 2022, Impact of a New Conceptualized Anti-Reflux Trumpet Stent on the Quality of Life of Patients With Advanced Carcinoma of the Cardio-Esophageal Junction. *Ghana Med J*, 56(2): 95–99. doi:10.4314/gmj.v56i2.6
- [7] Conio M, Savarese MF, Filiberti RA, et al., 2021, Palliation of Malignant Esophageal Obstruction Using an Anti-Migration Self-Expandable Metal Stent: Results of a Prospective Multicenter Study. *Clin Res Hepatol Gastroenterol*, 45(3): 101683. doi:10.1016/j.clinre.2021.101683
- [8] Fuccio L, Hassan C, Frazzoni L, et al., 2016, Clinical Outcomes Following Stent Placement in Refractory Benign Esophageal Stricture: A Systematic Review and Meta-Analysis. *Endoscopy*, 48(2): 141–148. doi:10.1055/s-0034-1393331
- [9] Ma L, Tang X, Fan Z, 2012, Recent Advances in Anti-Reflux Stents for the Esophagus. *China Medical Device Information*, 18(10): 12–16, 71.

- [10] Li B, Li B, Li L, et al., 2020, Progress in the Clinical Application of Esophageal Stents in Esophageal Diseases. *Continuing Medical Education*, 34(1): 74–76.
- [11] Katsanos K, Sabharwal T, Adam A, 2010, Stenting of the Upper Gastrointestinal Tract: Current Status. *Cardiovasc Intervent Radiol*, 33(4): 690–705.
- [12] Yang Z, Wu Q, Wang F, et al., 2013, A Systematic Review and Meta-Analysis of Randomized Trials and Prospective Studies Comparing Covered and Bare Self-Expandable Metal Stents for the Treatment of Malignant Obstruction in the Digestive Tract. *Int J Med Sci*, 10(7): 825–835.
- [13] Sabharwal T, Morales JP, Irani FG, Adam A, 2005, Quality Improvement Guidelines for Placement of Esophageal Stents. *Cardiovasc Intervent Radiol*, 28(3): 284–288.
- [14] Sabharwal T, Morales JP, Salter R, et al., 2005, Esophageal Cancer: Self-Expanding Metallic Stents. *Abdom Imaging*, 30(4): 456–464.
- [15] Uhlenhopp DJ, Then EO, Sunkara T, et al., 2020, Epidemiology of Esophageal Cancer: Update in Global Trends, Etiology and Risk Factors. *Clin J Gastroenterol*, 13(6): 1010–1021.
- [16] Halpern AL, McCarter MD, 2019, Palliative Management of Gastric and Esophageal Cancer. *Surg Clin North Am*, 99(3): 555–569.
- [17] Expert Group, 2020, Expert Consensus on the Clinical Application of Esophageal Cancer Stent Placement. *Chinese Journal of Interventional Radiology (Electronic Edition)*, 8(4): 291–296.
- [18] Dua KS, DeWitt JM, Kessler WR, et al., 2019, A Phase III, Multicenter, Prospective, Single-Blinded, Noninferiority, Randomized Controlled Trial on the Performance of a Novel Esophageal Stent With an Antireflux Valve. *Gastrointest Endosc*, 90(1): 64–74.e3.
- [19] Shim CS, Jung IS, Cheon YK, et al., 2005, Management of Malignant Stricture of the Esophagogastric Junction With a Newly Designed Self-Expanding Metal Stent With an Antireflux Mechanism. *Endoscopy*, 37(4): 335–339.
- [20] Savarino E, Bhatia S, Roman S, et al., 2022, Achalasia. *Nat Rev Dis Primers*, 8(1): 28. doi:10.1038/s41572-022-00356-8
- [21] Li MY, Wang QH, Chen RP, et al., 2023, Pathogenesis, Clinical Manifestations, Diagnosis, and Treatment Progress of Achalasia of Cardia. *World J Clin Cases*, 11(8): 1741–1752.
- [22] De Palma GD, Catanzano C, 1998, Removable Self-Expanding Metal Stents: A Pilot Study for Treatment of Achalasia of the Esophagus. *Endoscopy*, 30(8): S95–S96.
- [23] Tang S, Yuan H, Wang M, et al., 2009, Treatment of Achalasia With Coated Anti-Reflux Esophageal Stent. *Minimally Invasive Medicine*, 4(4): 365–366.
- [24] Katzka DA, Kahrilas PJ, 2020, Advances in the Diagnosis and Management of Gastroesophageal Reflux Disease. *BMJ*, 371: m3786.
- [25] Eusebi LH, Ratnakumaran R, Yuan Y, et al., 2018, Global Prevalence of, and Risk Factors for, Gastro-Oesophageal Reflux Symptoms: A Meta-Analysis. *Gut*, 67(3): 430–440.
- [26] Dunbar KB, 2024, Gastroesophageal Reflux Disease. *Ann Intern Med*, 177(8): ITC113–ITC128. doi:10.7326/AITC202408200
- [27] Yodice M, Mignucci A, Shah V, et al., 2021, Preoperative Physiological Esophageal Assessment for Anti-Reflux Surgery: A Guide for Surgeons on High-Resolution Manometry and pH Testing. *World J Gastroenterol*, 27(16): 1751–1769.
- [28] Hirdes MM, Vleggaar FP, Laasch HU, et al., 2012, Technical Feasibility and Safety of a New, Implantable Reflux Control System to Prevent Gastroesophageal Reflux in Patients With Stents Placed Through the Lower Esophageal

Sphincter. *Gastrointest Endosc*, 75(1): 174–178.

- [29] Qiu X, Jiao F, Liu Z, 2003, Long-Term Efficacy of CZES Anti-Reflux Esophageal Stent and Study on the Function of Anti-Reflux Valve. *China Journal of Endoscopy*, 9(1): 79–80, 82.

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Clinical Observation on the Efficacy of TCM Syndrome Differentiation in Treating Gouty Nephropathy

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Abstract: *Objective:* To investigate the clinical efficacy of traditional Chinese medicine (TCM) syndrome differentiation in the treatment of patients with gouty nephropathy. *Methods:* From June 2023 to December 2024, 80 patients with gouty nephropathy were selected as samples and randomly divided into two groups: group A received TCM syndrome differentiation treatment, while group B received conventional treatment. The efficacy, laboratory indicators, symptom scores, and safety were compared between the two groups. *Results:* The efficacy of group A was higher than that of group B ($P < 0.05$). The uric acid, blood urea nitrogen, serum creatinine, and 24-hour urinary protein levels in group A were lower than those in group B ($P < 0.05$). The symptom score of group A was lower than that of group B ($P < 0.05$). The adverse reactions of gouty nephropathy in group A were lower than those in group B ($P < 0.05$). *Conclusion:* TCM syndrome differentiation treatment for gouty nephropathy can alleviate symptoms, protect renal function, and is highly effective and feasible.

Keywords: Gouty nephropathy; TCM syndrome differentiation treatment; Efficacy

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1. Introduction

Gouty nephropathy is related to abnormal uric acid metabolism and increased uric acid production, which can induce hyperuricemia, aggravate kidney damage, and cause edema, uric acid stones, and other symptoms. It is a metabolic disease. Additionally, abnormal purine metabolism in the human body can increase the risk of chronic tophus and acute arthritis, involving the kidneys, which can lead to the deposition of uric acid crystals in areas such as renal tubules and interstitium, thereby inducing gouty nephropathy. As gouty nephropathy progresses, the glomerular filtration rate decreases, which can aggravate renal function damage, manifesting as proteinuria, hematuria, hypertension, etc. Symptomatic intervention with Western medicine cannot achieve both symptomatic and root treatment effects^[1]. TCM believes that gouty nephropathy is related to an insufficient innate endowment and weakness of spleen and kidney functions, coupled with external factors such as wind and cold, irregular diet,

and emotional distress. Over time, phlegm and blood stasis are generated, leading to impaired renal function. TCM often treats gouty nephropathy with dialectical programs, planning medication based on the patient’s etiology, constitution, and symptom manifestations, correcting Yin-Yang disorders, and accelerating the resolution of gouty nephropathy [2]. This study explores the efficacy of TCM syndrome differentiation treatment using 80 patients with gouty nephropathy who visited from June 2023 to December 2024 as samples.

2. Materials and methods

2.1. Materials

Eighty patients with gouty nephropathy who visited from June 2023 to December 2024 are selected as samples and randomly divided into groups. The baseline data of patients with gouty nephropathy in group A are compared with those in group B ($P > 0.05$), as seen in **Table 1**.

Table 1. Baseline data analysis of gouty nephropathy

Group	n	Gender(%)		Age (years)		Syndrome differentiation (%)			
		Male	Female	Range	Mean	Damp-heat obstruction type	Liver and kidney Yin deficiency type	Stasis and turbidity blockage type	Kidney deficiency and stone strangury type
Group A	40	21(52.50)	19(47.50)	34–77	54.91 ± 2.11	11(27.50)	12(30.00)	11(27.50)	6(15.00)
Group B	40	22(55.00)	18(45.00)	34–78	54.89 ± 2.08	12(30.00)	11(27.50)	10(25.00)	7(17.50)
X ² /t	-	0.0503		0.0427		0.0811			
P	-	0.8226		0.9661		0.9434			

2.2. Inclusion and exclusion criteria

The inclusion criteria of the study are: (1) Presence of urate deposition, hyperuricemia, and other related symptoms; (2) Disease duration exceeding 1 year; (3) Absence of acute infection, renal insufficiency, and other diseases.

Meanwhile, the exclusion criteria are: (1) Liver or heart disease; (2) Allergy to traditional Chinese medicine; (3) Not taking anti-gouty nephropathy medication before enrollment.

2.3. Treatment methods

2.3.1. Group A

Differential medication based on syndromes: For damp-heat obstruction syndrome, Ganlu Xiaodu Pill was administered, containing honeysuckle, *Hedyotis diffusa*, and talc (15g each); *Angelica sinensis* and *Patrinia* (12g each); and various other herbs (10g each). For liver and kidney Yin deficiency syndrome, Zhibai Dihuang Decoction was given, consisting of Chinese yam (30g); cortex lycii, *Rehmannia glutinosa*, moutan bark, and *Cornus* (15g each); and other herbs. For blood stasis and turbidity obstruction syndrome, Shentong Zhuyu Decoction was prescribed, which includes dandelion (20g); honeysuckle and *Patrinia* (15g each); and various other herbs. For kidney deficiency and stone strangury syndrome, Er Miao San and Shi Wei San were combined, containing *Vaccaria* seed (12g); white peony root, *Pyrrosia*, and *Poria* (15g each); and other herbs.

The herbs in the prescriptions are adjusted according to symptoms, boiled, and 300ml of the decoction was

taken warm in the morning and evening. The medication was administered for 3 months.

2.3.2. Group B

Patients in Group B received sodium bicarbonate tablets (0.5g each) from Tianjin Lisheng Pharmaceutical Co., Ltd., taking 1g three times a day, and febuxostat tablets (40mg each) from Jiangsu Wanbang Biochemical Pharmaceutical Group Co., Ltd., taking 40mg once a day. Medication is administered for 3 months.

2.4. Observation indicators

- (1) Efficacy: Symptom score reduction of $> 70\%$ (joint pain and swelling almost disappeared), $30\text{--}70\%$ (joint pain and swelling significantly relieved), and $< 30\%$ (no change in joint pain and swelling), noted as markedly effective, effective, and ineffective, respectively.
- (2) Laboratory indicators: Fully automated biochemical analyzer is used to detect uric acid, blood urea nitrogen, serum creatinine, 24-hour urinary protein, and other indicators.
- (3) Symptom scoring: Joint swelling and pain, nocturia, fatigue, and low back and spine pain are scored from 0 to 3 based on the degree of severity (none, mild, moderate, severe).
- (4) Adverse reactions: The number of patients with diarrhea, nausea and vomiting, and liver function impairment are recorded.

2.5. Statistical analysis

Data are processed using SPSS 23.0. Count data are tested using the χ^2 test (% recorded), and measurement data are tested using the t-test ($\bar{x} \pm s$ recorded). There was a comparative difference with $P < 0.05$.

3. Results

3.1. Efficacy of treatment for gouty nephropathy

The efficacy of Group A was higher than that of Group B ($P < 0.05$), as shown in **Table 2**.

Table 2. Analysis of the efficacy of treatment for patients with gouty nephropathy (n,%)

Group	Marked effect	Effective	Ineffective	Effective rate
Group A ($n=40$)	31(77.50)	8(20.00)	1(2.50)	39(97.50)
Group B ($n=40$)	23(57.50)	10(50.00)	7(17.50)	33(82.50)
χ^2	-	-	-	5.0000
P	-	-	-	0.0253

3.2. Laboratory indicators

After medication, the levels of uric acid, blood urea nitrogen, serum creatinine, and 24-hour urinary protein in Group A were all lower than those in Group B ($P < 0.05$), as shown in **Table 3**.

Table 3. Analysis of laboratory indicators for patients with gouty nephropathy ($\bar{x} \pm s$)

Group	Uric acid($\mu\text{mol/L}$)		Blood urea nitrogen(mmol/L)	
	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=40$)	474.29 \pm 2.43	407.26 \pm 1.85	14.11 \pm 0.25	5.71 \pm 0.36
Group B ($n=40$)	474.31 \pm 2.48	416.88 \pm 1.91	14.16 \pm 0.31	8.49 \pm 0.91
<i>t</i>	0.0364	22.8811	0.7941	17.9664
<i>P</i>	0.9710	0.0000	0.4296	0.0000

Group	Blood creatinine($\mu\text{mol/L}$)		24h urinary protein(g/24h)	
	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=40$)	143.22 \pm 1.88	108.43 \pm 0.48	1.51 \pm 0.32	0.78 \pm 0.12
Group B ($n=40$)	143.25 \pm 1.91	111.69 \pm 0.99	1.54 \pm 0.31	0.88 \pm 0.16
<i>t</i>	0.0708	18.7398	0.4259	3.1623
<i>P</i>	0.9437	0.0000	0.6714	0.0022

3.3. Symptom scores

The symptom scores in Group A were lower than those in Group B, with $P < 0.05$. The results are shown in **Table 4**.

Table 4. Analysis of symptom scores for patients with gouty nephropathy ($\bar{x} \pm s$)

Group	Joint swelling and pain (score)		Nocturia increase (score)	
	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=40$)	2.36 \pm 0.43	0.68 \pm 0.21	2.41 \pm 0.36	0.71 \pm 0.15
Group B ($n=40$)	2.39 \pm 0.44	1.37 \pm 0.29	2.43 \pm 0.37	1.39 \pm 0.33
<i>t</i>	0.3084	12.1881	0.2450	11.8643
<i>P</i>	0.7586	0.0000	0.8071	0.0000

Group	Fatigue and weakness (score)		Lumbar and spinal cold pain (score)	
	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=40$)	2.36 \pm 0.45	0.71 \pm 0.23	2.43 \pm 0.44	0.73 \pm 0.28
Group B ($n=40$)	2.38 \pm 0.46	1.36 \pm 0.36	2.44 \pm 0.42	1.37 \pm 0.33
<i>t</i>	0.1966	9.6230	0.1040	9.3528
<i>P</i>	0.8447	0.0000	0.9175	0.0000

3.4. Adverse reactions

The adverse reactions in Group A were lower than those in Group B for gouty nephropathy, with $P < 0.05$. The results are shown in **Table 5**.

Table 5. Analysis of adverse reactions for patients with gouty nephropathy (n,%)

Group	Diarrhea	Nausea and vomiting	Liver function damage	Incidence rate
Group A (n=40)	1(2.50)	0(0.00)	0(0.00)	1(2.50)
Group B (n=40)	3(7.50)	2(5.00)	1(2.50)	6(15.00)
X ²	-	-	-	3.9139
P	-	-	-	0.0479

4. Discussion

Patients with gouty nephropathy have large amounts of urate crystals deposited in their renal tubules and renal interstitial areas, which can block the urinary tract and induce inflammatory responses. Coupled with the effects of oxidative stress, endothelin, and lipid disorders, the incidence of gouty nephropathy has been increasing year by year [3]. In the early stages of gouty nephropathy, patients often present with azotemia, hypertension, urinary tract infections, and uric acid stones. As the disease progresses to the intermediate stage, persistent proteinuria appears, and a few patients may develop complications such as hypoproteinemia, lumbar soreness, and hypertension. In the later stages, secondary anemia may occur, and some patients may even develop renal failure. Western medicine often stimulates the body to metabolize uric acid and reduce uric acid production through symptomatic drugs, but the overall management and control quality is limited.

Therefore, it is necessary to explore other treatment options [4]. In traditional Chinese medicine theory, there is no disease name for “gouty nephropathy”. Based on initial joint pain symptoms, it can be categorized under the scopes of “severe joint pain” or “obstruction syndrome”. Later renal manifestations can be included in the categories of “lumbar pain” or “strangury syndrome” [5]. Traditional Chinese medicine classifies gouty nephropathy based on symptom manifestations and pathological types. It can be divided into the following pathological types: Invasion of damp-heat pathogen can cause spleen and stomach dysfunction, or damp-heat accumulation can lead to poor blood circulation and joint obstruction, or damage to the kidney meridian caused by damp-heat pathogen, all of which can trigger damp-heat obstruction type of gouty nephropathy. Treatment should focus on relieving pain, dredging meridians, and promoting urination. For those with congenital deficiency, liver and kidney Yin deficiency, inability to nourish blood, or internal heat generation, body fluid can be boiled to produce blood stasis and phlegm turbidity, which flows downward to the kidneys, causing liver and kidney Yin deficiency type of gouty nephropathy.

Treatment should aim to clear heat, nourish Yin, nourish the liver, and tonify the kidneys. Blood stasis, phlegm turbidity, and damp-heat can cause meridian obstruction, or toxic turbidity accumulated in the kidneys can damage the kidney meridians, leading to the turbid blood stasis type of gouty nephropathy. Treatment should be focused on dispelling blood stasis, dredging meridians, and promoting blood circulation. Kidney deficiency can cause water and fluid metabolism disorders, internal dampness and turbidity generation, or kidney meridian damage leading to liver failure, which can trigger kidney deficiency and stone strangury type of gouty nephropathy with stones. Treatment should be aimed at promoting strangury, expelling stones, promoting urination, and nourishing the kidneys [6].

Based on the data analysis in this study, the efficacy of Group A is higher than that of Group B, with $P < 0.05$. According to traditional Chinese medicine theory, kidney deficiency, blood stasis, turbid phlegm, dampness-heat, and other synergistic effects exacerbate kidney disease. Therefore, dialectical administration based on the overall concept of regulation and treatment is required to control the patient’s condition through multiple pathways and targets, such as accelerating uric acid metabolism and inhibiting uric acid production, resulting in excellent