

Advances in Precision Medicine

Whioce Publishing Pte. Ltd.

10 Anson Road #10-13a International Plaza

Singapore (079903)

Advances in Precision Medicine

Focus and Scope

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

About Publisher

Whioce Publishing was established in Singapore in 2014 with a global orientation. The core business of the company focuses on publication of academic journals and organization of international academic conferences, at the same time providing educational trainings, consultations on scientific and technological information, translation services and publications of e-books.

Albeit being a young company, Whioce Publishing has placed huge focus on initiating and publishing top quality international academic journals. The eventual aim is to be indexed by top-notch databases such as EI, SCI, SSCI and AHCI, at the same time growing to become a recognized international academic publishing company that provides a knowledge sharing and communication platform to top researchers all over the world.

EXPANSION STRATEGY: Constantly expanding and strengthening collaborations with publishing companies and relevant industry associations all over the world, building a group of knowledgeable academic personnel and a quality management team. Disseminate scientific and technical information of high quality, gradually growing to a publishing enterprise with worldwide influence.

Publisher Headquarter

WHIOCE PUBLISHING PTE. LTD.

Publishing Office: 10 Anson Road #10-13A International Plaza Singapore 079903

TEL: +65-91818774

Website: whioce.com

Email: info@whioce.com

C

ONTENTS

- 1 Efficacy and Clinical Safety Study of Rabeprazole Combined with Amoxicillin Dual Therapy for Type 2 Diabetes Mellitus Patients with *Helicobacter pylori* Infection**
Xiaofang Wu
- 7 Therapeutic Effect of Nasal Continuous Positive Airway Pressure Ventilation on Severe Pneumonia Complicated with Respiratory Failure in Children**
Xin Guo, Xusheng Qi
- 13 Research on the Anti-aging Effect of Golden Rejuvenating Hormone Containing PQQ, Spermidine, Ergothioneine, Cycloastragalol and Cordycepin**
Jun Yu
- 21 Clinical Observation on the Postoperative Rehabilitation Effect of Combining Traditional Chinese Medicine Techniques with Psychological Counseling in Patients with Mixed Hemorrhoids**
Tianyang Yun
- 27 Similarities and Differences Between Small Molecules and Biologics: Examples of Drugs for Alzheimer's Disease**
Qianshuai Zhang
- 35 Study on the Influence of Implementing Detail Management on Nursing Quality and Nursing Satisfaction in the Disinfection Supply Room**
Aihua Chen
- 41 Current Situation and Reform of Tumor Radiotherapy Education: Integration and Innovation of Curriculum System, Practical Ability, and Intelligent Technology**
Xiaojie Xia, Zeyuan Liu, Xiaolin Ge, Hui Chen, Lu Xu
- 48 Clinical Study on the Treatment of Alzheimer's Disease of Spleen Deficiency and Phlegm Obstruction Type by Wenpi Tongluo Kaiqiao Formula Combined with Acupuncture**
Lingfei Jiang, Qianqian Li, Wei Chen

C

ONTENTS

53 Construction of an Amputation Risk Prediction Model for Patients with Diabetic Foot (DF) in a Civil Aviation Hospital

Zhengfeng Liu , Sunhang Cao , Dongmei Zhai , Zhiqiang Huang , Yaochen Yang , Yunheng Song , Mai Zhou , Wuyi Deng

59 Optimization and Practice of the Emergency Response Mechanism of Primary Healthcare Institutions in Plague Prevention and Control

Yanhua Liu

66 Application of CT Whole Brain Perfusion Combined with CT Angiography in The Diagnosis of Acute Cerebral Infarction

Zhengwei Chen

72 Clinical Observation of Dachaihu Decoction in the Treatment of Bile Reflux Gastritis

Hao Zhou

77 Clinical Observation of Minimally Invasive Puncture Drainage Assisted by Robot Navigation for the Treatment of Hypertensive Cerebral Hemorrhage

Shichen Jiang, Hongbo Xiao

83 Exploring and Analyzing the Application Value of Endoscopic Nasal Septum Deviation Correction Combined with Low-Temperature Plasma Radiofrequency Ablation in the Treatment of Chronic Sinusitis

Chao Chen, Rui Wu

89 Linerixibat and the Future of Pruritus Therapy in Primary Biliary Cholangitis

Qishu He

97 Comparative Study of Immobilization vs. Non-Immobilization in the Treatment of Anterior Talofibular Ligament Injuries

Xinyi Wang

C

ONTENTS

- 105 Exploration of Ideological and Political Education in the Clinical Pharmacology Course for Postgraduate Medical Students in the AI Era**

Ning Huang, Lei Wang, Jiawu Zhu, Changbo Zheng

- 110 Research on the Current Status and Countermeasures of Family Doctor Contracted Services for Children Aged 0-6— Taking Wenzhou as an Example**

Xiaoxiao Liu, Jianfeng Wang, Xiaojing Fan, Zeyang Hu, Sensen Wu

- 117 An Analysis of the Causes of Communicable Diseases in the Lianyungang Area During the Period of the Republic of China: Investigation Based on Local Chronicles**

Xiaolong Yang

- 123 Effect of Comprehensive Intervention Measures of Education Rehabilitation Monitoring on Patients with Chronic Obstructive Pulmonary Disease**

Pingping Tang, Gang Cao

- 130 Research on the Critical Role of Medical Record Front Page Information in Healthcare Statistics**

Weihong Wang

- 136 Research on the Supply-Demand Matching Path for Personalized Smart Healthy Aging Services in Dalian under the Context of Integrated Medical and Elderly Care**

Yin Cong

- 143 Diabetes with Viral Pneumonia: Epidemiological Characteristics, Pathophysiological Mechanisms, and Clinical Management Strategies**

Zhengmei Qian, Xiaoxuan Chen, Ruilin Sun

- 151 Research on the Mechanism of Action of Traditional Chinese and Western Medicine and the Course of Treatment for Shenrongbian Pills in the Treatment of Impotence and Premature Ejaculation**

Chunlei Chen , Wei Yang, Bei Zhang, Zheng Li

C

ONTENTS

158 Glymphatic System Impairment in Type 2 Diabetes Mellitus Associated with Cognitive Function

Jie Gao, Peichun Pan, Jing Li, Bingqian Gao, Dongsheng Zhang, Min Tang, Xuejiao Yan, Kai Ai, Xiaoyan Lei, Zhongwei Liu, Yuming Zhang, Xiaoling Zhang

168 Efficacy of External High-Frequency Hyperthermia Combined with Circulating Hyperthermic Perfusion Chemotherapy in the Treatment of Malignant Pleural and Peritoneal Effusions

Aerhengbieke·Tuhanbai, Zixuan Wang, Guohui Sun

Efficacy and Clinical Safety Study of Rabeprazole Combined with Amoxicillin Dual Therapy for Type 2 Diabetes Mellitus Patients with *Helicobacter pylori* Infection

Xiaofang Wu*

Community Health Service Center, Huanzhu Longquan Street, Huzhou 313000, Zhejiang, China

*Author to whom correspondence should be addressed.

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical efficacy, safety, and impact on inflammatory factor levels of rabeprazole combined with amoxicillin dual therapy in the treatment of patients with type 2 diabetes mellitus (T2DM) and *Helicobacter pylori* (Hp) infection, providing a reference for clinical treatment. *Methods:* A total of 526 patients with T2DM and Hp infection who were treated in our hospital from January 2022 to December 2024 were selected as the study subjects. Among them, 33 patients withdrew due to allergies or other reasons, and 493 patients completed the treatment. They were divided into a control group (n = 246) and an observation group (n = 247) using a random number table method. The control group received quadruple therapy, while the observation group received high-dose dual therapy. The general information, clinical efficacy, serum interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), hypersensitive C-reactive protein (hs-CRP), Hp eradication rate, recurrence rate, and incidence of adverse reactions were compared between the two groups. *Results:* After treatment, the indicators of both groups improved compared to before treatment. The observation group showed significant advantages in various indicator improvements: In terms of clinical efficacy, the observation group (95.144%) was significantly better than the control group (83.74%) ($\chi^2 = 16.982$, $P = 0.000 < 0.001$). Regarding inflammatory factor levels, IL-6, TNF- α , and hs-CRP levels decreased more significantly in the observation group compared to the control group ($P = 0.000 < 0.001$). In terms of Hp eradication rate and recurrence rate, the Hp eradication rate was higher in the observation group than in the control group ($\chi^2 = 14.481$, $P = 0.000 < 0.001$), and the recurrence rate was lower ($\chi^2 = 32.740$, $P = 0.000 < 0.001$). In terms of safety, the incidence of adverse reactions (4.04%) was lower in the observation group than in the control group (14.63%) ($\chi^2 = 16.325$, $P = 0.000 < 0.01$). *Conclusion:* Rabeprazole combined with amoxicillin dual therapy is effective in the treatment of patients with T2DM and Hp infection. It can effectively reduce inflammatory factor levels, improve the Hp eradication rate, reduce recurrence, and has high safety. It is worthy of clinical promotion and application.

Keywords: Rabeprazole; Amoxicillin; Dual therapy; Quadruple therapy; Type 2 diabetes mellitus; *Helicobacter pylori*

Online publication: September 26, 2025

1. Introduction

Helicobacter pylori (Hp) is a common worldwide chronic infectious disease that is closely related to the pathogenesis of various gastrointestinal diseases such as gastritis, peptic ulcer, and gastric cancer^[1]. Type 2 diabetes mellitus (T2DM) is a metabolic disease in which patients often experience long-term hyperglycemia, leading to decreased immune function

and damage to the gastrointestinal mucosal barrier, making them susceptible to Hp infection. Additionally, Hp infection may worsen diabetes through various mechanisms, such as affecting gastrointestinal hormone secretion and disrupting glucose metabolism, creating a vicious cycle. Therefore, early and efficient eradication of Hp is crucial for improving the prognosis of patients with T2DM and concomitant Hp infection. Currently, quadruple therapy is the primary treatment for Hp. Although it has a certain therapeutic effect, it faces challenges such as multiple medications, long treatment courses, poor patient compliance, high incidence of side effects, and the potential for drug resistance. Given the increasing problem of antibiotic resistance, finding an efficient, safe, and simple treatment method is a current research focus. Rabeprazole, a new type of proton pump inhibitor, can effectively block gastric acid secretion and provide favorable conditions for the bactericidal effect of antibiotics in the stomach. Amoxicillin is a broad-spectrum antibiotic that has a good inhibitory effect on Hp. The combination of these two drugs forms a dual therapy that is simple to administer and has good patient compliance^[2]. This study compares the efficacy and safety of dual therapy with conventional quadruple therapy in the treatment of T2DM with concomitant Hp infection, aiming to provide new ideas for its clinical treatment.

2. Materials and methods

2.1. General Information

This study is a prospective investigation that enrolled 526 patients with T2DM combined with *Helicobacter pylori* infection who were treated in our hospital from January 2022 to December 2024. Among them, 33 withdrew due to allergies or other reasons, leaving 493 patients who completed the treatment. They were randomly divided into a control group ($n = 246$) and an observation group ($n = 247$) using a random number table method.

Inclusion criteria: (1) Meet the diagnostic criteria for type 2 diabetes established by the World Health Organization (WHO); (2) Confirmed diagnosis of Hp infection through urea breath test, rapid urease test of gastric mucosa biopsy, or pathological examination; (3) Age between 18–75 years old; (4) Voluntary participation in this study with signed informed consent.

Exclusion criteria: (1) Used antibiotics, proton pump inhibitors, bismuth agents, or other drugs that affect Hp detection or treatment in the past month; (2) Have severe cardiac, liver, kidney, or other important organ dysfunction; (3) Presence of severe gastrointestinal diseases such as gastrointestinal bleeding, perforation, or obstruction; (4) Allergic to the medications used in this study; (5) Pregnant or breastfeeding women; (6) Have mental illness, unable to cooperate with treatment and follow-up.

2.2. Methods

The control group received quadruple therapy, specifically rabeprazole enteric-coated tablets (10 mg/time, 2 times/day) + bismuth potassium citrate (220 mg/time, 2 times/day) + amoxicillin (1 g/time, 2 times/day) + clarithromycin (0.5 g, 2 times/day). Rabeprazole and bismuth potassium citrate were taken 30 minutes before meals, while amoxicillin and clarithromycin were taken after meals. The treatment course was 14 days.

The observation group was treated with high-dose dual therapy, specifically rabeprazole (10 mg/time, 4 times/day) + amoxicillin (0.75 g/time, 4 times/day), both taken 30 minutes before meals. The treatment course was also 14 days. During the treatment, both groups maintained their original diabetes treatment regimens and received dietary guidance to avoid spicy and stimulating foods, smoking, and alcohol consumption.

2.3. Observation indicators

- (1) General information: Record the gender, average age, and disease duration of the two groups.
- (2) Treatment effect: Four weeks after the treatment, the urea breath test was used to detect Hp infection, and the treatment effect was evaluated based on the improvement of clinical symptoms. Markedly effective: Complete resolution of clinical symptoms and negative urea breath test; Effective: Significant relief of clinical symptoms

and negative urea breath test; Ineffective: No improvement or worsening of clinical symptoms and positive urea breath test.

- (3) Inflammatory factor levels: Collect 5ml of fasting venous blood from patients in both groups before and after treatment. Use enzyme-linked immunosorbent assay (ELISA) to detect serum interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and high-sensitivity C-reactive protein (hs-CRP) levels.
- (4) Hp eradication rate and recurrence rate: Detect Hp eradication four weeks after treatment. The criterion for Hp eradication is a negative urea breath test. Six months after treatment, re-test for Hp infection and calculate the recurrence rate.
- (5) Incidence of adverse reactions: Monitor adverse reactions such as nausea, vomiting, abdominal distension, loss of appetite, bitter taste in the mouth, belching, and peripheral neuropathy during treatment in both groups.

2.4. Statistical methods

Analyze the data using SPSS 27.0 statistical software. Normally distributed measurement data are expressed as mean \pm standard deviation (SD), and paired *t*-tests are used for intra-group comparisons. Count data are expressed as [n(%)], and chi-square tests are used for inter-group comparisons. A *P*-value < 0.05 is considered statistically significant.

3. Results

3.1. Comparison of general information between the two groups

There were no statistically significant differences in age, gender, or disease duration between the two groups ($P > 0.05$). See **Table 1** for details.

Table 1. Comparison of general information between the two groups

Group	Number of cases (<i>n</i>)	Age (mean \pm SD, years)	Gender (Male/Female)	Disease duration (years)
Control group	246	47.21 \pm 4.38	126/120	5.18 \pm 1.31
Observation group	247	47.25 \pm 4.39	128/119	5.11 \pm 1.29
χ^2/t value		0.101	0.018	0.598
<i>p</i> -value		0.919	0.894	0.550

3.2. Comparison of treatment effects between the two groups

Compared with the control group, the total clinical effective rate of the observation group (95.144%) was better than that of the control group (83.74%) ($\chi^2 = 16.982$, $P = 0.000 < 0.001$). See **Table 2**.

Table 2. Comparison of clinical efficacy between two groups

Group	Markedly effective	Effective	Ineffective	Total clinical effectiveness rate
Control Group (<i>n</i> = 246)	84 (34.15%)	122 (49.59%)	40 (16.26%)	206 (83.74%)
Observation Group (<i>n</i> = 247)	150 (60.73%)	85 (34.41%)	12 (4.86%)	235 (95.14%)
χ^2 value				16.982
<i>p</i> -value				< 0.001

3.3. Comparison of inflammatory factor levels between the two groups

After treatment, the levels of IL-6, TNF- α , and hs-CRP decreased in both groups, but the decrease was more significant in the observation group ($P = 0.000 < 0.001$). See **Table 3**.

Table 3. Comparison of inflammatory factor levels between two groups

Group	IL-6 (pg/mL)		TNF- α (pg/mL)		hs-CRP (mg/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control group ($n = 246$)	8.63 ± 3.25	4.59 ± 1.82	9.46 ± 2.43	7.35 ± 1.34	12.48 ± 2.37	8.21 ± 1.87
Observation group ($n = 247$)	8.64 ± 3.26	3.90 ± 1.15	9.48 ± 2.49	6.21 ± 1.01	12.51 ± 2.40	6.35 ± 1.48
t -value	0.03	5.034	0.090	10.669	0.140	12.248
p -value	0.973	< 0.001	0.928	< 0.001	0.	

3.4. Comparison of Hp eradication rate and recurrence rate between the two groups

After treatment, the Hp eradication rate in the observation group was significantly higher than that in the control group ($95.95 > 86.18$), and the 1-year recurrence rate was lower than that in the control group ($4.05\% < 21.14\%$). See **Table 4**.

Table 4. Comparison of Hp eradication rate and recurrence rate between the two groups

Group	Hp eradication rate	1-year recurrence rate
Control group ($n = 246$)	212 (86.18%)	52 (21.14%)
Observation group ($n = 247$)	237 (95.95%)	10 (4.05%)
χ^2 value	14.481	32.740
p -value	0.000	0.000

3.5. Comparison of adverse reaction rates between the two groups

Compared with the control group, the total incidence of adverse reactions in the observation group (4.04%) was lower than that in the control group (14.63%) ($\chi^2 = 16.325$, $P = 0.000 < 0.01$). See **Table 5**.

Table 5. Comparison of adverse reactions between the two groups

Group	Nausea & vomiting	Abdominal distension	Decreased appetite	Bitter taste	Belching	Peripheral neuritis	Total adverse reaction rate
Control group ($n = 246$)	8 (3.25%)	3 (1.22%)	5 (2.03%)	6 (2.44%)	8 (3.25%)	6 (2.44%)	36 (14.63%)
Observation group ($n = 247$)	1 (0.01%)	0	1 (1.01%)	1 (1.01%)	1 (1.01%)	0	10 (4.04%)
χ^2 value							16.325
p -value							0.000

4. Discussion

T2DM is a metabolic disease caused by genetic and environmental factors^[3]. Oxidative stress and inflammatory reactions caused by long-term hyperglycemia can damage multiple systems in the body, leading to the occurrence of infections.

Helicobacter pylori is a microaerobic Gram-negative bacterium that invades the gastric mucus layer through its unique helical structure and flagellar movement, forms infections on the surface of gastric mucosal epithelium, induces inflammatory reactions, and causes diseases such as gastritis, peptic ulcer, and even gastric cancer ^[4]. Epidemiological investigations have found that compared with the general population, diabetics have a significantly higher rate of Hp infection due to their weakened immune function and gastrointestinal motility disorders ^[5]. Furthermore, the chronic inflammation caused by Hp infection leads to the production of many inflammatory factors in the body, disrupting the body's insulin signaling pathway, exacerbating insulin resistance, and thereby affecting blood glucose control levels. Therefore, eliminating Hp infection is the key to the treatment of type 2 diabetes.

Quadruple therapy is currently the most commonly used treatment method. Rabeprazole, a novel proton pump inhibitor, can specifically target the H⁺/K⁺-ATP enzyme in gastric parietal cells, inhibiting gastric acid secretion and increasing the pH level in the stomach. This provides a favorable environment for antibiotics to exert their bactericidal effects. In an acidic environment, bismuth potassium citrate can generate bismuth salt-protein complexes that cover the surface of the gastric mucosa, offering protective effects, and it also exhibits antibacterial activity against Hp ^[6]. Amoxicillin and clarithromycin achieve the elimination of *Helicobacter pylori* by disrupting cell wall synthesis and inhibiting protein synthesis, respectively. However, in recent years, due to the extensive use of antibiotics, the resistance of *Helicobacter pylori* to clarithromycin, metronidazole, and other drugs has been increasing year by year, which has become a significant factor contributing to the failure of quadruple therapy to eradicate Hp infection. Additionally, the variety of quadruple therapy drugs and the frequent dosing lead to low patient compliance, and the combination of multiple drugs can cause side effects such as nausea, vomiting, abdominal distension, and decreased appetite, thereby adversely affecting the efficacy and quality of life of patients ^[7].

In high-dose dual therapy, the active metabolite of rabeprazole has more binding sites and stronger affinity for the H⁺/K⁺-ATP enzyme, enabling faster and more sustained inhibition of gastric acid secretion. This maintains a higher pH level in the stomach for a prolonged period, significantly enhancing the antibacterial activity of amoxicillin ^[8]. Amoxicillin belongs to the class of β -lactam antibiotics, and its antibacterial activity is enhanced in a near-neutral environment, exerting a bactericidal effect by inhibiting bacterial cell wall synthesis. The high-dose and high-frequency application of amoxicillin can increase its duration of action in the stomach and elevate its concentration in the body, thereby enhancing the clearance of Hp. The use of high-dose dual therapy in Hp infection is gradually increasing. Numerous studies have demonstrated that this approach yields high cure rates with few side effects, both in initial treatment and rescue therapy.

Previous research has confirmed the advantages of high-dose dual therapy in improving the effectiveness of Hp infection treatment. The results of this study indicate that the efficacy of the observation group was significantly better than that of the control group. This is primarily due to the continuous and potent inhibition of gastric acid secretion by high-dose rabeprazole, which provides a favorable gastric microenvironment for amoxicillin to exert its bactericidal effects, enhancing its ability to kill Hp and subsequently improving the clinical manifestations of patients. Complete eradication of Hp can significantly reduce inflammatory responses in the body and improve the inflammatory status of patients ^[9]. High-dose dual therapy can more thoroughly eradicate Hp, alleviate inflammatory reactions induced by pathogenic bacteria and virulence factors, and further inhibit the secretion of inflammatory cytokines. This is consistent with the research conclusions presented in this article. Additionally, the Hp eradication rate in the observation group was significantly higher than that in the control group, and the recurrence rate was also significantly lower. This is because high-dose dual therapy effectively addresses the challenge of resistance development encountered in conventional quadruple therapy, optimizing the dose of proton pump inhibitors and the frequency of amoxicillin administration. Complete eradication of Hp effectively reduces the risk of bacterial remnants and secondary infections, thereby decreasing the recurrence rate. Numerous previous studies have confirmed the safety of dual therapy ^[10]. This is attributed to the relatively fewer types of drugs used in high-dose dual therapy, which reduces the risk of drug interactions and adverse reactions. Simultaneously, the simplicity of the high-dose dual therapy regimen enhances patient compliance, further decreasing the probability of adverse reactions caused by missed or incorrect drug administration.

5. Conclusion

In summary, the combination of rabeprazole and amoxicillin as a dual therapy for the treatment of T2DM patients with concurrent Hp infection demonstrates significant efficacy. It effectively reduces inflammatory cytokine levels, improves the Hp eradication rate, reduces recurrence, and exhibits high safety. This approach is worthy of clinical promotion and application.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wu H, Li X, Chen M, 2024, Clinical Effect of Modified Shenling Baizhu Powder Combined with High-Dose Dual Therapy in the Treatment of Spleen Deficiency Type Helicobacter pylori Infection. *Rational Drug Use in Clinic*, 17(31): 86–89.
- [2] Wang N, Xie Q, 2024, Research Progress on the Treatment of Helicobacter pylori Infection. *Medical Innovation of China*, 21(32): 184–188.
- [3] Yang L, Chen Y, 2024, Application Effect of Anti-Hp Quadruple Therapy in Diabetic Patients with Hp Infection and Its Influence on Serum Inflammatory Factor Levels. *Clinical Medical Research and Practice*, 9(29): 55–58.
- [4] Huang H, Wang H, Li X, et al., 2024, Effects of Quadruple Therapy and High-Dose Dual Therapy on Helicobacter pylori Eradication Rate and Recurrence Rate. *Medical Innovation of China*, 21(26): 141–144.
- [5] Wu X, Ren H, Yang Y, et al., 2024, Research Progress on the Impact of Helicobacter pylori Infection on Type 2 Diabetes. *Shanghai Medical Journal*, 45(14): 17–21.
- [6] Zhao Q, Liu X, Chen J, 2024, The Effect of Quadruple Therapy on Helicobacter pylori Eradication Rate and Inflammatory Factor Levels in Patients with Helicobacter pylori-Associated Gastric Ulcer. *Primary Medical Forum*, 28(33): 54–57.
- [7] Zhou J, 2024, Analysis of the Efficacy of Lansoprazole and Amoxicillin Dual Therapy in the Treatment of Helicobacter pylori-Associated Chronic Gastritis. *China Practical Medicine*, 19(08): 111–113.
- [8] Mao M, 2022, Clinical Effect of Quadruple Therapy with Esomeprazole Magnesium Enteric-Coated Tablets in the Treatment of Helicobacter pylori-Associated Gastric Ulcer. *Journal of Clinical Rational Drug Use*, 15(19): 81–83.
- [9] Li M, Zhu Z, 2024, Comparison of the Efficacy of High-Dose Dual Therapy and Classic Quadruple Therapy in Eradicating Helicobacter pylori. *Chinese Journal of Modern Drug Application*, 18(11): 108–110.
- [10] Lin C, Liu Y, Zhong P, et al., 2024, Effects of High-Dose Dual Therapy for Helicobacter pylori Eradication on Intestinal Microecology and the Intervention Effect of Corresponding Probiotics. *Jilin Medical Journal*, 45(10): 2447–2450.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Therapeutic Effect of Nasal Continuous Positive Airway Pressure Ventilation on Severe Pneumonia Complicated with Respiratory Failure in Children

Xin Guo, Xusheng Qi*

Pediatric Outpatient Department, Taihe Hospital of Shiyan City (Affiliated Hospital of Hubei University of Medicine), Shiyan 442000, Hubei, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical effect of nasal continuous positive airway pressure (nCPAP) in children with severe pneumonia complicated with respiratory failure. *Methods:* 80 children were randomly divided into a control group and an observation group, 40 cases in each group. The control group was given routine treatment, and the observation group was given nCPAP intervention. The changes of oxygenation index, ventilation efficiency, respiratory load and inflammatory index were compared between the two groups. *Results:* After treatment, A-ADO decreased significantly, $\text{PaO}_2/\text{FiO}_2$ and Cdyn increased, PaCO_2 decreased, pH increased, VE and VT improved, and f/VT decreased in the observation group. The ratio of CRP, PCT, WBC and neutrophil was significantly lower than that of the control group, with statistical significance ($P < 0.05$). *Conclusion:* nCPAP can effectively improve lung oxygenation, ventilation function and inflammatory state, reduce respiratory load, and promote recovery of children, and its clinical application value is significant.

Keywords: Transnasal; Continuous positive airway pressure ventilation; Severe pneumonia in children; Respiratory failure; Observation of curative effect

Online publication: September 26, 2025

1. Introduction

Severe pneumonia is a common acute respiratory disease in children. The course of the disease progresses rapidly, often accompanied by significant ventilation disorder, which easily leads to hypoxemia and carbon dioxide retention, leading to acute respiratory failure. Because of poor lung compliance and weak compensatory ability, respiratory load and unstable vital signs often appear in the clinic ^[1]. As a noninvasive and well-tolerated ventilation method, nasal continuous positive airway pressure (nCPAP) can effectively maintain alveolar opening and improve oxygenation function, and it is increasingly widely used in pediatric severe respiratory support ^[2]. How to accurately apply nCPAP in the acute phase and explore its mechanism, timing, and individual response law is the key direction of current research.

2. General information and methods

2.1. General information

Eighty children with severe pneumonia complicated with respiratory failure who were treated in our hospital from December 2023 to December 2024 were included. The children ranged in age from 6 months to 12 years old, with an average of (4.87–2.15) years old, including 45 male children and 35 female children. All of them were diagnosed as severe pneumonia by clinical diagnosis and imaging examination, and showed symptoms of respiratory failure to different degrees. According to the difference in treatment methods, the children were randomly divided into the control group and the observation group, with 40 cases in each group. The control group received conventional oxygen inhalation, anti-infection, and symptomatic support treatment, while the observation group received additional nasal continuous positive airway pressure treatment based on the control group. There was no statistical difference between the two groups in terms of gender, age and severity of illness ($P > 0.05$), which was comparable.

Inclusion criteria:

- (1) Children between 6 months and 12 years old, regardless of sex.
- (2) Severe pneumonia was diagnosed by clinical manifestations, chest imaging (X-ray or CT) and laboratory examination.
- (3) Combined with type I or type II respiratory failure, which accords with the Diagnostic Criteria for Respiratory Failure in Children.
- (4) The patient's condition is stable and his consciousness is clear, and he has the basic conditions to cooperate with nasal continuous positive airway pressure (nCPAP) treatment.
- (5) Interventional treatment was started within 48 hours after admission, with complete clinical follow-up data.

Exclusion criteria:

- (1) Congenital cardiopulmonary malformation, severe cardiac insufficiency or other serious basic diseases affect the curative effect evaluation.
- (2) Patients with nCPAP contraindications such as pneumothorax, mediastinal emphysema, severe upper respiratory tract obstruction or active bleeding.
- (3) Children who are in urgent need of invasive mechanical ventilation or have been treated with tracheal intubation.
- (4) Nervous system diseases such as status epilepticus and disturbance of consciousness.
- (5) Have a history of repeated lung infections or chronic lung diseases.

2.2. Methods

2.2.1. Control group

The children in the control group were treated with routine comprehensive treatment, including continuous low-flow nasal catheter oxygen inhalation to ensure the smooth breathing of the children; Anti-infection treatment can effectively resist the invasion of germs on children's bodies; Relieve fever and pain, and relieve the discomfort of children; Bronchial relaxation helps children's respiratory tract unobstructed; Sucking and expelling phlegm to keep the respiratory tract clean; A series of general symptomatic support measures such as water and electrolyte balance adjustment, ensuring the stability of children's internal environment, and nutritional support.

2.2.2. Observation group

Based on the basic treatment plan of the control group, the observation group was additionally treated with nasal continuous positive airway pressure (nCPAP), and its specific operation mode was as follows:

- (1) Equipment preparation and interface selection: Use a special double-pipe nCPAP device for infants, and match the nasal plug to ensure good airtightness and prevent air leakage.
- (2) Parameter setting and dynamic adjustment: the initial pressure is 4–6 cm H₂O, and the maximum pressure does not exceed 8 cm H₂O; The oxygen concentration is set to 40% and dynamically adjusted to maintain 92–96%

according to SpO₂.

- (3) Ventilation duration and monitoring frequency: ventilation should be no less than 6 hours per day, and intermittent ventilation should be decided according to the fatigue degree and blood gas condition. Vital signs (SpO₂, respiratory rate, heart rate) were recorded every 4 hours.
- (4) Prevention of skin and complications: Strengthen nasal care to prevent pressure sores, and clean oral cavity to prevent common complications such as nosebleeds and bloating.
- (5) Standard and transition of weaning: When the SpO₂ is stable $\geq 95\%$, the respiratory frequency is normal and there is no obvious respiratory distress, gradually decompress and switch to low-flow oxygen therapy.
- (6) Efficacy evaluation: Blood gas, SpO₂ and respiratory rate were evaluated before treatment, 48 hours later and before weaning, and the hospitalization days and complications were recorded ^[3].

2.3. Observation indicators

2.3.1. Pulmonary oxygenation and ventilation efficiency index

- (1) Alveolar-arterial oxygen pressure difference (A-ADO) to evaluate the improvement of oxygenation disorder and reflect alveolar gas diffusion efficiency.
- (2) Partial arterial oxygen pressure (PAO) and its ratio (PaO₂/FiO₂).
- (3) Dynamic lung compliance (C_{dyn}), combining with the pressure waveform to evaluate the ventilation elasticity of lung tissue, and to judge the effect of nCPAP on lung dilation mechanics.

2.3.2. Gas exchange and acid-base state adjustment index

- (1) Arterial partial pressure of carbon dioxide (PaCO₂)
- (2) Blood pH and bicarbonate concentration (HCO)
- (3) Dynamic change trend of respiratory quotient (RQ).

2.3.3. respiratory system load response index

- (1) Ventilatory volume per minute (VE) and tidal volume (VT)
- (2) Respiratory frequency-tidal volume ratio (f/VT)
- (3) Auxiliary respiratory index score.

2.3.4. Inflammatory state and systemic response index

- (1) The changes of C-reactive protein (CRP) and procalcitonin (PCT) levels can be used to evaluate the control trend of pulmonary infection.
- (2) White blood cell count and neutrophil ratio can reflect the differences in immune response between acute infection and recovery.
- (3) Combine the actual temperature data to describe the inflammatory reaction cycle, and get the temperature change curve and thermal range length.

2.4. Statistical methods

The data were analyzed by SPSS 28.0. The measurement data were expressed by mean \pm standard deviation (SD), the counting data by rate, and the difference was statistically significant if $P < 0.05$.

3. Results

3.1. Compare the lung oxygenation and ventilation efficiency between the two groups

From Table 1, it can be seen that the A-ADO of the observation group decreased obviously after 48 hours of treatment and

before weaning, while the $\text{PaO}_2/\text{FiO}_2$ and Cdyn showed a great upward trend. These three indexes were better than those of the control group, and the difference between them was statistically significant ($P < 0.05$).

Table 1. Pulmonary oxygenation and ventilation efficiency in two groups of children

Index	Alveolar-arterial oxygen pressure difference (a-ado, mmHg)			$\text{PaO}_2/\text{FiO}_2$ ratio (mmHg)			Pulmonary dynamic compliance cdyn (mL/cm H_2O)		
	Before treatment	Treatment for 48 hours	Before aircraft withdrawal	Before treatment	Treatment for 48 hours	Before aircraft withdrawal	Before treatment	Treatment for 48 hours	Before aircraft withdrawal
Control group (mean \pm SD)	62.14 \pm 6.83	48.36 \pm 6.25	40.74 \pm 5.87	164.25 \pm 18.41	215.83 \pm 21.65	244.11 \pm 23.08	0.82 \pm 0.14	1.12 \pm 0.16	1.21 \pm 0.17
Observation group (mean \pm SD)	62.39 \pm 6.77	38.22 \pm 5.91	32.83 \pm 5.44	163.76 \pm 17.93	278.34 \pm 22.17	304.29 \pm 20.94	0.84 \pm 0.15	1.45 \pm 0.18	1.58 \pm 0.19
<i>t</i> value	1.248	12.476	11.139	1.357	13.938	14.273	1.118	10.774	11.835
<i>P</i> value	< 0.05								

3.2. Compare the gas exchange and acid-base state adjustment between the two groups

From **Table 2**, it can be found that after 48 hours of treatment, the PaCO_2 of the children in the observation group decreased, the pH value increased, and the HCO_3^- level became more stable. The improvement rate of ventilation and the compliance rate of internal environment regulation in the observation group were better than those in the control group. Nasal continuous positive airway pressure ventilation can effectively improve the ventilation function and internal environment stability ($P < 0.05$).

Table 2. Analysis of gas exchange and acid-base state adjustment in two groups of children

Index	Partial pressure of arterial blood carbon dioxide (PaCO_2 , mmHg)	Blood pH value	Bicarbonate concentration (HCO , mmol/L)	Dynamic trend of Respiratory Quotient (RQ)	The number of cases with improved ventilation ($\text{SPO} > 92\%$, RR close to normal)	Number of cases of internal environment adjustment reaching the standard ($\text{PaCO}_2\downarrow$, pH normal range)
Control group ($n = 40$)	45.13 \pm 4.76	7.29 \pm 0.05	24.25 \pm 2.08	0.77 \pm 0.06	27 cases (67.50%)	25 cases (62.50%)
Observation group ($n = 40$)	38.92 \pm 3.64	7.36 \pm 0.03	22.51 \pm 1.67	0.85 \pm 0.05	36 cases (90.00%)	35 cases (87.50%)
<i>t</i> value	11.734	10.589	10.021	9.883	8.327	6.839
<i>P</i> value	< 0.05					

3.3. Compare the respiratory system load response index between the two groups

As can be seen from **Table 3**, after 48 hours of treatment, the ventilation volume and tidal volume of the observation group are significantly higher than those of the control group, and the f/VT ratio is lower, and the number of cases of assisted breathing signs is also more, with statistical significance, which means that nCPAP can effectively reduce the respiratory load and improve the ventilation function ($P < 0.05$).

Table 3. Responsive indexes of respiratory system load in two groups of children

Index	Ventilation per minute (VE, L/min)	Tidal volume (VT, mL)	Respiratory frequency- tidal volume ratio (f/ VT)	Improvement rate of auxiliary respiratory signs (%)
Control group (<i>n</i> = 40)	6.82 ± 0.91	205.3 ± 25.6	0.338 ± 0.057	25 cases (62.50%)
Observation group (<i>n</i> = 40)	8.13 ± 0.86	243.8 ± 27.2	0.294 ± 0.042	35 cases (87.50%)
<i>t</i> value	11.327	9.863	10.237	6.472
<i>P</i> value	< 0.05			

3.4. Compare the inflammatory status and systemic response index between the two groups

Table 4 shows that the CRP, PCT, WBC and neutrophil ratio of children in the observation group are significantly lower than those in the control group, suggesting that nCPAP can effectively reduce the inflammatory reaction, control the infection process and promote the recovery of children ($P < 0.05$).

Table 4. Inflammatory status and systemic response indexes of two groups of children

Index	C-reactive protein (CRP, mg/L)	Procalcitonin (PCT, ng/mL)	White blood cell count (WBC, × 10/L)	Neutrophil ratio (%)
Control group (<i>n</i> = 40)	27.34 ± 5.63	1.26 ± 0.42	13.45 ± 2.13	76.13 ± 5.84
Observation group (<i>n</i> = 40)	18.96 ± 4.51	0.84 ± 0.35	10.72 ± 1.98	69.41 ± 4.92
<i>t</i> value	10.364	9.256	9.843	9.129
<i>P</i> value	< 0.05			

4. Discussion

As a non-invasive respiratory support method, nasal continuous positive airway pressure (nCPAP) shows multiple clinical advantages in the treatment of severe pneumonia complicated with respiratory failure in children [4]. It can maintain alveolar opening through continuous positive pressure, effectively improve alveolar diffusion disorder and oxygenation function, significantly improve PaO₂/FiO₂ and lung dynamic compliance, and optimize ventilation-blood flow matching. NCPAP can also reduce the compensatory burden of respiratory muscles, improve tidal volume and ventilation efficiency, reduce the f/VT value, improve children's spontaneous breathing ability and reduce the need for tracheal intubation. At the same time, the intervention is helpful to alleviate the pro-inflammatory reaction related to hypoxia, reduce the inflammatory indices such as CRP, PCT and WBC, shorten the thermal course and accelerate the recovery of the focus. The results of this study suggest that nCPAP can be optimized in many aspects, such as lung function, respiratory mechanics and inflammation control, and has a good acute intervention effect and early prevention and control potential [5].

As a non-invasive respiratory support method, nasal continuous positive airway pressure ventilation can comprehensively improve the pathological conditions of children from alveolar ventilation, gas exchange, respiratory mechanics, and inflammation control. This method has obvious advantages in improving lung oxygenation efficiency, stabilizing the acid-base environment, reducing respiratory muscle compensation load, and reducing inflammatory factors. In the future, we can study its synergistic approach with drug intervention and pathogen spectrum control based on larger samples, and provide a reference for the construction of more accurate and safe respiratory management strategies for critically ill children.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wang X, 2024, Study on the Value of Early Continuous Positive Airway Pressure Ventilation in the Treatment of Severe Pneumonia Complicated with Respiratory Failure in Children. *China Disaster Rescue Medicine*, November(9): 1052–1054 + 1078.
- [2] Guo J, Zhang J, 2022, Observation on the Effect of High-Quality Nursing Mode in the Treatment of Severe Pneumonia Complicated with Respiratory Failure in Children by NCPAP. *Guizhou Medicine*, 46(11): 1834–1835.
- [3] Lin Y, 2022, Therapeutic Value of Nasal Continuous Positive Airway Pressure Ventilation in Children with Severe Pneumonia Complicated with Respiratory Failure. *China Modern Drug Application*, 16(7): 28–30.
- [4] Zhou W, Wei S, Zhang X, 2022, Influential Factors of Nasal Continuous Positive Airway Pressure Combined with Gamma Globulin in the Treatment of Severe Pneumonia Complicated with Respiratory Failure in Children. *Chinese Journal of Woman and Child Health Research*, 33(2): 76–80.
- [5] Bai J, Que X, Feng X, 2021, Effect of Whole-Course Responsibility Nursing Mode on Neonates with Severe Pneumonia Complicated with Respiratory Failure Treated by Nasal Continuous Positive Airway Pressure. *Henan Medical Research*, 30(33): 6329–6332.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on the Anti-aging Effect of Golden Rejuvenating Hormone Containing PQQ, Spermidine, Ergothioneine, Cycloastragalol and Cordycepin

Jun Yu*

Guangzhou No-Additive Biotechnology Co., LTD., Guangzhou 510000, Guangdong, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To study the effect of Golden Rejuvenation Hormone on consumers' anti-aging. *Method:* Sixty test subjects from October to December 2024 were selected as the research subjects. They took one bottle of AGEVIVE Rejuvenation Drink before going to bed every day. Through consumer experience tests, anti-aging efficacy tests, etc., the sensory experience and skin test conditions of the test subjects were regularly detected, and the retention test values of the test subjects were statistically analyzed. *Result:* By taking Golden Rejuvenation Hormone containing PQQ, spermidine, ergothioneine, cycloastragalol cordycepin, the telomere length of the test subjects could be effectively maintained, cell vitality could be delayed, and the quality of life of the test subjects could be improved at the same time. The anti-aging effect was significant ($P < 0.05$). *Conclusion:* The golden rejuvenation hormone containing PQQ, spermidine, ergothioneine, cycloastragalol, and cordycepin, which can prolong telomeres, can present a good anti-aging effect. Based on various excellent components, it is conducive to restoring human mitochondria, promoting cell autophagy and repair, and has strong application and promotion value.

Keywords: Pyrroloquinoline quinone; Spermidine; Ergothioneine; Cycloastragalus alcohol; Cordycepin; Telomere

Online publication: September 26, 2025

1. Introduction

With the development of modern society and the intensification of population aging, anti-aging has become a research hotspot in the field of biomedicine, better meeting the current needs of consumers. Telomeres, as protective structures at the ends of chromosomes, gradually shorten in length as cells divide. Once they reach a critical length, cells will enter states such as senescence and apoptosis, and they are one of the cellular bases of human aging. The Golden Rejuvenation Essence is rich in natural components such as PQQ (pyrroquinolinone), spermidine, ergothioneine, cycloastragalone, and cordycepin. Through a synergistic effect, it can effectively extend the telomeres in the human body, thereby delaying the aging process and achieving anti-aging effects. This article aims to study the specific application effects of Golden Rejuvenation Extract, explore the influence mechanisms of various components within it, provide new ideas for research in the field of anti-aging, and promote the innovative development of anti-aging products. The report is as follows.

2. Data and methods

2.1. General information

Sixty test subjects from October to December 2024 were selected as the research subjects. The ratio of female to male was 4:1. The age of the test subjects ranged from 30 to 60 years old, with an average age of (43.67 ± 6.85) years old. 25% had normal skin, 30% had combination skin, 20% had oily skin, 15% had dry skin, and 10% had sensitive skin. The general data of the test subjects had no statistical significance ($P > 0.05$), so the contents of the subsequent studies were comparable.

2.2. Methods

The test subjects should take one vial of AGEVIVE Rejuvenation Drink 30 minutes before going to bed every night. The tests should be conducted on the 1st, 7th, 2nd, 4th, 6th and 8th weeks to analyze the application effect of the Golden Rejuvenation Essence.

2.3. Observation indicators

Develop a consumer sensory experience test. Through questionnaire surveys, collect the test subjects' feelings about the use of AGEVIVE Rejuvenation Drink. The test items include skin anti-aging, improvement of sleep quality, defecation, increase of energy, increase of appetite, increase of skin moisture, whitening, etc. The evaluation indicators include very obvious, relatively obvious, slight improvement, no improvement, deterioration, etc. Only the first three benign indicators were included in the study.

Anti-aging efficacy skin tests were conducted on the test subjects. The detection indicators included the water content of the stratum corneum, skin gloss, brightness of the cheek skin, brightness of pigmentation spots, ITA value of the cheek skin, ITA value of pigmentation spots, smoothness of wrinkles, and roughness of wrinkles etc.

2.4. Statistical methods

Data analysis was performed using SPSS 21.0 statistical software. Quantitative data were expressed as mean \pm standard deviation (SD), and qualitative data were expressed as percentage (%). The 2-test was used for comparison between groups. When $P < 0.05$, it indicates that the data difference was statistically significant.

3. Result

3.1. Sensory experience test results

As can be seen from **Table 1** below, compared with the 1st and 7th days, each efficacy indicator has significantly improved. Moreover, except for the whitening item, the positive evaluation of each other efficacy exceeds 90%, indicating that the test subjects have a good sensory experience.

3.2. Anti-aging efficacy test results

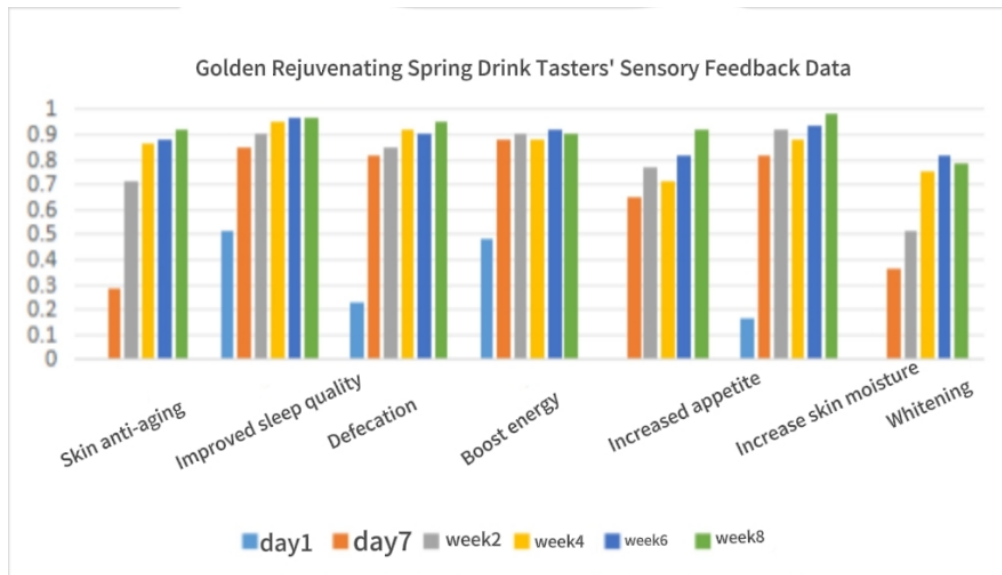
As can be seen from **Table 2** below, after using the AGEVIVE Rejuvenation Drink, the water content of the stratum corneum, gloss, brightness of the cheek skin, brightness of pigmentation spots, ITA value of the cheek skin, and ITA value of pigmentation spots of the test subjects at the 4th and 8th weeks all significantly increased, and the data differences were statistically significant ($P < 0.05$). After using AGEVIVE Rejuvenation Drink, the smoothness of skin wrinkles in the test subjects improved significantly ($P < 0.05$) after the 4th and 8th weeks. The roughness of wrinkles improved to some extent in the 4th week, but not significantly. It was not until the 8th week that a significant improvement was shown ($P < 0.05$).

2.3. Telomere length

As shown in **Table 3** below, based on the comparison of the absolute values of telomere length before and after the test for

Table 1. Test results of the testers' sensory experience

Project	Day 1	Day 7	Week 2	Week 4	Week 6	Week 8
Skin anti-aging	0	28.33%	71.67%	86.67%	88.33%	91.67%
Improved sleep quality	51.67%	85%	90%	95%	96.67%	96.67%
Defecation	23.33%	81.67%	85%	91.67%	90%	95%
Boost energy	48.33%	88.33%	90%	88.33%	91.67%	90%
Increased appetite	0	65%	76.67%	71.67%	81.67%	91.67%
Increase skin moisture	16.67%	81.67%	91.67%	88.33%	93.33%	98.33%
Whitening	0	36.67%	51.67%	75%	81.67%	78.33%

**Figure 1.** Golden rejuvenating spring drink tasters' sensory feedback data.**Table 2.** Test results of the anti-aging efficacy of the test subjects

Indicator	Day 1	Week 4	Week 8
The water content of the stratum corneum	36.28 ± 2.49	44.93 ± 2.45**	49.65 ± 2.44**
Skin luster	5.87 ± 0.29	6.77 ± 0.37**	7.43 ± 0.36**
Cheek skin brightness	58.67 ± 0.85	59.91 ± 0.80*	61.78 ± 0.79**
The brightness of the color spot	57.57 ± 1.05	58.64 ± 1.02*	59.99 ± 1.00**
The ITA values of cheek skin	26.89 ± 2.16	29.76 ± 1.15**	34.79 ± 2.03**
The ITA values of the pigmentation spots	22.50 ± 2.68	24.41 ± 1.57*	27.39 ± 2.13**
Wrinkle smoothness	2.21 ± 0.48	1.89 ± 0.38*	1.65 ± 0.35**
Wrinkle roughness	39.38 ± 7.94	37.15 ± 6.01	35.44 ± 5.08*

Note: Compared with the first day, * $P < 0.05$, ** $P < 0.005$

Table 3. Telomere test data table before and after the test

Number	Test the front-end particle length (bp)	Ranking of the same age group	Test the telomere length for 3 months (bp)	Ranking of the same age group
1	5554	66%	5613	75%*
2	5907	81%	5989	85%*
3	7076	84%	7023	79%
4	7488	76%	7566	81%*
5	7194	75%	7158	74%
6	6747	64%	6815	70%*
7	8751	72%	8824	78%*
8	8343	63%	8379	65%*
9	7016	71%	6971	66%
10	6094	77%	6154	82%*
11	8329	78%	8347	79%*
12	6132	62%	6048	58%
13	5880	69%	5917	71%*
14	8134	75%	8169	78%*
15	7755	59%	7694	54%
16	7529	69%	7570	72%*
17	5700	58%	5753	65%*
18	6763	61%	6700	55%
19	7956	87%	8026	95%*
20	7037	76%	6988	71%
21	8685	89%	8730	93%*
22	8145	85%	8180	89%*
23	8359	81%	8430	88%*
24	6759	77%	6692	68%
25	7977	79%	8008	83%*
26	5977	67%	6014	72%*
27	7513	78%	7554	83%*
28	8379	73%	8460	82%*
29	8816	91%	8867	94%*
30	5901	67%	5840	60%
31	6798	79%	6749	73%

Note: Compared with the first day, * $P < 0.05$

the 31 test subjects, 67.74% of the test subjects saw an increase in telomere length after using AGEVIVE Rejuvenation Drink. Among the same age group, the rate of telomere length exceeding was significantly increased, indicating that Golden Rejuvenation Extract has a promoting effect on telomere length in the human body. And the data differences were statistically significant ($P < 0.05$).

3. Discussion

As a cofactor of REDOX enzymes, PQQ will directly affect mitochondrial biosynthesis and functional maintenance, and thereby influence the rate of telomere decay. From the molecular level, the natural component PQQ is conducive to activating peroxisome proliferators, which in turn activate PGC-1 α (receptor γ coactivator), affecting mitochondrial biosynthesis^[1]. The activated PGC-1 α interacts with nuclear respiratory factors such as NRF1 and NRF2, promoting the expression of TFAM (mitochondrial transcription factor A), facilitating the combination of TFAM with mtDNA (mitochondrial DNA) to form a certain regulatory region, thereby driving the replication and transcription of mtDNA and achieving an increase in the number of mitochondria. Meanwhile, PQQ is also beneficial for increasing the frequency of the mitochondrial respiratory chain, thereby enhancing the ATP generation capacity of cells, providing sufficient energy for cell metabolism, and delaying the rate of cell attenuation^[2]. At the antioxidant defense level, PQQ can activate the NRF2-ARE signaling pathway, induce the expression of antioxidant enzymes within cells, simultaneously disrupt the binding of Nrf2 and Keap1, accelerate the transcription of antioxidant enzymes, further enhance the cell's ability to clear reactive oxygen species such as silver superoxide ions, maintain the stability of the intracellular environment, and play a certain role in anti-aging.

Pyrroloquinoline quinone (PQQ) is naturally found in some foods and is available as a dietary supplement in its disodium crystal form. The potential health benefits of PQQ have been studied, considering its antioxidant and anti-inflammatory properties. Furthermore, PQQ has been demonstrated to significantly influence the functions of mitochondria, the organelles responsible for energy production within cells, and their dysfunction is associated with various health conditions, including obesity complications^[3].

The anti-aging effect of spermidine is reflected in inducing autophagy and regulating senescence-related signaling pathways. Autophagy, as a mechanism for teaching cells to degrade and recycle, with the help of spermidine, is conducive to activating autophagy-related protein complexes, initiating the autophagy process, and promoting the nucleation and extension of autophagosome membranes^[4]. In addition, spermidine can further inhibit the activity of mTORC1 (mammalian target of rapamycin complex 1), relieve the inhibitory effect of this complex on the autophagy initiation protein ULK1, thereby accelerating the occurrence of autophagy. During the process of autophagy in cells, damaged organelles, such as mitochondria and misfolded protein aggregates, are encapsulated to form autophagosomes^[5]. After combining with lysosomes, autophagolysosomes are formed, thereby maintaining the stability of the intracellular environment^[6]. In the regulation of aging signals, spermidine can down-regulate the expression of aging-related proteins, such as p53, p16INK4a, etc. Among them, p53, as a key regulatory protein of the cell cycle, will accelerate cell aging when overly activated. Spermidine can effectively reduce the transcriptional activity of p53 and decrease the expression of downstream aging-related genes by inhibiting the acetylation modification of p53, presenting a certain anti-aging effect. As an inhibitor of CDK (cyclin-dependent kinase), p16INK4a inhibits the binding of CDK4/6 to cyclin D, leading to cell cycle arrest and accelerating its decline^[7]. Spermidine, based on the epigenetic regulatory mechanism, can effectively reduce the methylation level of the p16INK4a gene and decrease its expression, thereby enhancing the cell proliferation ability. Achieve the purpose of anti-aging.

Ergothioneine has a unique chemical structure and exhibits superior antioxidant and metal chelating capabilities. It can be specifically transported into cells by OCTN2 (organic cation transporter 2) and achieve high-concentration aggregation of ergothioneine in mitochondria through its active transport function^[8]. As the key site for ROS production within cells, the enrichment of ergothioneine in mitochondria can efficiently eliminate ROS produced by the mitochondrial

respiratory chain, such as superoxide and silver ions, and further inhibit lipid peroxidation of the mitochondrial membrane, thereby ensuring the integrity of the mitochondrial membrane. In addition, ergothioneine, based on its own imidazole structure, can directly react with ROS, promote ROS reduction, and continuously exert antioxidant effects through the action of the cellular reduction system^[9]. In addition to direct antioxidation, ergothioneine can also reduce the generation of extracellular ROS by regulating the activity of NADPH oxidase (NOX). NOX is an important source of extracellular ROS. Under stimuli such as inflammation, NOX is activated, generating a large amount of ROS and triggering oxidative stress^[10]. Ergothioneine can inhibit the expression and assembly of NOX subunits, reduce the activity of NOX, and decrease the generation of ROS. Meanwhile, ergothioneine has a high affinity for transition metal ions such as Fe²⁺ and Cu²⁺, which can chelate these metal ions, block the Fenton reaction, prevent the generation of hydroxyl radicals, and protect intracellular biological macromolecules from oxidative damage^[11]. In addition, ergothioneine can also regulate the opening of mitochondrial permeability transition pores (mPTP). Abnormal opening of mPTP can lead to the collapse of mitochondrial membrane potential, the release of cytochrome C, and trigger apoptosis. Ergothioneine delays cellular senescence by maintaining the closed state of mPTP, keeping the mitochondrial membrane potential stable, and reducing the occurrence of apoptosis^[12].

The anti-aging effect of cycloastragalol is mainly reflected in the regulation of telomerase activity and the maintenance of chromosomal stability. Telomeres are repetitive DNA sequences at the ends of chromosomes. As cells divide, they keep shortening^[13]. When telomeres shorten to a certain extent, cells will enter a state of senescence or apoptosis. Telomerase is a reverse transcriptase capable of prolonging telomere length, consisting of an RNA component (hTR) and a catalytic subunit (hTERT). Cycloastragalol can bind to the specific stem-ring structure of hTR, stabilize the structure of the total telomerase enzyme, and enhance the activity of hTERT. hTERT uses hTR as a template and adds the TTAGGG repeat sequence to the ends of chromosomes, thereby prolonging telomere length. Studies have shown that cycloastragalol can further promote the assembly and activity of telomerase by regulating the expression and localization of telomerase-related proteins^[14]. In addition to activating telomerase, cycloastragalol is also involved in the process of DNA damage repair in cells and maintains the stability of chromosomes. When telomeres are damaged, cells will activate DNA damage repair mechanisms, such as the ATM/ATR-CHK1/2 signaling pathway. Cycloastragalol can activate the ATM/ATR-CHK1/2 signaling pathway, promote the phosphorylation of γ -H2AX (a biomarker of DNA double-strand breaks) and the recruitment of repair proteins such as BRCA1 and Rad51, and accelerate the repair of DNA damage. Meanwhile, cycloastragalol can also regulate the expression and activity of telomere-binding proteins, such as TRF1 (telomere repeat binding factor 1) and TRF2 (telomere repeat binding factor 2). TRF1 and TRF2 can bind to telomere DNA, protect the telomere structure, prevent telomere terminal fusion and degradation, and maintain the integrity of chromosomes. Thereby delays the aging process of cells caused by telomere shortening and damage.

Cordycepin can achieve multi-target intervention in cellular senescence by interfering with nucleic acid metabolism and regulating signal pathways, etc. Its chemical structure is similar to that of adenosine. It can effectively inhibit the activity of ADK (adenosine kinase), increase the intracellular adenosine level, change the AMP/ATP ratio, and thereby activate the AMPK signaling pathway. As a cellular energy receptor, AMPK, once activated, can phosphorylate downstream target proteins, effectively regulate cellular metabolic processes, accelerate fatty acid oxidation, glucose uptake, and autophagy, thereby improving the cellular energy metabolism state and enhancing the anti-aging effect of Golden rejuvenation hormone. In terms of regulating gene expression, cordycepin can also regulate the expression of genes related to aging, such as down-regulating CDKN2A, IL6, etc., while up-regulating the expression of anti-aging genes, such as SIRT1, FOXO1, etc., achieving certain anti-aging effects. In addition, cordycepin can also affect the activity of gene transcription factors and their binding sites, adjust the level of gene transcription, and thereby regulate the process of cellular senescence^[15]. For instance, cordycepin can achieve efficient regulation of inflammation by inhibiting the activation of the NF- κ B signaling pathway, preventing the phosphorylation and degradation of I κ B, and reducing the release of pro-inflammatory factors. This is beneficial for alleviating the inflammatory response in the human body, avoiding accelerated cell aging, and slowing down the aging process.

In the Golden Rejuvenation Essence, these five natural ingredients do not act independently but work together to achieve the goal of anti-aging. PQQ and ergothioneine can effectively protect mitochondrial function from different perspectives. For instance, PQQ promotes mitochondrial biosynthesis and further enhances their energy metabolism, while ergothioneine strengthens the peroxidation protection of mitochondria, thereby reducing oxidative damage to cells, providing them with a stable and sufficient energy supply, further prolonging cell telomeres, and demonstrating anti-aging effects. Spermidine and cordycepin can both regulate autophagy and its inflammatory response in cells, effectively remove intracellular waste, create favorable conditions for the autophagy process, and synergistically control aging-related signaling pathways to reduce the expression of aging-related proteins. Cycloastragalol further enhances chromosomal stability by lengthening telomeres, promotes continuous cell proliferation, and facilitates the function of telomerase. Under the combined effect of other components, it achieves a comprehensive delay in cell aging and drives continuous innovation in the field of anti-aging.

In conclusion, the Golden Rejuvenating Extract, by integrating natural components such as PQQ, spermidine, ergothioneine, cycloastragalol, and cordycepin, can effectively extend telomeres, regulate aging-related signaling pathways and gene expression, and up-regulate the expression of anti-aging genes, thereby demonstrating excellent anti-aging application effects. At the theoretical level, it will reveal the molecular mechanism by which multiple natural active ingredients cooperatively regulate telomeres, enriching the biological theory of aging. At the application level, if the research is successful, Golden Rejuvenation is expected to become a safe and efficient anti-aging product, providing new strategies for the prevention and treatment of aging-related diseases such as cardiovascular diseases and neurodegenerative diseases. At the same time, it can also improve the quality of life of the elderly and reduce the medical burden on society, with broad market prospects and social benefits.

4. Conclusion

The application of Golden Rejuvenation Extract can not only increase the number of telomeres in the human body but also improve the quality of life of users. Its anti-aging effect is relatively significant and it has strong application value.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Guo H, Kang C, Yang S, et al., 2024, The Anti-Aging Effect of the Skin Care Complex Containing Sodium Hyaluronate, Ergothioneine and Lactobacillus Fermentation Products. *Flavors, Fragrances and Cosmetics*, 2024(4): 131–135.
- [2] Hofer J, Daskalaki I, Bergmann M, et al., 2024, Spermidine Is Essential for Fasting-Mediated Autophagy and Longevity. *Nature Cell Biology*, 2024(publish): 1–14.
- [3] Syafiqah N, Kazuto I, 2023, Pyrroloquinoline-Quinone to Reduce Fat Accumulation and Ameliorate Obesity Progression. *Frontiers in Molecular Biosciences*, 10: 1200025–1200025.
- [4] Haofeng H, Jian X, Quanquan G, et al., 2021, Cycloastragenol and Astragaloside IV Activate Telomerase and Protect Nucleus Pulposus Cells Against High Glucose-Induced Senescence and Apoptosis. *Experimental and Therapeutic Medicine*, 22(5): 1326–1326.
- [5] Jin M, Huang W, Zhao Y, et al., 2021, Research Progress on the Immunomodulatory Function and Molecular Mechanism of Cordycepin. *Biomedical Sciences*, 11(4): 227–234.
- [6] Zhu L, Chen Y, Tong T, et al., 2024, Study on the Mechanism of Spermidine Regulating Autophagy Through the PI3K/

- AKT/mTOR Pathway to Inhibit Myocardial Cell Hypertrophy. *Chinese Journal of Hospital Pharmacy*, 44(22): 2563–2568 + 2575.
- [7] Dai T, Xu Y, Chen Y, et al., 2024, Spermidine Alleviates Doxorubicin-Induced Myocardial Cell Senescence Through Mir-451-Mediated Autophagy. *Journal of Huazhong University of Science and Technology (Medical Science Edition)*, 53(6): 791–795.
- [8] Ren J, Yu T, Gao X, et al., 2024, Research Progress on the Biological Activity of Spermidine and Its Development and Application. *Chinese Herbal Medicine*, 55(16): 5714–5722.
- [9] Liu X, Qiu X, Liu Z, 2024, Research Progress on the Function, Preparation and Application of Ergothioneine. *China Food and Drug Administration*, 2024(6): 116–128.
- [10] Li H, Chen Z, Lyu X, 2024, Research Progress of Spermidine in Alleviating Cellular Senescence and Aging-Related Diseases. *Progress in Biotechnology*, 14(3): 388–398.
- [11] Zhang X, Mi X, Lin X, et al., 2024, The Effect of Spermidine on Autophagy and the Expression of Inflammatory Cytokines in Human Endometrial Stromal Cells. *Chinese Journal of Immunology*, 40(5): 1023–1029.
- [12] Xu Y, Wan W, 2024, Spermidine Inhibits Ribosomal DNA Transcription. *Chinese Science Bulletin*, 69(15): 2072–2080.
- [13] Xu X, Zhu L, Liu Z, et al., 2024, Study on the Effect and Mechanism of Salidroside on the Natural Aging of Hippocampal Neurons. *Chinese Journal of Health Preservation and Care*, 42(8): 16–19+23.
- [14] Niu X, Huang M, Zeng J, 2024, Development of Ergothioneine and Its Preliminary Application in Clinical Medicine. *Advances in Microbiology and Immunology*, 52(1): 97–102.
- [15] Li X, 2023, A Preliminary Study on the Anti-Aging Effect and Mechanism of New Food Ingredient PQQ. *Modern Food*, 29(15): 189–192.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Observation on the Postoperative Rehabilitation Effect of Combining Traditional Chinese Medicine Techniques with Psychological Counseling in Patients with Mixed Hemorrhoids

Tianyang Yun*

Jingzhou First People's Hospital, Jingzhou 434000, Hubei, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical effect of combining traditional Chinese medicine techniques with psychological counseling on the postoperative rehabilitation of patients with mixed hemorrhoids. *Methods:* A total of 100 patients with mixed hemorrhoids who underwent surgical treatment at our hospital from January 2024 to December 2024 were randomly selected. According to a random number table, they were divided into two groups: 45 patients receiving routine care (control group), and 45 patients receiving routine care combined with traditional Chinese medicine techniques and psychological counseling (observation group). The nursing interventions included herbal hot compresses, herbal sitz baths, acupoint application, auricular acupuncture, and psychological counseling. The rehabilitation indicators, VAS (Visual Analog Scale) scores, anal heaviness scores, anal edema scores, bowel movement conditions, and complication rates were compared between the two groups. *Results:* The wound healing time in the observation group was (12.97 ± 3.15) days, the recovery time for wound edema was (4.62 ± 1.15) days, and the time of postoperative bleeding after defecation was (5.92 ± 0.86) days. In the control group, the corresponding times were (15.52 ± 3.96) days, (5.45 ± 1.59) days, and (7.12 ± 1.24) days. The observation group showed significantly shorter times ($P < 0.05$). The VAS scores, anal heaviness scores, anal edema scores, difficulty in defecation, stool frequency, sensation of incomplete defecation, and stool characteristics at 3 days and 7 days postoperative were lower in the observation group compared to the control group ($P < 0.05$). The total complication rate in the observation group was lower than that in the control group ($P < 0.05$). *Conclusion:* The combination of traditional Chinese medicine techniques and psychological counseling helps promote early recovery and health restoration in patients with mixed hemorrhoids postoperatively, reduces wound healing time and edema recovery time, alleviates postoperative pain, and lowers the incidence of complications. This approach is worth adopting.

Keywords: Traditional Chinese Medicine techniques; Psychological counseling; Mixed hemorrhoids

Online publication: September 26, 2025

1. Introduction

Mixed hemorrhoids are a common high-incidence anorectal disease. Typically, patients present with symptoms such as prolapse of anal masses and rectal bleeding, and some may experience anal itching, anal heaviness, and pain,

significantly reducing the quality of life for patients. In clinical practice, surgical treatment is the primary method for treating mixed hemorrhoids, and as a key therapeutic intervention, it offers a curative effect ^[1]. However, complications such as urinary retention and rectal bleeding are common after surgery, which not only increases the patient's suffering but also extends the treatment duration and reduces the overall rehabilitation effect. Routine care mainly involves symptomatic monitoring, disease observation, and routine medication intervention. However, due to abnormal defecation and pain post-surgery, patients experience increasing psychological pressure, leading to negative emotions that hinder rapid recovery from the disease ^[2]. In recent years, research related to traditional Chinese medicine (TCM) has increased, and the combination of TCM techniques with psychological counseling has gradually been applied in clinical settings. Among these, acupoint application, based on the theory of meridians, involves applying herbal patches to corresponding acupoints, which not only facilitates patient care but also ensures high safety and maximizes the therapeutic effects of the medicine. Auricular acupuncture, which involves acupoint needling, effectively adjusts the functions of the internal organs and promotes the circulation of blood, thereby alleviating postoperative pain ^[3]. Furthermore, integrating psychological counseling addresses the emotional and mental needs of patients, aiming to eliminate negative emotions and accelerate recovery. Based on this, the study analyzes the application effects of combining TCM techniques with psychological counseling, as detailed below.

2. Materials and methods

2.1. Materials

Selected 100 patients with mixed hemorrhoids who underwent surgical treatment at our hospital from January 2024 to December 2024. They were randomly divided into two groups using a random number table, with 50 patients in each group. Control group: 26 male patients, 24 female patients; age: 25–67 years old, mean (42.56 ± 3.14) years old. Observation group: 28 male patients, 22 female patients; age: 23–69 years old, mean (43.15 ± 3.26) years old. In terms of general data, there was little difference between the two groups ($P > 0.05$).

2.2. Methods

The control group received routine nursing interventions. Postoperatively, vital signs such as body temperature, blood pressure, respiration, and pulse were closely monitored to ensure stability of these indicators. Wound changes were carefully observed to maintain a dry and clean wound to prevent infection. Additionally, the patients' dietary preferences were taken into account to ensure a light and easily digestible diet, reducing the incidence of diarrhea, rectal bleeding, and other complications.

The observation group received routine nursing interventions along with the addition of traditional Chinese medicine (TCM) techniques and psychological counseling, as follows:

- (1) Herbal hot compress: Wu Zhu Yu (*Evodia rutaecarpa*) was used for herbal hot compress treatment. The combination of heat therapy and herbal permeation accelerated local blood circulation and alleviated spasms and symptoms of anorectal diseases.
- (2) Red and blue light therapy: On postoperative day 1, red and blue light therapy was used to promote tissue healing.
- (3) Herbal sitz bath: On postoperative day 2, patients were guided to use an anorectal sitz bath device combined with nanomist technology, utilizing the permeation of the medicine to accelerate blood circulation around the anus. The anal medication was changed and the skin and anal area were monitored to prevent infection.
- (4) Acupoint application: Acupoint application was performed at bilateral Tian Shu (ST25) and Shen Que (CV8) points. By stimulating these meridian points, the treatment regulated Qi stagnation and the bowel, preventing constipation and bloating.
- (5) Auricular acupuncture: Chinese medicine seeds (Wang Bu Liu Xing) were placed at the anal and Shen Men (HT7) points in the ear. Ear acupoint pressure therapy was applied, and the procedure was stopped once the patient

experienced a sensation of soreness, numbness, distension, or pain.

- (6) Psychological counseling: When patients experienced anxiety or pain, the nursing staff provided successful case examples and explained the effects of surgery and prognosis. Through psychological suggestions and non-verbal communication, such as touch and eye contact, patients were encouraged to trust the nursing staff, increasing their sense of security.
- (7) Music therapy: Based on the patient's condition, soft and relaxing music was played to guide patients to patiently listen, thereby releasing tension and anxiety and alleviating postoperative pain.
- (8) Cognitive-behavioral intervention: The rehabilitation process after mixed hemorrhoid surgery, possible complications, and prevention and treatment strategies were explained in a patient-friendly manner.
- (9) Personalized psychological care: Active care and comfort were provided to patients, understanding their psychological needs. Based on individual circumstances, communication with patients was increased to guide them in expressing their feelings, helping them feel the care and affection from medical staff and family members, and boosting their confidence in fighting the disease.

2.3. Observation indicators

- (1) Record postoperative rehabilitation indicators, including wound healing time, wound edema recovery time, and time of bleeding after defecation.
- (2) Assess pain score (VAS), anal heaviness score, and anal edema score. Higher scores indicate more severe pain, anal heaviness, and anal edema.
- (3) Observe defecation conditions, including difficulty in defecation, stool frequency, sensation of incomplete defecation, and stool characteristics. Higher scores indicate more difficulty in defecation.
- (4) Count the occurrence of complications, including urinary retention, postoperative bleeding, and defecation difficulty.

2.4. Statistical methods

Data in this study were processed using the statistical software SPSS 20.0. The measurement data and count data were expressed as mean \pm standard deviation (SD) and rate (%), respectively, and analyzed using *t*-test and χ^2 test. For comparisons between the two groups, a significant difference was considered when $P < 0.05$.

3. Results

3.1. Postoperative rehabilitation indicators

The observation group showed better postoperative rehabilitation indicators compared to the control group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of postoperative rehabilitation indicators between the two groups (mean \pm SD, days)

Group	Number of cases	Wound healing time	Wound edema recovery time	Bleeding after defecation time
Control group	50	15.52 \pm 3.96	5.45 \pm 1.59	7.12 \pm 1.24
Observation group	50	12.97 \pm 3.15	4.62 \pm 1.15	5.92 \pm 0.86
<i>t</i>		3.563	2.991	5.623
<i>P</i>		0.000	0.004	0.000

3.2. VAS score, anal heaviness score, and anal edema score

Compared with the control group, the observation group had lower VAS scores, anal heaviness scores, and anal edema scores at 3 days and 7 days postoperatively ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of VAS scores, anal heaviness scores, and anal edema scores between the two groups (mean \pm SD, points)

Group	Number of cases	VAS score		Anal heaviness score		Anal edema score	
		Postoperative3d	Postoperative7d	Postoperative3d	Postoperative7d	Postoperative3d	Postoperative7d
Control group	50	2.41 \pm 0.59	1.89 \pm 0.54	2.32 \pm 0.71	1.47 \pm 0.31	2.32 \pm 0.74	2.16 \pm 0.53
Observation group	50	1.69 \pm 0.41	1.12 \pm 0.35	1.54 \pm 0.42	0.59 \pm 0.12	1.58 \pm 0.47	0.69 \pm 0.15
<i>t</i>		7.086	8.461	6.686	18.719	5.969	18.871
<i>P</i>		0.000	0.000	0.000	0.000	0.000	0.000

3.3. Bowel movement conditions

The observation group had lower bowel movement scores compared to the control group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of bowel movement conditions between the two groups (mean \pm SD, points)

Group	Number of cases	Difficulty in defecation		Stool frequency		Sensation of incomplete defecation		Stool Characteristics	
		Postoperative 3d	Postoperative 7d	Postoperative 3d	Postoperative 7d	Postoperative 3d	Postoperative 7d	Postoperative 3d	Postoperative 7d
Control group	50	2.41 \pm 0.65	1.46 \pm 0.34	2.32 \pm 0.68	1.83 \pm 0.39	2.43 \pm 0.74	1.94 \pm 0.52	2.23 \pm 0.69	1.74 \pm 0.38
Observation group	50	1.67 \pm 0.32	0.69 \pm 0.12	1.59 \pm 0.31	0.94 \pm 0.12	1.69 \pm 0.36	1.19 \pm 0.27	1.57 \pm 0.31	0.79 \pm 0.15
<i>t</i>		7.222	15.101	6.907	15.423	6.359	9.051	6.169	16.443
<i>P</i>		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

3.4. Complication occurrence

The overall complication rate was lower in the observation group compared to the control group ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of complication occurrence rates between the two groups [$n(\%)$]

Group	Number of cases	Urinary retention	Postoperative bleeding	Defecation difficulty	Total incidence
Control group	50	5	2	3	10 (20.00)
Observation group	50	1	1	1	3 (6.00)
χ^2					4.332
<i>P</i>					0.037

4. Discussion

In anorectal surgery, mixed hemorrhoids are a common condition characterized by the connection of internal and external

hemorrhoidal nodules with varicose veins forming lumps. The typical symptoms include anal pain, rectal bleeding, and prolapse. Factors such as irregular diet, prolonged sitting, and poor defecation management contribute to the complex development of mixed hemorrhoids. During the postoperative recovery process, patients often experience severe pain, and complications such as infections and edema may arise, severely affecting the patient's postoperative recovery and quality of life ^[4].

Under conventional medical models, methods such as wound cleaning, pain management, and dietary interventions are typically used. While these can improve the patient's condition, they do not alleviate postoperative pain, reduce psychological stress, or accelerate the recovery process. Acupoint application is a traditional therapy that continuously stimulates specific acupoints to adjust blood circulation, thereby reducing swelling and pain and promoting the smooth flow of meridians. Auricular acupuncture, based on the close relationship between the ear and various organs and meridians of the body, stimulates ear acupoints to regulate organ functions and alleviate postoperative discomfort. Due to their unique theoretical frameworks and significant effects, both therapies play an important role in accelerating the postoperative recovery of mixed hemorrhoid patients. Furthermore, as most patients experience anxiety, tension, and depression post-surgery, the addition of psychological counseling alongside TCM techniques helps patients gain a correct understanding of their condition and treatment methods. Techniques like relaxation training and cognitive-behavioral therapy reduce mental tension, increase disease-fighting confidence, and ultimately create a rehabilitation plan that addresses both physical and psychological aspects ^[5]. The results showed that the observation group had shorter wound healing time, wound edema recovery time, and bleeding after defecation compared to the control group. This suggests that combining TCM techniques and psychological counseling aids in early wound healing and alleviates symptoms like bleeding after defecation and wound edema.

The reasons are as follows: TCM techniques (such as acupoint application, auricular acupuncture, and herbal hot compresses) use herbal hot compresses to apply heated herbal packs externally. The combined effect of thermal therapy and herbal permeation accelerates local blood circulation and reduces muscle spasms and anorectal symptoms. Acupoint application uses herbal essence patches that directly penetrate the skin to activate acupoints, preventing constipation after surgery. Auricular acupuncture, with Wang Bu Liu Xing seeds applied to ear acupoints (such as the anal and Shen Men points), regulates the neuroendocrine system and alleviates anal sphincter spasms. On top of this, psychological counseling helps relieve and release patients' negative emotions, such as anxiety and tension, playing a crucial role in reducing postoperative pain and anxiety. The results indicated that the observation group had lower VAS scores, anal heaviness scores, and anal edema scores, and also showed lower defecation difficulty, stool frequency, sensation of incomplete defecation, and stool characteristics scores compared to the control group. This result suggests that the combination of TCM techniques and psychological counseling significantly alleviates postoperative pain, anal heaviness, and anal edema, and improves defecation outcomes. The reasons are as follows: Auricular acupuncture and acupoint application directly intervene in postoperative pain. Acupoint application significantly improves blood circulation, while auricular acupuncture uses ear acupoints associated with various organs to regulate the whole body, thereby reducing pain. Most mixed hemorrhoid patients suffer from negative emotions like tension and anxiety. With professional and systematic psychological counseling, patients can better understand their condition, release negative emotions, increase their confidence in treatment, and accelerate the recovery of physiological functions ^[6].

5. Conclusion

In conclusion, the combination of traditional Chinese medicine techniques and psychological counseling plays a significant role in the postoperative rehabilitation of mixed hemorrhoid patients. It not only accelerates the recovery of the patients' physiological functions but also helps reduce the incidence of complications.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wen X, Xie L, Xie Y, 2024, The Application Effect of Acupoint Application Combined with Herbal Hot Compress Nursing on Bowel Movements and Anal Pain in Postoperative Patients with Mixed Hemorrhoids. *Chinese Journal of Medical Science*, 14(17): 144–147.
- [2] Ren J, Gao C, 2024, The Intervention Effect of Herbal Hot Compress Combined with Acupoint Application on Postoperative Pain in Patients with Mixed Hemorrhoids. *Chinese Journal of Drug Abuse Prevention and Treatment*, 30(6): 1113–1117.
- [3] Tang J, 2024, The Application of Humanistic Care Intervention in Nursing for Patients with Mixed Hemorrhoid Surgery and Its Effect on Postoperative Pain and Urination Function. *Chinese Medical Guidelines*, 22(16): 170–172.
- [4] Zeng F, 2024, The Effect of Psychological Nursing Intervention on Improving Postoperative Urination Disorders in Patients with Mixed Hemorrhoids. *Chinese Practical Rural Doctor Journal*, 31(3): 32–35.
- [5] Lu L, Wang Q, Sun Q, 2023, The Effect of Herbal Sitz Bath Combined with Acupoint Application on Wound Healing and Pain Mediators in Postoperative Mixed Hemorrhoid Patients. *Journal of Modern Integrated Traditional Chinese and Western Medicine*, 32(21): 2977–2981.
- [6] Zhang Z, Wang Y, Kong S, 2023, Clinical Observation of Si Mo Run Chang Fang Combined with Acupoint Application for the Treatment of Qi Stagnation-Type Constipation After Mixed Hemorrhoid Surgery. *Chinese Pharmacy*, 32(4): 91–94.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Similarities and Differences Between Small Molecules and Biologics: Examples of Drugs for Alzheimer's Disease

Qianshuai Zhang^{1,2*}

¹The University of Hong Kong, Hong Kong 999077, China

²China Pharmaceutical University, Nanjing 210000, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Alzheimer's disease is a neurodegenerative disease with a hidden onset. Existing therapeutic drugs can only delay the progression of the disease and relieve symptoms. Small interfering RNAs show potential for the treatment of Alzheimer's disease by cleaving mRNA encoding target genes, but many challenges need to be overcome by stably delivering small interfering RNA to the lesions. This paper describes the pathological mechanism of Alzheimer's disease, existing drug targets, the advantages and challenges of small interfering RNA therapy, research progress in the transblood-brain barrier delivery system, new small interfering RNA delivery system and ongoing clinical trials of Alzheimer's disease drugs, etc., and strives to provide reference and reference for related research on small interfering RNA therapy for Alzheimer's disease.

Keywords: Biological small molecules; Drugs for Alzheimer's disease; Drug research and development

Online publication: September 26, 2025

1. Introduction

Alzheimer's disease (AD) is an age-related neurodegenerative disorder caused by nerve cell damage, affecting around 45 million people globally^[1]. Neuropathologically, AD develops in parallel with the accumulation of amyloid- β (A β) and phosphorylated tau protein (p-tau)^[2], accounting for the cognitive decline in affected individuals. Nowadays, medications used to treat AD include small molecules and biologics and could be classified as symptomatic treatment and disease-modifying therapy (DMT)^[3,4]. Small molecules are typically low molecular weight (MW) compounds that can be synthesized through chemical processes, while biologics are larger molecules derived from living organisms or cells^[5]. Currently, several monoclonal antibodies (mAbs) for AD have been approved by the United States Food and Drug Administration (FDA), providing new hope to AD patients^[6].

2. Drug design and mechanism of drug action

2.1. Small molecules

2.1.1. Cholinesterase inhibitors (ChEIs)

Acetylcholine (ACh) is a neurotransmitter related to brain functions, such as attention and memory. Acetylcholinesterase

(AChE) is a cholinesterase enzyme that hydrolyses the ACh and terminates the nerve impulses transmitted to cholinergic synapses conducted by ACh^[7]. It is believed that during AD development, cholinergic synapses experience a massive loss^[8], followed by the cholinergic deficit, resulting in memory dysfunction and ultimately dementia^[9]. Therefore, the usage of ChEIs to block the AChE and maintain the ACh level becomes a promising strategy for treating AD. Currently, donepezil, rivastigmine, and galantamine constitute the pivotal ChEIs that have been approved for AD treatment by the FDA in 1996, 2000, and 2001, respectively. Besides, the first ChEI once authorized in 1993 was tacrine, and was withdrawn due to hepatotoxicity in 2013^[10].

2.1.2. N-methyl-D-aspartate receptor (NMDAR) antagonists

Glutamate is the agonist of the NMDAR and an excitatory transmitter in the nervous system, which is considered a neurotoxin as well, accounting for several neurodegenerative disorders^[11]. This implies that inhibiting the NMDAR and the glutamate-mediated neurotoxicity may ameliorate the cognitive decrease in AD patients^[12]. Memantine approved in 2003 is applied to moderate the overactivation of NMDAR^[13]. In addition, Namzaric, a fixed-dose combination of donepezil and memantine, was approved in 2014 (**Figure 1**). However, these five medications are symptomatic treatments that only alleviate the symptoms instead of resolving the underlying cause to discontinue the long-term progression of AD; thus, the efficacy is temporary and fleeting^[14].

2.2. Biologics

Accumulation of A β and p-tau is thought to play an essential role in the development of AD^[15]. A β is a fragment of amyloid precursor protein (APP), which is similar to a cell surface receptor and could produce A β as soluble monomers^[16]. Apart from monomers, A β exists as dimers, oligomers, protofibrils, fibrils, and eventually forms plaques. Additionally, these A β forms can convert from each other (**Figure 2**)^[16].

In recent years, some biologics targeting A β have been approved. In 2021, aducanumab (Aduhelm), was approved via the accelerated approval (AA) pathway by the FDA. Aducanumab was a human mAb that targets the A β soluble oligomers and insoluble fibrils^[17], reducing the amyloid plaque in the brain^[18]. It was also the first approval of DMT for AD^[4,19]. However, since the follow-up studies failed to confirm the anticipated clinical benefit, aducanumab was withdrawn in 2024^[20,21]. Lecanemab (Leqembi) was another humanized mAb targeting A β soluble oligomers and protofibrils^[22], approved via the AA pathway in 2023 and converted to a traditional approval 6 months later. Furthermore, another A β -targeted mAb for AD called donanemab (Kisunla)^[23], received full FDA approval directly in 2024, which can target the pyroglutamate-modified A β and bind to the amyloid plaques selectively (**Table 1**).

3. Pharmaceutical production process

3.1. Manufacturing process

The manufacturing processes for small molecules include the identification of drug targets and the active pharmaceutical ingredient (API) first. Then, the API was synthesized through the chemical synthetic pathways, including substitution, addition and elimination, oxidation and reduction reactions, and more. Lastly, these chemical synthesis pathways are scaled up. Moreover, the chemical synthetic processes of small molecules are standardized with manageable and scalable steps, which ensures a high batch consistency.

In contrast, advanced biotechnologies are conventionally utilized for the manufacturing process of most biologics, making the processes more complicated. Firstly, the target for drug action and a specific protein interacting with the target are identified, with a functional DNA sequence created based on the chosen protein and its genetic code. After that, the functional sequence is inserted into different host cells to screen for the cell line that could produce the chosen protein most effectively. Then, the cell line is cultured and grown in the bioreactors and undergoes the fermentation process to produce the target protein. Lastly, the target protein is separated by filtration, followed by purification, stabilization

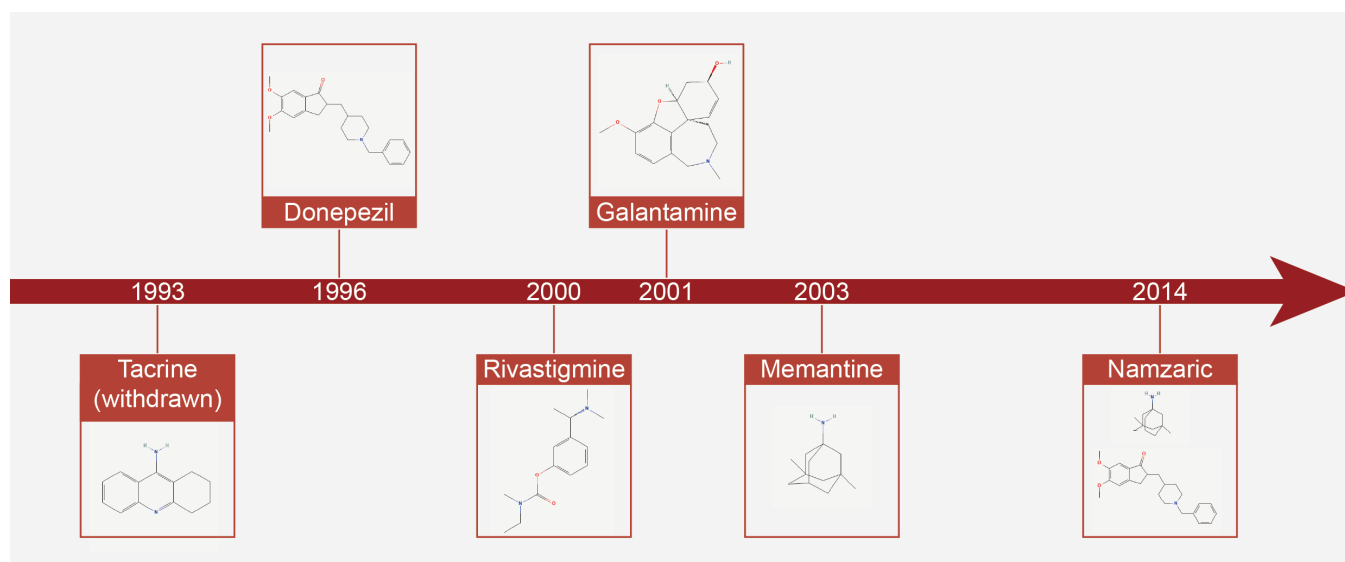


Figure 1. Development history of small molecules approved by FDA for AD and their structure.

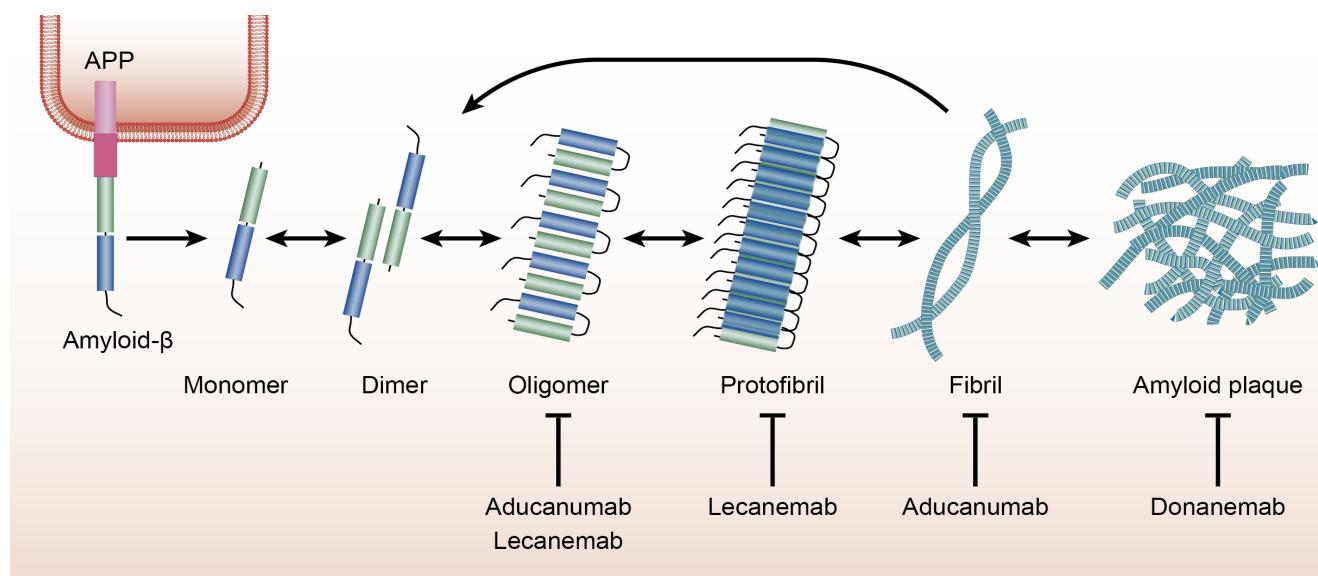


Figure 2. Aβ cycle and its aggregation species, and different targets of mAbs approved by the FDA.

Table 1. Details of the three mAbs targeting Aβ, once approved by the FDA

Drug	Target	Approval pathway	Approval status
Aducanumab	Aβ soluble oligomers and insoluble fibrils	AA pathway (2021)	Withdrawn (2024)
Lecanemab	Aβ soluble oligomers and protofibrils	AA pathway (2023)	Traditional approval (2023)
Donanemab	Pyroglutamate-modified Aβ and amyloid plaques	Traditional approval (2024)	Traditional approval (2024)

and then processed into a medicine. Consequently, due to the complex manufacturing process, there could be a longer manufacturing time and a wider variation between batches for biologics compared to small molecules.

3.2. Dosage forms

Small molecule drugs are readily formulated in various dosage forms due to their stable physical and chemical properties, such as tablets, capsules, granules and solutions for oral administration; liquid preparations and lyophilized powder for injection; semisolid dosage forms, transdermal preparations and inhaled powder for topical administration, and more. Different dosage forms demonstrate the capacity to satisfy various purposes, such as higher bioavailability and effectiveness, lower required dose or administration frequency, and fewer adverse events (AEs). Compared to small molecules, the dosage forms of biologics are more monotonous. Since biologics are mostly proteins that cannot preserve activity in the acidic environment of the stomach, biologics are generally formulated as liquid injections (**Table 2**).

Table 2. Information about FDA-approved dosage forms of AD medications

Type	Drug	Brand-name	Dosage form	Market Status
Small molecules	Donepezil	Aricept	Tablet	Prescription
			Solution	Discontinued
		Aricept ODT	Disintegrating tablet	Discontinued
		Adlarity	Transdermal preparation	Prescription
	Rivastigmine	Exelon	Capsule, solution	Discontinued
			Transdermal preparation	Prescription
	Galantamine	Razadyne	Tablet, solution	Discontinued
		Razadyne ER	Extended-release capsule	Discontinued
		Zunveyl	Delayed-release tablet	Prescription
	Memantine	Namenda	Tablet	Prescription
			Solution	Discontinued
		Namenda XR	Extended-release capsule	Discontinued
	Donepezil and memantine	Namzaric	Extended-release capsule	Prescription
Biologics	Lecanemab	Leqembi	Injection	Prescription
	Donanemab	Kisunla	Injection	Prescription

3.3. Quality control (QC)

It is indispensable to conduct quality tests for drug development, regulatory acceptance, and batch consistency, as well as to ensure safety and efficacy. Commonly utilized analytical technologies in QC for API of small molecules include high-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) for the purity examination; X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), Raman spectroscopy for the structural characterization; dynamic light scattering (DLS), differential scanning calorimetry (DSC), potentiometric titration for the physical properties analysis^[24].

Distinct from small molecules, in the purity examination, technologies utilized mainly include sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), size exclusion chromatography (SEC) and DLS. Mass spectrometry (MS), liquid chromatography-tandem mass spectrometry (LC-MS/MS), time of flight mass spectrometer

(TOF-MS), and circular dichroism (CD) are applied for structural characterization. Capillary isoelectric focusing (CIEF), DSC and SDS-PAGE are used for physical properties analysis. Additionally, bioactivity assay for biologics includes enzyme-linked immunosorbent assay (ELISA), antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytotoxicity (CDC) assays (**Table 3**).

Table 3. Some analytical technologies applied in QC for API

Test items	Analytical technologies	
	Small molecules	Biologics
Purity	HPLC, UPLC, LC-MS, GC-MS	SDS-PAGE, SEC, DLS
Structure	XRD, FTIR, Raman spectroscopy	MS, LC-MS/MS, TOF-MS, CD
Physical property	DLS, DSC, potentiometric titration	CIEF, DSC, SDS-PAGE
Bioactivity	/	ELISA, ADCC, CDC

4. Regulatory issues

4.1. Brand-name small molecules and biologics

Newly discovered candidate drugs and synthesized biological products are applied via the new drug application (NDA) ^[25] and biologics license application (BLA) ^[26], respectively. It is necessary for novel drugs applied via NDA or BLA pathways to undergo clinical trials, which would cost a great amount of resources, capital and time, leading to the high price of the brand-name drugs and the high failure rate of the application ^[27]. After approval, they are also called brand-name small molecules and biologics. In addition, the period of market monopoly for small molecules and biologics is determined by the patents and regulatory exclusivity, providing market protection for new drugs ^[28].

4.2. Generic small molecules and biosimilars

Both generic small molecule drugs and biosimilars refer to the generic products of reference-listed drug (RLD) products, providing alternatives to brand-name drugs. Generic drugs are approved via the abbreviated NDA (ANDA) and are strictly required to be identical to the corresponding RLD products in the dosage form, safety, effectiveness, administration strategy, and more ^[29]. No additional clinical studies and only the bioavailability and bioequivalence data are required for a generic drug application ^[30], thus less resource is required. Differently, biosimilars only need to illustrate highly similar properties to RLD products in purity, safety and potency ^[31] but need additional clinical trials to demonstrate the therapeutic equivalence to RLD products and get approval via the BLA pathway ^[32], causing a higher price in comparison with generic small molecules.

5. Discussion

It is generally accepted that both small molecules and biologics play an inevitable role in disease treatment and public health. It could be argued that biologics could have a more promising prospect for AD treatment from an industrial perspective. Firstly, biologics are more selective with higher safety and efficacy than small molecules. As mentioned before, ChEIs and NMDAR antagonists could only delay the progression of symptoms rather than address the underlying causes, while biologics for DMTs provide the possibility of curing AD. Secondly, from the factual perspective, since the approval of memantine in 2003, no completely novel small molecules have been approved. With the advances in biotechnology and the pathology of AD, more potential targets and pathways leading to the disease have been identified and validated, facilitating the new generation of biologics development ^[33].

In addition, in terms of commercial prospects, on one hand, the biologics price tends to be more expensive ^[34], and

a report ^[5] indicated that in the USA, although only 2% of prescriptions are taken up by biologics, spending on biologics accounts for around half of the total drug spending, illustrating an increasing market value of biologics. On the other hand, according to the Biologics Price Competition and Innovation Act (BPCIA), brand-name biologics have regulatory exclusivity for 12 years, which is longer than 5 years for small molecules, thus ensuring a longer period of market monopoly protection from biosimilar competition. Furthermore, since the requirement of additional clinical trials for approval of biosimilars, the price of biosimilars could be relatively higher than that of generic small molecules, thus it may reasonably be concluded that the approval of biosimilars will have less impact on the price of brand-name biologics, compared with that of approved generic small molecules on the price of brand-name small molecules, guaranteeing adequate returns on investment.

Last but not least, patient compliance is also an essential component to consider. Due to the longer half-life of biologics compared to small molecules, the frequency of administration for biologics is lower. For example, twice a day. Admittedly, it takes longer, about half an hour, to receive each intravenous infusion, but the possibility of missing a dose or overdosing is reduced. Moreover, the metabolism of small molecules in the liver can readily be affected by food or other medications, increasing the risk of AEs. Collectively, biologics may be more worthy of investment, with higher safety and efficacy, fewer side effects, rapid advancements in biotechnology, better business prospects, and regulatory support, as well as higher patient compliance.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Ahn E, Park J, 2025, Molecular Mechanisms of Alzheimer's Disease Induced by Amyloid- β and Tau Phosphorylation Along with RhoA Activity: Perspective of RhoA/Rho-Associated Protein Kinase Inhibitors for Neuronal Therapy. *Cells*, 14(2): 89.
- [2] Scheltens P, Strooper B, Kivipelto M, et al., 2021, Alzheimer's Disease. *The Lancet*, 397(10284): 1577–1590.
- [3] Zhang J, Zhang Y, Wang J, et al., 2024, Recent Advances in Alzheimer's Disease: Mechanisms, Clinical Trials and New Drug Development Strategies. *Signal Transduct Target Ther*, 9(1): 211.
- [4] Cummings J, Fox N, 2017, Defining Disease Modifying Therapy for Alzheimer's Disease. *J Prev Alzheimer's Dis*, 4(2): 109–115.
- [5] Wouters O, Vogel M, Feldman W, et al., 2024, Differential Legal Protections for Biologics vs Small-Molecule Drugs in the US. *JAMA*, 332(24): 2101–2108.
- [6] Liu J, Ting J, Al-Azzam S, et al., 2021, Therapeutic Advances in Diabetes, Autoimmune, and Neurological Diseases. *Int J Mol Sci*, 22(6): 2805.
- [7] Pohanka M, 2012, Acetylcholinesterase Inhibitors: A Patent Review (2008–Present). *Expert Opinion on Therapeutic Patents*, 22(8): 871–886.
- [8] Dawood D, Anwar M, 2025, Recent Advances in the Therapeutic Insights of Thiazole Scaffolds as Acetylcholinesterase Inhibitors. *European Journal of Medicinal Chemistry*, 287: 117331.
- [9] Bartus R, Dean R, Beer B, et al., 1982, The Cholinergic Hypothesis of Geriatric Memory Dysfunction. *Science*, 217(4558): 408–414.
- [10] Ríos C, Marco-Contelles J, 2019, Tacrines for Alzheimer's Disease Therapy. III. The PyridoTacrines. *European Journal of Medicinal Chemistry*, 166: 381–389.

- [11] Chang C, Lin C, Lane H, 2020, d-Glutamate and Gut Microbiota in Alzheimer's Disease. *Int J Mol Sci*, 21(8): 2676.
- [12] Greenamyre J, Maragos W, Albin R, et al., 1988, Glutamate Transmission and Toxicity in Alzheimer's Disease. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 12(4): 421–IN4.
- [13] Reisberg B, Doody R, Stöffler A, et al., 2003, Memantine in Moderate-to-Severe Alzheimer's Disease. *N Engl J Med*, 348(14): 1333–1341.
- [14] Schneider L, Sano M, 2009, Current Alzheimer's Disease Clinical Trials: Methods and Placebo Outcomes. *Alzheimer's Dement*, 5(5): 388–397.
- [15] Pradeepkiran J, Baig J, Islam M, et al., 2024, Amyloid- β and Phosphorylated Tau are the Key Biomarkers and Predictors of Alzheimer's Disease. *Aging Dis*, 16(2): 658–682.
- [16] Kang J, Lemaire H, Unterbeck A, et al., 1987, The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor. *Nature*, 325(6106): 733–736.
- [17] Sevigny J, Chiao P, Bussière T, et al., 2016, The Antibody Aducanumab Reduces A β Plaques in Alzheimer's Disease. *Nature*, 537(7618): 50–56.
- [18] Haeblerlein S, Aisen P, Barkhof F, et al., 2022, Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. *J Prev Alzheimer's Dis*, 9(2): 197–210.
- [19] Cummings J, Zhou Y, Lee G, et al., 2024, Alzheimer's Disease Drug Development Pipeline: 2024. *Alzheimer's Dement (N Y)*, 10(2): e12465.
- [20] Alexander G, Knopman D, Emerson S, et al., 2021, Revisiting FDA Approval of Aducanumab. *N Engl J Med*, 385(9): 769–771.
- [21] Rosen J, Jessen F, 2025, Patient Eligibility for Amyloid-Targeting Immunotherapies in Alzheimer's Disease. *Journal of Prevention of Alzheimer's Disease*, 12(4): 100102.
- [22] Dyck C, Swanson C, Aisen P, et al., 2023, Lecanemab in Early Alzheimer's Disease. *New England Journal of Medicine*, 388(1): 9–21.
- [23] Sims J, Zimmer J, Evans C, et al., 2023, Donanemab in Early Symptomatic Alzheimer's Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. *JAMA*, 330(6): 512–527.
- [24] Han G, Priefer R, 2023, A Systematic Review of Various pKa Determination Techniques. *International Journal of Pharmaceutics*, 635: 122783.
- [25] Salminen W, Wiles M, Stevens R, 2019, Streamlining Nonclinical Drug Development Using the FDA 505(b)(2) New Drug Application Regulatory Pathway. *Drug Discovery Today*, 24(1): 46–56.
- [26] Nugent B, Ramamoorthy A, Pippins J, et al., 2025, Confirmatory Evidence Used in Non-Oncologic Rare Disease New Molecular Entity Marketing Applications Approved by FDA, 2020–2023. *Clin Pharmacol Ther*, 117(6): 1627–1631.
- [27] Hay M, Thomas D, Craighead J, et al., 2014, Clinical Development Success Rates for Investigational Drugs. *Nature Biotechnology*, 32(1): 40–51.
- [28] Kesselheim A, Sinha M, Avorn J, 2017, Determinants of Market Exclusivity for Prescription Drugs in the United States. *JAMA Internal Medicine*, 177(11): 1658–1664.
- [29] Kulkarni S, Gaikwad V, 2023, Common Chemistry, Manufacturing, and Control Deficiencies in Abbreviated New Drug Applications Assessed by the US Food and Drug Administration: Hurdle to Access Cost-Effective Medicines. *Journal of Pharmacological and Toxicological Methods*, 123: 107295.
- [30] Zhu H, Zhou H, Seitz K, 2009, Chapter 15 - Bioavailability and Bioequivalence. In: Qiu Y, Chen Y, Zhang GGZ, Liu L, Porter WR, editors. *Developing Solid Oral Dosage Forms*. Academic Press, San Diego, 341–364.
- [31] Ranjan R, 2025, Development of Complex Generics and Similar Biological Products: An Industrial Perspective of Reverse Engineering. *AAPS PharmSciTech*, 26(4): 95.

- [32] Monga A, Gagan, Jamwal P, et al., 2025, Biosimilars: A Critical Review of Development, Regulatory Landscape, and Clinical Implications. *AAPS PharmSciTech*, 26(1): 46.
- [33] Cummings J, Aisen P, DuBois B, et al., 2016, Drug Development in Alzheimer's Disease: The Path to 2025. *Alzheimer's Res Ther*, 8: 39.
- [34] Rome B, Egilman A, Kesselheim A, 2022, Trends in Prescription Drug Launch Prices, 2008–2021. *JAMA*, 327(21): 2145–2147.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Study on the Influence of Implementing Detail Management on Nursing Quality and Nursing Satisfaction in the Disinfection Supply Room

Aihua Chen*

Xuzhou Tongshan maternal and Child Health Hospital, Xuzhou 221100, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the influence of detail management on nursing quality and nursing satisfaction in the disinfection supply room (CSSD). *Methods:* The study period was selected from August 2023 to August 2024, and 92 pieces of CSSD instruments (artificial abortion kit instruments) in our hospital were selected as the research subjects, which were divided into the study group and the control group according to the random grouping method, with 46 pieces in each group. The control group received routine management, and the study group received detailed management. The nursing quality, professional skills, and satisfaction of medical staff in each group were evaluated, and the occurrence of adverse events of devices in each group was analyzed. *Results:* the scores of nursing quality, professional skills of medical staff and satisfaction of medical staff in the study group were at a higher level, and the incidence of adverse events was at a lower level; the difference was more significant than that in the control group ($P < 0.05$). *Conclusion:* Detail management plays an important role in CSSD, which can comprehensively improve the quality of nursing, reduce the risk of adverse events, and has positive significance in improving the professional skills and satisfaction of medical staff.

Keywords: Detail management; Disinfection and supply room; Nursing quality; Nursing satisfaction

Online publication: September 26, 2025

1. Introduction

CSSD is one of the indispensable departments in the hospital. Its responsibilities are the recovery, cleaning, disinfection and sterilization of hospital instruments, which play an important role in ensuring the sterility of instruments and dressings. The work quality and management efficiency of the Department can affect the treatment effect and prognosis of patients, and have a direct impact on the overall medical level of the hospital. Therefore, improving the management quality of CSSD has become an important research topic^[1]. The CSSD function is not only for the disinfection and sterilization of devices, but also covers the management and distribution of medical devices. Each work link has an important connection with hospital infection control, patient safety, and satisfaction. With the improvement of medical quality standards, CSSD is facing more stringent management requirements, and the disadvantages of the traditional decentralized management mode are gradually revealed, such as improper management links, poor management skills, decentralized management mode, insufficient resource integration, and low work efficiency. Therefore, it is urgent to choose a scientific and high-

quality management. Detail management pays attention to the refinement of intervention measures. It can divide the work according to the CSSD work content and the responsibilities of the medical staff. It can use more effective and high-quality measures for management, which is of positive significance to improve the quality of CSSD work and the satisfaction of medical staff. In this paper, 92 pieces of CSSD devices in the hospital were analyzed, and the implementation value of detail management was evaluated.

2. Data and methods

2.1. General information

The research period was from August 2023 to August 2024. The subjects of the study were 92 pieces of instruments selected from the CSSD in the hospital. They were randomly divided into a study group ($n = 46$) and a control group ($n = 46$). All instruments were abortion kit-related instruments, and there was no difference between the two groups ($P > 0.05$). During the study period, there were no changes in CSSD managers, a total of 4, all female, with an average age of (39.00 ± 3.82) years old, ranging from 30 to 48 years old. The working hours ranged from 1 to 7 years, with an average of (4.00 ± 0.72) years.

2.2. Research criteria

Inclusion criteria: (1) The processing data of the included devices are complete without loss or damage; (2) The study was supported by the hospital ethics committee; (3) CSSD managers have professional qualification certificates and have received professional training and assessment.

Exclusion criteria: (1) Devices lost during the study; (2) Devices to be eliminated; (3) Severely damaged, deformed, and without a production license or certificate.

2.3. Method

The control group implemented routine management and carried out management work according to the hospital rules and regulations. The specific content involved the recovery, cleaning, disinfection, sterilization, etc. of the equipment. The equipment was reasonably stored and distributed according to the type of equipment, and the relevant records of the equipment were improved to ensure accurate tracking.

The research group implements detailed management, specifically as follows:

(1) Build a detailed management team

Organize the hospital CSSD staff to carry out systematic training, comprehensively learn CSSD and detail management related knowledge, and the head nurse of the department acts as the team leader to ensure that all members master CSSD management knowledge and operation skills. At the same time, organize the importance of CSSD work of staff, promote the improvement of safety awareness and prevention awareness, and ensure that the management work is carried out in strict accordance with the standards. The staff conducted an in-depth analysis of the existing problems and formulated higher-quality management measures based on the current situation to promote the improvement of nursing quality.

(2) Receiving and inventory details

Refine the access standards to ensure that all devices meet the use specifications and quality standards. After the device is sent to CSSD, a special person is responsible for receiving the device, analyzing the appearance of the device to ensure that there is no damage, corrosion, etc., and verifying whether the accessories are complete according to the device list to ensure normal use. The receiving and counting work is completed by experienced personnel to ensure the seamless connection of all work links.

(3) Detailed workflow

Classify the management according to the device model, optimize the management for the disinfection and

cleaning process, divide the work area in detail and mark it, such as the inspection area, recycling area, cleaning area, guarantee area, sterilization area, and carry out the work in strict accordance with the process. In case of sharp objects, warning signs shall be made, and they shall be recycled and cleaned separately. If there is a cavity in the instrument, it is necessary to clean it with a high-pressure water gun, and then take aseptic hemostatic forceps to clamp the articles after completion, to minimize contact with the instrument. In the process of removing bacteria, intervention should be carried out in strict accordance with the standards. After completion, packaging should be carried out according to the device type, and attention should be paid to the implementation of aseptic requirements.

(4) Quality supervision

Regularly organize the testing staff to carry out professional knowledge training, covering quality testing standards, testing methods, and relevant laws and regulations, to ensure that the inspectors master the latest industry trends and technologies. Carry out in-depth analysis and Discussion on the case, comprehensively improve the inspectors' understanding of the importance of quality monitoring, and promote the enhancement of work risk awareness and responsibility. According to the CSSD work of the hospital, the quality inspection standard operating procedures were formulated to promote the standardization of the inspection process and comprehensively improve the reliability and consistency of the inspection work. The testing work shall be recorded in detail, including the testing personnel, testing date, testing results, and handling opinions, and a complete traceability system shall be established according to the actual situation.

2.4. Observation indexes

(1) Quality of care

The CSSD self-designed questionnaire (100 points, the reliability and validity of the scale and Cronbach's α coefficient are 0.824 and 0.829, respectively), and the score is directly proportional to the quality of management.

(2) Professional skills of medical staff

A self-made questionnaire (100 points) was used to score, and the score was in direct proportion to the professional skills of the medical staff.

(3) Satisfaction of medical staff

The hospital's self-made questionnaire was used to evaluate the satisfaction of medical staff for device management, and the score was proportional to the satisfaction.

(4) Occurrence of adverse device events

It involves device defects, incomplete information records, and device classification errors.

2.5. Statistical treatment

The research data were comprehensively processed and analyzed by SPSS 23.0 software. The measurement data and counting data were expressed by " $(\pm s)$ " and " $[n/(%)]$ ", respectively. The differences between groups were tested by " t " and " P " respectively, and $P < 0.05$ proved that the differences were significant.

3. Results

3.1. Nursing quality assessment

Table 1 shows that the score of nursing quality in the study group is higher, and the difference is more significant than that in the control group ($P < 0.05$).

Table 1. Nursing quality assessment (mean \pm standard deviation, points)

Time	Device acceptance	Disinfection and sterilization	Instrument cleaning	Instrument packaging	Standard operation	Environmental management	Device management
Research group ($n = 46$)	93.24 \pm 2.26	92.49 \pm 2.09	94.75 \pm 2.75	94.14 \pm 2.64	93.65 \pm 2.37	92.53 \pm 2.52	94.39 \pm 2.37
Control group ($n = 46$)	91.59 \pm 2.41	90.64 \pm 2.27	92.47 \pm 2.48	92.75 \pm 2.36	91.48 \pm 2.43	90.33 \pm 2.26	91.43 \pm 2.29
<i>t</i> value	3.387	4.066	4.175	2.662	4.335	4.408	6.091
<i>P</i> value	0.001	0.000	0.000	0.009	0.000	0.000	0.000

3.2. Analysis of professional skills of medical staff

Table 2 shows that the score of professional skills of medical staff in the study group is higher, and the difference is more significant than that in the control group ($P < 0.05$).

Table 2. Analysis of professional skills of medical staff (mean \pm standard deviation, points)

Group	Processing flow	Sterilization packaging	Theoretical knowledge	Cleaning and disinfection	Information traceability
Research group ($n = 4$)	94.97 \pm 2.41	92.69 \pm 2.64	94.78 \pm 2.36	92.54 \pm 2.68	94.42 \pm 2.36
Control group ($n = 4$)	90.62 \pm 2.36	90.43 \pm 2.36	90.25 \pm 2.42	90.46 \pm 2.53	90.08 \pm 2.64
<i>t</i>	2.579	2.970	2.680	2.854	2.451
<i>P</i>	0.041	0.024	0.036	0.029	0.049

3.3. Satisfaction analysis of medical staff

Table 3 shows that the satisfaction score of medical staff in the study group is higher, and the difference is more significant than that in the control group ($P < 0.05$).

Table 3. Satisfaction analysis of medical staff (mean \pm standard deviation, points)

Group	Feasibility of management mode	Device processing efficiency	Risk Management	Work flow	Work environment
Research group ($n = 4$)	95.42 \pm 2.25	95.36 \pm 2.17	93.53 \pm 2.36	96.36 \pm 2.47	95.27 \pm 2.35
Control group ($n = 4$)	90.47 \pm 2.52	90.58 \pm 2.31	91.27 \pm 2.52	91.47 \pm 2.74	90.37 \pm 2.42
<i>t</i>	2.930	3.016	2.467	2.651	2.905
<i>P</i>	0.026	0.023	0.004	0.038	0.027

3.4. Analysis of adverse events of devices

There were 4 (8.70%) cases of adverse events in the control group. The incidence of adverse events in the study group was lower than that in the control group ($\chi^2 = 4.181$, $P = 0.040$).

4. Discussion

CSSD plays an important role in the prevention and control of nosocomial infection. The main responsibilities of the Department are to recycle, wash, disinfect and supply hospital-related equipment. With the rapid development of medical technology, the clinical demand for medical devices is increasing, and the workload of CSSD is also increasing. Based on the characteristics of CSSD work, if the management personnel do not operate in accordance with the relevant standards, it is very easy to cause the failure of equipment disinfection and sterilization, which will increase the risk of nosocomial infection and threaten the safety of medical staff and patients^[2]. Based on the analysis of the CSSD routine management work, it is found that the traditional management work mainly depends on the static standard procedures, and the dynamic monitoring and feedback mechanism is significantly insufficient, which is difficult to adapt to the current CSSD working environment and needs. In addition, the routine management work focuses on implementation, and no effective supervision mechanism has been established, leading to the related problems that cannot be solved in time^[3]. Based on the lack of conventional management, how to promote the quality of CSSD management has become one of the key projects of hospital management.

In this paper, the nursing quality score of the study group was higher, and the difference was more significant than that of the control group ($P < 0.05$). The main reason for the analysis was that the routine management work was mainly carried out according to the CSSD standard, which was contrary to the actual medical work. According to the latest nursing standard in China, the central position of patients should be fully highlighted during nursing, the people-oriented policy should be strictly implemented, and patients should always be taken as the service subject, to provide higher quality nursing services. The detail management not only emphasizes the operation technology and service technology standards, but also uses the personalized and humanized service concept, which fully highlights the moral, cultural, and spiritual implications of nursing staff^[4]. Based on the characteristics of CSSD in the hospital, through the construction of a detailed team and the systematic training and learning for all members, the management staff's work quality can be improved, the ability of cleaning, disinfection and sterilization can be effectively improved, and the control of relevant work processes and systems can be strengthened, which is conducive to the improvement of nursing quality.

In this paper, the score of professional skills of medical staff in the study group was higher, and the difference was more significant than that in the control group ($P < 0.05$). The main reason for the analysis was that detailed management involved more detailed operating procedures, which could provide clearer work guidance for medical staff, and effectively reduced the operation inconsistency caused by personal understanding differences by refining each operation step. According to the characteristics of the equipment, the cleaning, disinfection, and other work processes are refined, special management is carried out for weak links, and the nursing and management operations are standardized, which can improve the professional skills of the staff^[5].

In this paper, the satisfaction score of medical staff in the study group was higher, and the difference was more significant than that in the control group ($P < 0.05$). The main reasons were analyzed as follows: the detailed management measures optimized the workflow, reduced repeated steps or unnecessary operations, and promoted the improvement of the efficiency of device management through the rational division and division of regions, which could avoid the cross-over situation, reduce the workload of medical staff, and then improve the satisfaction^[6]. The detail management measures emphasize the collaborative intervention between staff. By strengthening the quality supervision, it can ensure the seamless connection of all links, avoid the waste of time, and solve the existing problems in time^[7].

In this paper, there were no adverse events during the device management in the study group, and 4 (8.70%) adverse events occurred during the device management in the control group. The incidence of adverse events in the study group was lower, which was more valuable than that in the control group ($P < 0.05$). The main reasons for analysis were that compared with the conventional management measures, the detailed management established a more standardized and high-quality detection procedure, reduced the impact of human factors on the management quality, strictly controlled the device management link, ensured the traceability of the operation process, and therefore reduced the risk of adverse events^[8].

5. Conclusion

In conclusion, the use of detail management in CSSD plays an important role in improving the quality of care, reducing the risk of adverse events, and improving the professional skills and satisfaction of medical staff.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wang X, 2024, Effect of Detail Management under Process Reengineering on Prevention and Control of Nosocomial Infection in Disinfection and Supply Room. *Jiangsu Health Management*, 35(11): 1582–1585.
- [2] Liu S, 2024, Study on the Impact of Detail Management on the Management Quality and Device Treatment Status of Disinfection and Supply Room. *China Medical Device Information*, 30(4): 163–165.
- [3] Song Y, 2024, Effect of Detail Management on Improving the Nursing Quality of Disinfection Supply Room. *China Urban and Rural Enterprise Health*, 39(2): 34–36.
- [4] Jiang Q, Hu A, 2023, Application Value of Detail Management in Nursing Management of Disinfection and Supply Room. *Modern Diagnosis and Treatment*, 34(23): 3608–3610.
- [5] Cui X, 2023, The Application Effect of Nursing Quality Control Management in Disinfection and Supply Room and Its Influence on the Comprehensive Quality of Nursing Staff and the Qualified Rate of Cleaning, Disinfection and Sterilization Items. *Clinical Medical Research and Practice*, 8(9): 146–130.
- [6] Wang Y, 2022, Effect of Refined Quality Control Management Mode on the Qualified Rate of Disinfection and Sterilization of Surgical Instruments and the Incidence of Risk Events in the Disinfection and Supply Room. *China Medical Device Information*, 46(20): 177–179.
- [7] Zheng K, Chen H, Lin H, et al., 2022, Effect of Detail Management Intervention on the Quality of Nursing Management and Equipment Treatment in Disinfection and Supply Room. *Tibet Medicine*, 43(2): 76–78.
- [8] Tian Y, Zheng W, Guo H, 2022, Analysis of the Impact of Implementing Detail Management on Nursing Quality and Nursing Satisfaction in Disinfection Supply Room. *Modern Hospital*, 22(2): 232–235.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Current Situation and Reform of Tumor Radiotherapy Education: Integration and Innovation of Curriculum System, Practical Ability, and Intelligent Technology

Xiaojie Xia, Zeyuan Liu, Xiaolin Ge, Hui Chen, Lu Xu*

Jiangning Clinical Medical College, Kangda College of Nanjing Medical University, Nanjing 211100, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: This study systematically analyzes the current situation of tumor radiotherapy education and reveals the core contradictions it faces: lagging curriculum content, weak practical teaching, and insufficient interdisciplinary knowledge leading to deviations in clinical competence cultivation. Based on the current situation analysis, propose an innovative training model: (1) Curriculum reconstruction: Integrating OBE concept and ADDIE model, constructing a three-level curriculum system of “basic clinical frontier”; (2) Advanced Practice: Establishing a five level capability ladder using the EPA model (basic operations → conventional design → precise implementation → multidisciplinary integration → technological innovation), with supporting dynamic monitoring mechanisms; (3) Technological empowerment: Realizing clinical scene visualization training through digital twins, AI personalized learning systems, and VR/AR technology. The implementation path emphasizes the deep integration of intelligent technology, the incubation of clinical research projects, and the construction of a collaborative ecosystem between industry, academia, and research. The conclusion indicates that this model solves the lack of linkage between educational ecological elements, promotes the transformation of radiotherapy education towards “intelligence, personalization, and globalization,” and provides a systematic solution for the strategic delivery of composite radiotherapy talents for a healthy China.

Keywords: Education in tumor radiotherapy; Innovative training mode; OBE-ADDIE curriculum system; EPAs competency advancement; Intelligent educational technology

Online publication: September 26, 2025

1. Introduction

Radiation therapy, as an important component of the comprehensive management of malignant tumors, has become an indispensable treatment method in clinical intervention. According to statistics, about 60% to 70% of cancer patients require radiation therapy during their disease progression^[1]. In the three-level discipline system of clinical medicine in China, tumor radiotherapy, tumor surgery, and oncology together constitute the three pillars of tumor diagnosis and treatment. Its core value lies in relying on the biological effects of ionizing radiation to achieve precise destruction of tumor targets^[2]. This discipline exhibits significant interdisciplinary integration characteristics. From a theoretical perspective, it is necessary to integrate

multidimensional knowledge systems such as radiation physics, molecular biology, and medical imaging. From a practical perspective, it emphasizes the organic unity of clinical logical reasoning and precise technical execution^[3]. As a highly specialized clinical course, its educational goal is to cultivate composite professionals with solid theoretical foundations, the ability to independently design personalized treatment plans, and the ability to prevent and control complications. The core teaching content covers key modules such as tumor pathology diagnosis, evidence-based evaluation of radiation therapy indications, individualized treatment plan development and implementation, aiming to promote the efficient transformation of multidisciplinary knowledge into clinical competence^[4].

The report of the 20th National Congress of the Communist Party of China for the first time established “people’s health” as a national strategic priority goal, emphasizing “placing the protection of people’s health in a strategic position of priority development”^[5]. This policy orientation not only promotes the deepening reform of the medical and health service system, but also puts forward systematic reconstruction requirements for the medical talent training mode. As a clinical specialty with high technological dependence and interdisciplinary characteristics, radiation therapy urgently needs to keep up with the times in its talent cultivation mode to respond to the urgent demand for comprehensive and innovative medical talents in clinical practice^[6].

This article intends to systematically sort out the structural bottlenecks in China’s current radiation therapy education system, deeply analyze their mechanisms, and propose a future-oriented training model reconstruction path, providing theoretical support and practical reference for the high-quality development of radiation therapy professionals.

2. Multidimensional analysis of the current status of radiation therapy training in medical education

2.1. Structural challenges in undergraduate education

In the undergraduate education system of clinical medicine in China, tumor radiotherapy has long been on the periphery, resulting in a serious lack of depth and breadth in its curriculum content and teaching practice. The educational dilemma is mainly reflected in three aspects: firstly, the updating of course content lags, still relying mainly on the traditional knowledge system of radiation physics, and failing to effectively integrate cutting-edge knowledge such as radiomics and radiogenomics. Secondly, the practical teaching process is weak, and the teaching process highly relies on the clinical experience of individual teachers, lacking a unified standardized case library and ability assessment system. Thirdly, the design of the assessment mechanism is single, still focusing on memory-based knowledge testing, neglecting the systematic evaluation of students’ clinical reasoning, decision-making ability, and technological innovation potential^[7]. Due to the aforementioned shortcomings, students’ knowledge structure exhibits fragmented characteristics, making it difficult to construct a systematic clinical thinking system. Some medical colleges have taken the lead in carrying out teaching reform pilot projects, attempting to integrate flipped classroom and problem-based learning (PBL) methods^[8]. Through the construction of virtual simulation laboratories and the introduction of artificial intelligence-assisted teaching systems^[9,10], the interactivity and effectiveness of teaching have been improved to a certain extent, providing a reference path for subsequent reforms.

2.2. Transformation challenges of graduate education

Due to the educational gap at the undergraduate level, graduate students majoring in tumor radiotherapy generally face the dilemma of starting from a “zero foundation.” This educational gap prolongs the formation cycle of professional abilities and also puts higher demands on the curriculum design and practical training at the graduate level^[11]. Although standardized training for resident physicians has played a certain role in improving clinical skills, the current textbook system generally lags: it fails to integrate emerging technologies such as radiomics analysis and adaptive radiotherapy promptly^[12]. This deficiency forces graduate students to rely on unstructured knowledge acquisition pathways, resulting in a significant gap between theoretical learning and clinical application, seriously restricting the development of their

scientific research and innovation abilities, reflecting the systematic deficiencies of the current training mechanism in knowledge updating, skill transformation, and ability evaluation.

2.3. Analysis of structural contradictions

The shortage of radiation therapy professionals is not only due to insufficient educational coverage, but also closely related to the high threshold training requirements determined by their professional characteristics. From the perspective of epidemiology, the incidence rate of cancer continues to rise, which makes the demand for radiotherapy talents continue to expand, and the teaching content of radiotherapy in undergraduate education and clinical practice is obviously insufficient; At the level of professional characteristics, the cultivation of qualified talents requires a systematic training cycle of 3-5 years, and the existing education structure is difficult to meet this demand. There are two structural contradictions in the current education system: (1) The systematic disconnection between theory and practice, and the significant temporal and spatial separation between knowledge transmission and clinical scenarios. The traditional curriculum system keeps theoretical cognition at the level of abstract concepts and cannot support complex clinical decision-making needs. The assessment mechanism overly focuses on knowledge reproduction ability and neglects the effective evaluation of clinical thinking ability, resulting in a significant deviation between educational output and job competency requirements; (2) The curriculum system lacks interdisciplinary integration and follows a linear logic of “foundation clinical specialty.” The teacher’s background is single, making it difficult for students to establish a comprehensive understanding of the radiotherapy technology system. Clinical skills training is limited within the radiotherapy department and has not established a collaborative training mechanism with multiple disciplines, such as oncology, surgery and internal medicine, which cannot meet the practical needs of modern medicine for multidisciplinary diagnosis and treatment (MDT).

These structural contradictions reveal that the systematic reconstruction of radiation therapy education is imperative. The reform of radiation therapy education needs to go beyond local improvement paths and establish a comprehensive education ecosystem that deeply integrates theory and practice and cross-disciplinary linkage through the reconstruction of the “interdisciplinary clinical integration technological innovation” training system, in order to cultivate high-level talents who can truly meet future medical challenges.

3. Construction of an innovative training mode

3.1. Curriculum system paradigm reconstruction

Result-oriented education is a student-centered teaching method, first established as a core concept by American educator Spady in the 1990s. The ADDIE model (Analysis Design Development Implementation Evaluation) is a structured approach that helps teachers effectively set teaching objectives and evaluate learning outcomes. It determines teaching objectives through a structured approach, by determining what to learn, how to learn, and how to determine if learners have achieved learning outcomes, to assist teachers in implementing effective teaching. OBE focuses on the achievement of students’ ultimate competence, emphasizing the development of teaching objectives based on what they can do. The ADDIE model provides clear process support and strengthens the structured organization of teaching content and methods. In the theoretical curriculum system of radiation therapy, based on the integration framework of Outcome-Based Education (OBE) and ADDIE model, the ultimate goal is to master the basic theory of radiation therapy, integrate multidisciplinary knowledge systems, and achieve the core competence of radiation oncologists. The three-level curriculum modules of radiation therapy are constructed with “basic clinical frontier”, corresponding to three types of educational objectives: knowledge integration, clinical ability cultivation, and innovative expansion:

- (1) Basic stage curriculum architecture: Focusing on the theoretical cornerstone of radiation therapy, focusing on integrating multidisciplinary basic knowledge. The curriculum includes Introduction to Radiobiology, Medical Imaging Anatomy, Radiotherapy Physics, and AI, guiding students to understand the interdisciplinary logic from radiation effect mechanisms to imaging and dose calculation. The teaching method should adopt a modular

design, promote cognitive integration through embedding real cases and problem-driven learning. Highlight the construction of “knowledge networking.” Through contextualized case teaching, students can understand the connection between radiobiological effects and therapeutic mechanisms, and construct a systematic knowledge framework from molecular mechanisms to dose delivery.

- (2) Clinical stage competency development: Focusing on the improvement of clinical competence, the course introduces a “clinical decision tree” orientation, with typical cases as the main line, covering the complete clinical process from treatment indication evaluation, scheme formulation, target area delineation to dose verification, including indication evaluation, target area delineation, plan design, and efficacy feedback. Cooperate with virtual simulation platforms and AI-assisted training systems to achieve interactive training for students in near-real scenarios, improving clinical judgment and operational proficiency.
- (3) Frontier stage innovation expansion: Focus on the integration and improvement of cutting-edge technology and humanistic literacy. The course covers modules such as radiomics, biological dose prediction, clinical ethics, and technical risk assessment. Combining ethics, communication skills, and medical humanities courses, it promotes the cultivation of critical thinking, moral judgment, and collaborative spirit. Strengthen their doctor-patient communication skills and humanistic awareness through ethical decision-making sand tables, role-playing, and other situational simulations.

3.2. Advanced construction of practical teaching system

The Entrustable Professional Activities (EPAs) education model, established by Professor Ten Cate’s team in the early 21st century, deconstructs complex clinical work into a series of specific, observable, and assessable behavioral units. Through detailed evaluation criteria and feedback mechanisms, it effectively improves the clinical competence and professional ethics of resident physicians. Research has shown that a diversified teaching program designed based on the six-dimensional competency model of “professional knowledge, clinical skills, communication skills, teamwork, research ability, and professional ethics” constructed based on EPAs significantly improves the comprehensive abilities of resident physicians compared to traditional training methods that combine learning and rotational practice. In the field of radiotherapy, a “5-level advanced system” has been constructed based on practical abilities, scientific research innovation, and interdisciplinary cooperation, combining EPAs with the actual clinical needs in China. It covers basic operations, conventional treatment, precision radiotherapy, interdisciplinary integration, and technological innovation.

The first stage is the basic operational level, emphasizing the standard operation of radiotherapy equipment, the standardized execution of treatment processes, and training in radiation safety knowledge and management processes. The focus is on mastering the usage norms of radiotherapy equipment, radiation safety protection, and operational process standards to ensure preliminary competence in routine treatment room operations. The second stage is the ability to design conventional plans, including the development of three-dimensional conformal radiotherapy plans, dose distribution optimization, and basic quality control skills, to enhance the ability to develop treatment plans for three-dimensional conformal radiotherapy and conventional IMRT, and to learn to independently complete target segmentation, dose calculation, and plan evaluation. The third stage involves precise radiotherapy capabilities, where the system masters the application and quality control methods of high-precision technologies such as IGRT, SBRT, and adaptive radiotherapy, and achieves precise implementation and adjustment through real case simulations, such as the operation and quality control of IGRT, adaptive radiotherapy, and SBRT. In the fourth stage, the study will expand the cultivation of interdisciplinary collaborative abilities, combine MDT simulation exercises to train students to propose reasonable treatment suggestions in interdisciplinary contexts, promote collaborative work between students and departments such as oncology, surgery, and imaging, and enhance their ability to design personalized treatment plans through interdisciplinary collaboration. The fifth stage is technological innovation capability, including AI assisted program design, radiomics analysis, and feasibility assessment of new technologies. Students are encouraged to identify technical bottlenecks during clinical training, carry out small-scale scientific research projects, explore research directions such as AI-assisted therapy

and radiomics modeling, and enhance their innovation awareness and transformation ability.

4. Implementation path and safeguard measures

4.1. Intelligent technology empowers educational innovation

Faced with the rapidly developing trend of radiation therapy technology, traditional teaching models are no longer able to meet the requirements of modern education for refinement, visualization, and interactivity, as well as the practical needs of future medical talent cultivation. Therefore, it is necessary to actively introduce intelligent technological means, adapt to the trend of deep integration of technology and education, and construct a new teaching paradigm of “technology-driven virtual real integration”. Among them, digital twin technology can achieve precise modeling of clinical equipment and processes in virtual space, create a virtual training environment that can be operated repeatedly and provide feedback in real-time, significantly improve teaching safety and efficiency, and achieve full process visualization training from case input, target area delineation to dose distribution. Artificial intelligence technology can be used to construct personalized learning paths. By analyzing students’ learning behavior data through deep learning models, real-time recognition of knowledge mastery blind spots, and providing accurate learning feedback based on intelligent recommendation systems, a precise teaching path is constructed to improve learning efficiency and pertinence. In addition, virtual reality (VR) and augmented reality (AR) technologies can be used to simulate complex radiotherapy operation scenarios into interactive training modules, allowing students to complete practical exercises of complex skills such as target area delineation and dose distribution regulation in a risk-free environment, reducing the risk of novice misoperation and improving training effectiveness. Furthermore, a dynamic treatment model can be constructed by combining real patient data to promote the visualization and deduction of dose distribution and biological effects. Students can enhance their clinical adaptability through the full process training of “simulated reception treatment decision-making scheme formulation efficacy feedback”, and help students understand the application of biological effects in individual treatment.

4.2. Student development support system

Build a student-centered “ability development transformation” closed-loop support system to promote the transformation of medical students from passive learners to active knowledge constructors. Firstly, implement a multidimensional competency assessment system that covers core dimensions such as professional knowledge, clinical skills, scientific research ability, communication and collaboration, and ethical judgment. Based on the assessment results, customize personalized training paths for students. Secondly, establish a “scientific research clinical” integrated platform, and through project-based training during the clinical rotation period, require students to start from actual clinical problems and complete a complete research path from mechanism exploration to technology transformation. Encourage them to design and implement technological innovation solutions based on actual clinical needs to enhance their research thinking and problem-solving abilities. Ultimately, an excellent project incubation mechanism will be established by setting up a “Hospital Innovation Workshop” to provide seed funding, mentor resources, and technical transformation support for high-potential projects, accelerate the implementation of results, and stimulate students’ innovative vitality and professional identity.

4.3. Collaborative evolution of the education ecosystem

The system needs to break away from the closed operation mode of the traditional medical education system and shift towards an open education ecosystem with multi-party collaboration. The specific path includes: in terms of the integration mechanism of industry, academia, and research, co-building teaching, research, and development integrated laboratories with high-end medical equipment manufacturing enterprises, and promoting the integration path of “demand technology product.” By incorporating frontline clinical needs into the R&D process of enterprises, we aim to enhance students’ engineering thinking and technical application abilities. At the level of the education feedback system, establish a medical

education innovation fund to return a portion of the profits from the transformation of medical research achievements to the education sector for talent cultivation and teaching reform, forming a virtuous cycle of “research transformation education.” Strengthening the embedding mechanism of social responsibility in the empowerment process of social responsibility: integrating public health science popularization into radiotherapy teaching content, organizing students to participate in community tumor screening and health education practices, enhancing their sense of professional mission and social responsibility, improving the public’s impression of “radiation damage” in radiotherapy, and creating a social public opinion environment conducive to the development of the discipline.

5. Conclusion

This study systematically identifies the structural barriers in the current education system for tumor radiotherapy, pointing out multiple bottlenecks such as outdated course content, weak practical links, and incomplete ability evaluation mechanisms. It reveals that the lack of linkage mechanisms between elements in the education ecosystem is the fundamental reason for the deviation in clinical competence cultivation. The current education ecosystem has failed to achieve organic linkage between teaching elements, resulting in a gap between students’ theoretical cognition, skill mastery, and innovation ability, which makes it difficult to meet the needs of the era of precision medicine and interdisciplinary integration development. On this basis, this article proposes an innovative training model with “curriculum system reconstruction-practical ability advancement-technology integration driven” as the core. This model takes ability orientation as the core and intelligent means as tools to promote the transformation of teaching from “knowledge imparting” to “competence cultivation.” It strives to build a composite education system that integrates multidisciplinary knowledge, enhances practical ability, and technology innovation orientation, providing theoretical support and operational path for the high-quality development of radiation therapy professionals in the new era.

Overall, the education of tumor radiotherapy is undergoing a deep transformation from “traditional indoctrination” to “intelligent empowerment.” The innovative training path constructed by our research institute is closely aligned with the national strategic goal of “Healthy China 2030” in strategic logic, and is in line with the development trend of new medicine in educational practice. We are committed to cultivating new era radiotherapy experts with technical capabilities, clinical thinking, and a humanistic spirit, and continuously injecting high-quality talent into China’s cancer prevention and treatment industry.

Funding

Research and Development Fund of Kangda College, Nanjing Medical University (Project No.: KD2023 KYJJ265).

Disclosure statement

The author declares no conflict of interest.

References

- [1] Lin B, Gao F, Yang Y, et al., 2021, FLASH Radiotherapy: History and Future. *Frontiers in Oncology*, 11: 644400.
- [2] Li Y, 2018, *Tumor Radiotherapy*. China Union Medical College Press, Beijing, 5th ed.
- [3] Zhao L, Mao J, Yin R, et al., 2017, Evaluation of the Effectiveness of Different Teaching Modes in Tumor Radiotherapy. *Chinese Journal of Cancer Prevention and Treatment*, 24(22): 1600–1603.
- [4] Walls G, Hanna G, McAleer J, 2020, Learning Radiotherapy: The State of the Art. *BMC Medical Education*, 20(1): 150.

- [5] The Central People's Government of the People's Republic of China, 2022, Holding High the Great Banner of Socialism with Chinese Characteristics and Working Together to Build a Socialist Modernized Country in an All-round Way – Report at the 20th National Congress of the CPC, visited on June 20, 2025, http://www.gov.cn/20thcpc/2022-10/25/content_5721685.htm.
- [6] Li K, Qu S, 2022, Preliminary Application of Exploratory Learning Mode in Tumor Radiotherapy Teaching. *Continuing Medical Education*, 36(7): 73–76.
- [7] Jin Y, Guo Y, Wang Y, et al., 2022, Research on the Practice and Effect of Bloom's Vertebral Teaching Method in Evidence-based Medicine English Teaching for International Students. *Research on Medical Teaching in Universities*, 12(1): 11–15.
- [8] Zhan Q, Ma J, Duan Y, 2024, Application of Flipped Classroom Combined with PBL in Clinical Teaching of Tumor Radiotherapy. *China Health Industry*, 21(10): 168–170.
- [9] Xin Z, Zhang T, 2023, Application of Problem-based Teaching Method Combined with Simulation Laboratory in the Teaching of Target Area Delineation in Tumor Radiotherapy. *China Higher Medical Education*, 2023(8): 110–111.
- [10] Xu J, Cai H, 2023, The Application and Progress of Virtual Reality Technology in Radiotherapy Teaching. *China Continuing Medical Education*, 15(8): 186–189.
- [11] Li M, Siqin G, 2018, Preliminary Exploration of Teaching Reform in Tumor Radiotherapy. *Anhui Pharmaceutical*, 22(4): 793–794.
- [12] Hong L, Guo L, 2016, Exploration on the Construction of Innovative Talent Training Model in Collaborative Innovation Centers of Chinese Universities. *Chongqing Higher Education Research*, 4(1): 72–75.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Study on the Treatment of Alzheimer's Disease of Spleen Deficiency and Phlegm Obstruction Type by Wenpi Tongluo Kaiqiao Formula Combined with Acupuncture

Lingfei Jiang¹, Qianqian Li¹, Wei Chen^{2*}

¹Graduate School of Guangxi University of Chinese Medicine, Nanning 530200, Guangxi, China

²The First Affiliated Hospital of Guangxi University of Chinese Medicine, Nanning 530023, Guangxi, China

*Corresponding author: Wei Chen, jlfcm@foxmail.com

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To observe the clinical efficacy of Wenpi Tongluo Kaiqiao Formula combined with acupuncture in the treatment of Alzheimer's disease (AD) of spleen deficiency and phlegm obstruction type. *Methods:* 90 cases with AD of spleen deficiency and phlegm obstruction type who were admitted to the Department of Encephalopathy of the First Affiliated Hospital of Guangxi University of Chinese Medicine from December 2023 to October 2024 were selected and randomly divided into the control group, the decoction group, and the acupuncture-medication group, with 30 cases in each group. The control group was given donepezil hydrochloride tablets orally; the decoction group was given Wenpi Tongluo Kaiqiao Formula in addition to the treatment in the control group; the acupuncture-medication group was given acupuncture method of invigorating the spleen, resolving phlegm, and opening the orifices in addition to the treatment in the decoction group. The treatment course for each group was 4 weeks. After treatment, the clinical total effective rate of the three groups was compared, and their safety was evaluated. *Results:* 81 cases completed the trial (27 cases in the control group, 26 cases in the decoction group, and 28 cases in the acupuncture-medication group). There was a statistically significant difference in the total effective rate among the three groups ($P < 0.05$), with the acupuncture-medication group having the best efficacy, followed by the decoction group, and the control group having the poorest efficacy. There were no adverse reactions reported in any group during the treatment course. *Conclusion:* Wenpi Tongluo Kaiqiao Formula combined with acupuncture is more effective than either taking donepezil hydrochloride tablets alone or taking donepezil hydrochloride tablets combined with Wenpi Tongluo Kaiqiao Formula for this type of AD, and it is worthy of clinical promotion.

Keywords: Wenpi Tongluo Kaiqiao Formula; Acupuncture; Alzheimer's disease; Spleen Deficiency and Phlegm Obstruction Type; Clinical Observation

Online publication: September 26, 2025

1. Introduction

Alzheimer's disease (AD) is a common neurodegenerative disorder in the elderly, characterized by cognitive decline, memory impairment, and behavioral abnormalities. Its pathogenesis involves cholinergic dysfunction, amyloid beta (A β) deposition, tau protein phosphorylation. Existing medications (e.g., acetylcholinesterase inhibitors) can alleviate symptoms, but have high costs and toxic side effects. In traditional Chinese medicine (TCM), AD is categorized as dementia.

Professor Zihui Wu, a renowned TCM expert from Guangxi, proposed that spleen deficiency and phlegm obstruction is the key pathogenesis, and used Wenpi Tongluo Kaiqiao Formula to warm the spleen, resolve phlegm, unblock collaterals, and open orifices. Clinically, this formula has been shown to improve TCM symptoms. Additionally, acupuncture can intervene in the pathogenesis of AD and improve neurological function. This study investigates the therapeutic efficacy of combining these two approaches, as reported below.

2. Background and methods

2.1. General information

90 cases with Alzheimer's disease (AD) of the spleen deficiency and phlegm obstruction type were enrolled and randomly divided into 3 groups (30 cases in each group). During the study, 3 cases dropped out of the control group (1 due to medication-related pain, 1 lost to follow-up, and 1 due to dizziness), 4 cases dropped out of the decoction group (2 lost to follow-up and 2 unexpectedly withdrew), and 2 cases dropped out of the acupuncture-medication group (both due to voluntary withdrawal). The baseline characteristics (age, gender, education level, disease duration) showed no statistically significant differences ($P > 0.05$) among the three groups, indicating comparability. This study was approved by the hospital ethics committee (Approval No.: 2023-015-01), and informed consent was obtained from all patients and their families.

2.2. Diagnostic criteria

2.2.1. Western medicine diagnosis

Refer to the diagnostic criteria for AD in the International Classification of Diseases, Tenth Revision (ICD-10) ^[1].

2.2.2. Chinese medicine diagnosis

Refer to the syndrome differentiation of spleen deficiency and phlegm obstruction type in the Internal Medicine of Traditional Chinese Medicine (2017 Edition) ^[2] (main symptoms include cognitive decline, combined with secondary symptoms, tongue and pulse signs).

2.3. Inclusion and exclusion criteria

2.3.1. Inclusion criteria

- (1) Meet the diagnostic criteria for both Western medicine and Traditional Chinese Medicine (TCM);
- (2) Aged 65–85 years old;
- (3) Mini-Mental State Examination (MMSE) score of 10–24 and Clinical Dementia Rating (CDR) score of 1.0–2.0;
- (4) Provide informed consent.

2.3.2. Exclusion criteria

- (1) CDR score of 3.0, illiteracy, or severe sensory impairment;
- (2) Other comorbidities (e.g., sequelae of cerebral infarction, Parkinson's disease);
- (3) Use of antidepressants, antipsychotics, or nootropic drugs not specified in this study within the past month, which cannot be discontinued;
- (4) History of allergies, major organ dysfunction, or suicidal tendencies.

2.4. Treatment methods

2.4.1. Control group

Onepezil hydrochloride tablets (5 mg/tablet; National Medicine Approval Number H20050978) , 10 mg per time, once daily before bedtime, for 4 weeks.

2.4.2. Decoction group

In addition to the treatment in the control group, Wenpi Tongluo Kaiqiao Formula was added [Huangqi (Radix Astragali seu Hedysari) 30 g, Yizhiren (Fructus Alpiniae Oxyphyllae) 10 g, Sanqi (Radix et Rhizoma Notoginseng) 10 g, Chichangpu (Rhizoma Acori Tatarinowii) 10 g, Heshouwu (Radix Polygoni Multiflori) 10 g, Jiaogulan (Herba Gynostemmae Pentaphylli) 10 g], decocted in water, 200 mL per pack, twice daily, take it warm after breakfast and dinner, for 4 weeks.

2.4.3. Acupuncture-medication group

In addition to the treatment in the decoction group, the acupuncture method of invigorating the spleen, resolving phlegm, and opening the orifices was added. The selected acupoints included Baihui (GV20), Sishencong (EX-HN1), Fengfu (GV16), Taixi (KI3), Xuanzhong (GB39), Zusanli (ST36), Fenglong (ST40), Zhongwan (CV12). Neutral reinforcement and reduction, retaining needle for 30 min, once daily, 5 times per week, for 4 weeks.

2.5. Efficacy evaluation criteria

Refer to efficacy index assessment based on the Mini-Mental State Examination (MMSE) [3]: Efficacy index = (Post-treatment Score – Pre-treatment Score) / Pre-treatment Score × 100%. Clinical recovery: efficacy index ≥ 85%; Markedly effective: 50% ≤ efficacy index < 85%; Effective: 20% ≤ efficacy index < 50%; Ineffective: efficacy index < 20%. Total effective rate = (Number of Cases with Clinical Recovery + Markedly Effective + Effective) / Total Cases × 100%.

2.6. Statistical methods

SPSS 21.0 was used for analysis. The Kruskal-Wallis H test was employed to compare the overall differences in efficacy among the three groups. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of clinical efficacy among the three groups

The Kruskal-Wallis H test revealed statistically significant differences in overall efficacy among the three groups (*P* < 0.05). The total effective rates were as follows: control group (59.26%, 16/27), decoction group (78.57%, 22/28), and acupuncture-medication group (92.59%, 25/27). The acupuncture-medication group demonstrated the highest efficacy, followed by the decoction group, while the control group showed the lowest efficacy. See **Table 1** for details.

Table 1. Comparison of clinical efficacy among the three groups [n (%)]

Group	Cases	Ineffective	Effective	Markedly effective	Clinical recovery	Total effective
Control	27	11 (40.74)	16 (59.26)	0 (0.00)	0 (0.00)	16 (59.26)
Decoction	28	6 (21.43)	18 (64.29)	4 (14.28)	0 (0.00)	22 (78.57)
Acupuncture-Medication	27	2 (7.40)	11 (40.74)	13 (48.15)	1 (3.70)	25(92.59)

4. Discussion

The pathogenesis of AD is complex, involving Aβ deposition [4], Tau protein phosphorylation [5], and cholinergic dysfunction [6]. The commonly used drugs like donepezil hydrochloride can alleviate symptoms, but may cause adverse reactions such as gastrointestinal discomfort, insomnia, dreaminess, and muscle spasms [7]. In Traditional Chinese Medicine, the pathogenesis of spleen deficiency with phlegm obstruction type is characterized by dysfunction

of the spleen in transportation, leading to malnourishment of the brain marrow and phlegm turbidity blocking the brain collaterals. Therefore, Wenpi Tongluo Kaiqiao Formula is used for intervention (with Huangqi and Yizhiren as sovereign medicinal to invigorate the spleen and benefit intelligence, Shichangpu and Sanqi as minister medicinal to resolve phlegm and unblock collaterals, Heshouwu and Jiaogulan as assistant medicinal to tonify the liver and kidney and resolve phlegm accumulation). Modern pharmacological studies have shown that astragaloside can reduce A β generation^[8]. Yizhiren extract can improve cognitive impairment and neuroinflammatory reactions induced by A β ^[9]. Shichangpu extract can inhibit A β misfolding^[10]. Notoginsenoside can downregulate Tau phosphorylation^[11]. Acupuncture at the Governor Vessel points (GV20, EX-HN1, GV16) and spleen-kidney strengthening points (ST36, ST40, KI3, etc.) can regulate neurotransmitters and inhibit neuroinflammation^[12,13], which works together with herbal medicine to regulate zang-fu organs and unblock meridians, offering a multi-target approach to improve AD pathology.

5. Conclusion

In conclusion, the combination of Wenpi Tongluo Kaiqiao Formula and acupuncture demonstrates definite efficacy and good safety in treating AD of spleen deficiency and phlegm obstruction type, providing a novel integrative Chinese and Western medicine approach for AD management.

Funding

High-level Talent Team of “Qihuang Project” at Guangxi University of Chinese Medicine (Project No.: 202410)

Disclosure statement

The author declares no conflict of interest.

References

- [1] World Health Organization, 1992, International Classification of Diseases, 10th Revision (ICD-10). WHO Press, Geneva: 338–342.
- [2] Zhang B, Wu M, 2017, Internal Medicine of Traditional Chinese Medicine. China Traditional Chinese Medicine Press, Beijing: 289–295.
- [3] Yang H, 2017, The Clinical Observation on Alzheimer Disease of Spleen Deficiency and Sputum Resistance Type with Modified Wenpi Tongluo Kaiqiao Decoction, thesis, Guangxi University of Chinese Medicine.
- [4] Salim S, 2017, Oxidative Stress and the Central Nervous System. J Pharmacol Exp Ther, 360(1): 201–205.
- [5] Mijalkov M, Vereb D, Canal-Garcia A, et al, 2023, Nonlinear Changes in Delayed Functional Network Topology in Alzheimer’s Disease: Relationship with Amyloid and Tau Pathology. Alzheimers Res Ther, 15(1): 112.
- [6] Hampel H, Mesulam M, Cuello A, et al, 2018, The Cholinergic System in the Pathophysiology and Treatment of Alzheimer’s Disease. Brain, 141(7): 1917–1933.
- [7] Pan J, 2021, Analysis of the Effect of Donepezil Hydrochloride in the Treatment of Senile Dementia. The Medical Forum, 25(08): 1172–1173.
- [8] Yan Y, 2016, Protective Effect and Its Oxidation Mechanisms of the Main Components of Astragalus on A β 25-35-Induced Alzheimer’s Disease Rat Model, thesis, Wuhan University.
- [9] Shi S, Zhang C, Liu B, et al, 2013, Study on Anti-Senile Dementia Function of Different Polar Extracts of Alpinia

Oxyphylla. China Pharmacy, 24(27): 2507–2510.

- [10] Zhou Y, Li W, Li H, 2023, Research Progress on Mechanism of Action of Rhizoma Acori Tatarinowii in Prevention and Treatment of Alzheimer's Disease. China Medical Herald, 20(27): 64–67.
- [11] Sun T, Li W, Wang D, 2020, Network Pharmacology Analysis of Panax Notoginseng in Alzheimer's Disease. Journal of Guangdong Medical University, 38(05): 556–561.
- [12] Qin H, 2020, Clinical Observation on the Treatment of Mild Cognitive Impairment in Alzheimer's Disease by Acupuncture Combined with Donepezil Hydrochloride Based on Governor Channel Theory, thesis, Heilongjiang University of Chinese Medicine.
- [13] Wang F, Wang M, 2017, Acupuncture at Wushen Points in Treatment of Vascular Dementia of Relieving Delay Detention. Liaoning Journal of Traditional Chinese Medicine, 44(11): 2403–2405.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Construction of an Amputation Risk Prediction Model for Patients with Diabetic Foot (DF) in a Civil Aviation Hospital

Zhengfeng Liu¹, Sunhang Cao², Dongmei Zhai³, Zhiqiang Huang¹, Yaochen Yang¹, Yunheng Song¹, Mai Zhou⁴, Wuyi Deng^{1*}

¹Vascular Surgery Department, Civil Aviation General Hospital, Beijing 100123, China

²Physical Examination and Rehabilitation Center, Civil Aviation General Hospital, Beijing 100123, China

³China Travel Sky Holding Company, Beijing 101318, China

⁴General Surgery Department, Civil Aviation General Hospital, Beijing 100123, China

*Corresponding author: Wuyi Deng, 1164132935@qq.com

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To construct a prediction model to predict the amputation risk of patients with diabetic foot (DF) in a civil aviation hospital, identify key influencing factors of amputation risk, and predict the probability of amputation, thereby providing a reference for condition evaluation and medical management of DF patients. *Methods:* Basic data, DF data, and laboratory index data were collected from 48 DF patients (selected based on inclusion and exclusion criteria) who visited a civil aviation hospital in Chaoyang District, Beijing, from 2023 to 2024. Descriptive statistics were performed to establish baseline characteristics, followed by univariate analysis (comparison between groups). Variables with P-values less than 0.05 were selected for multivariate binary logistic regression analysis to form a regression model. The prediction performance of the model was analyzed to establish a robust prediction model that provides a reference for predicting amputation risk in DF patients. *Results:* Whether the Wagner score is greater than 3, the presence of PAD, and abnormal CRP levels were identified as independent risk factors for amputation in DF patients. A prediction model was formed with an AUC of 0.970, indicating good performance. This model can serve as an effective tool for predicting amputation risk in DF patients and provide a reference for clinical decision-making.

Keywords: Diabetic foot; Amputation risk; Prediction model; Regression model

Online publication: September 26, 2025

1. Introduction

Diabetic foot (DF) is a common complication among diabetic patients, which can easily progress to amputation, thereby affecting the quality and duration of patients' lives ^[1]. Statistics show that among a large number of diabetic patients, nearly 10% suffer from DF. DF is prone to recurrence and has a high amputation rate, with one DF patient undergoing amputation every 20 seconds globally ^[2]. Therefore, it is of great significance to effectively predict the risk of amputation in DF patients. This study

aims to identify the risk factors that affect amputation in DF patients, construct a prediction model, and forecast the risk of amputation, thereby providing a reference for early clinical prediction of patients' amputation probability. This study can assist in the accurate selection of treatment plans and improve treatment effectiveness, as well as offer guidance for patients' daily care and other aspects.

2. Materials and methods

2.1. Clinical data

A total of 48 DF patients who visited the Civil Aviation General Hospital in Chaoyang District, Beijing, from 2023 to 2024 were selected. Among them, 29 were male (60.42%) and 19 were female (39.58%). The patients' ages ranged from 40 to 89 years, with an average age of (68.58 ± 12.14) years old. The study was approved by the ethics committee.

Inclusion criteria: (1) Met the diagnostic criteria for DF published by the International Working Group on the Diabetic Foot (IWGDF) in 2015^[3]; (2) aged ≥ 18 years old; (3) had complete relevant data.

Exclusion criteria: (1) aged < 18 years old; (2) foot ulcers caused by non-diabetic conditions; (3) history of lower limb amputation; (4) comorbidity with other severe systemic diseases such as cancer, severe liver or kidney failure, etc., and (5) mental or cognitive disorders that prevent cooperation with the study.

2.2. Collection of research variables

This is a retrospective study that collects clinical data of patients with DF through the medical record system of Civil Aviation General Hospital, including but not limited to basic information such as age^[4] and gender^[5], DF disease course^[6], Wagner classification^[7], comorbidities (such as peripheral arterial disease), wound condition, necrosis, amputation, and other disease information; as well as laboratory indicators such as uric acid, CRP^[8], and N%.

Data definition and preprocessing: Amputation includes major amputation and foot amputation. Researchers are divided into amputation and non-amputation groups. Wagner is bounded by a median of 3, divided into >3 and ≤ 3 groups, represented by 1 and 0, respectively; comorbidities are indicated by 0 or 1; wound condition and necrosis are evaluated by experts and divided into 0 and 1; uric acid, CRP, and N% are divided into abnormal and normal values based on medical standards, also represented by 0 and 1. After data collection, they are imported into the research database. The import process is verified by two people. After data collection, preprocessing operations such as data cleaning are performed.

2.3. Statistical analysis

Data is entered using EXCEL, processed using SPSS 29.0 software, and graphs are drawn using R 4.5. Descriptive statistical process: For continuous variables, according to the normal distribution compliance, mean \pm standard deviation (SD) and M(IQR) are used to represent them respectively. Categorical variables are represented by frequency. In the comparison between groups, independent sample *t*-tests, χ^2 -tests, Mann-Whitney U tests, and Fisher's exact tests are used according to different situations. Variables with statistically significant differences in univariate analysis ($P < 0.05$) are further included in multivariate binary logistic regression analysis to screen independent predictors ($P < 0.05$) to form a prediction model. ROC curves are drawn, AUC is used to evaluate the model effect, DCA curves are drawn using R, and the full intervention curve and the overall intervention curve are compared to evaluate clinical practicality.

3. Results

3.1. Baseline characteristics of participants and results of univariate analysis

The study sample consisted of 48 cases, including 29 males (60.42%) and 19 females (39.58%). The age range was 40 to 89 years, with an average age of (68.58 ± 12.14) years old. There were 36 amputation cases (75.00%) and 12 non-

amputation cases (25.00%). In the amputation samples, males were more numerous than females, while in the non-amputation samples, the male-female ratio was balanced (**Table 1**). In the univariate analysis, variables with statistically significant differences between the two groups ($P < 0.05$) were: Wagner grade > 3 , presence of Pad, abnormalities in N%, abnormalities in CRP, necrosis, and wound condition.

Table 1. Baseline characteristics of participants and results of univariate analysis

Variable	Amputation Group ($n = 36$)	Non-amputation group ($n = 12$)	t/z/ χ^2	P-value
Age (years)	71.00 \pm 11.46	67.78 \pm 12.41	0.793	0.432
Gender (Male/Female)	23/13	6/6	-	0.501
Wagner Grade > 3 (Y/N)	34/2	3/9	-	< 0.001
PAD (Y/N)	33/3	5/7	-	< 0.001
Abnormal Neutrophil% (Y/N)	28/8	4/8	-	0.011
Abnormal Uric Acid (Y/N)	16/20	5/7	-	0.569
Abnormal CRP (Y/N)	34/2	4/8	-	< 0.001
DF Duration (days)	35 (IQR = 158)	75 (IQR = 254)	-0.526	0.599
Gangrene (Y/N)	19/17	2/10	4.769	0.029
Large Wound (Y/N)	26/10	4/8	-	0.036

3.2. Prediction model construction

Using the variables with $P < 0.05$ from the univariate analysis (Wagner grade > 3 , presence of Pad, abnormalities in N%, abnormalities in CRP, necrosis, and wound condition) as independent variables, and amputation status as the dependent variable, a multivariate binary logistic regression was performed. The results are shown in Table 2. As can be seen from **Table 2**, Wagner grade > 3 , presence of Pad, and abnormalities in CRP are independent risk factors for predicting the risk of amputation in patients with DF.

Table 2. Results of multivariate binary logistic regression analysis

Variable	B	SE	Wald χ^2	P-value	OR (95% CI)
Wagner Grade > 3 (Y/N)	3.412	1.600	4.547	0.033	30.34
PAD (Y/N)	3.970	1.995	3.959	0.047	52.98
Abnormal Neutrophil% (Y/N)	2.043	1.751	1.361	0.243	7.72
Abnormal CRP (Y/N)	4.377	2.210	3.924	0.048	79.58
Gangrene (Y/N)	1.530	1.649	0.861	0.353	4.62
Large Wound (Y/N)	-1.085	1.567	0.480	0.488	0.34
Constant	-8.344	3.799	4.823	0.028	0.00

3.3. Prediction model performance analysis

The Hosmer-Lemeshow test value for this model was 0.742, indicating good model fit. The ROC curve for this model is shown in **Figure 1** (due to step size and sample size effects, the ROC curve has a significant turn), with an AUC of 0.970. The model demonstrates good discrimination and performance.

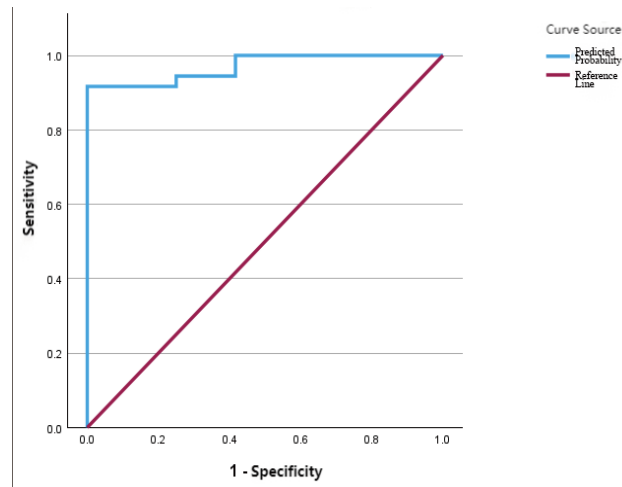


Figure 1. ROC curve.

The DCA curve in **Figure 2** illustrates that within the probability threshold range of 0.1 to 0.5, the model curve is higher than the benchmark curves for both full intervention and no intervention (thresholds greater than 0.5 are not considered, as treatment is required in this range). This suggests that using this model to guide clinical decision-making within this threshold range can yield a positive net benefit. Specifically, at the commonly used 30% threshold in clinical practice, the net benefit of the model is higher than both the full intervention and no intervention strategies, indicating the model's overall strong clinical utility.

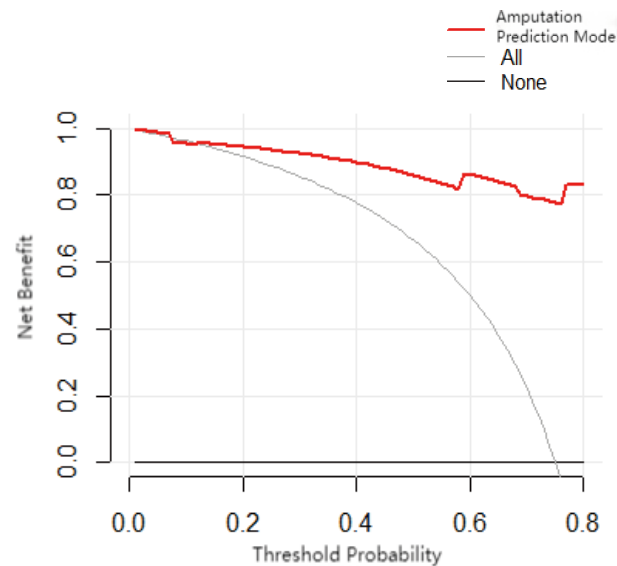


Figure 2. DCA curve.

4. Discussion

Diabetic foot (DF) refers to foot infections, ulcers, or tissue damage in diabetic patients due to factors such as infection, peripheral neuropathy, or vascular disease. It is characterized by high morbidity, mortality, and recurrence rates. For DF patients who do not respond well to conservative treatment, amputation is the ultimate therapeutic approach to avoid disease progression. Statistics show that the 5-year mortality rate after amputation for DF patients is $> 70\%$, and the 10-year survival rate is only 24% ^[9], indicating that amputation has a significant impact on patients' survival duration and

quality of life. To provide early assessment of amputation risk for DF patients, develop individualized assessment tools, formulate early intervention strategies, optimize resource allocation, and improve medical decision-making, this study constructed a predictive model for amputation risk in DF patients. The model identified three independent risk factors: Wagner score (whether > 3), peripheral artery disease (PAD) status, and C-reactive protein (CRP) level. The Wagner score assesses the severity of DF PAD can cause local ischemia, infection, necrosis, etc., and elevated CRP levels indicate active inflammatory responses closely related to infection. These risks have also been suggested in other studies in the field [10,11,12]. The performance and clinical effectiveness of the model constructed in this study suggest that it can help identify high-risk patients early, enabling intervention measures to reduce amputation rates and improve patients' survival duration and quality of life. Additionally, this study provides a foundation for further optimizing prediction models, integrating multi-center data, improving prediction accuracy, and realizing prediction tooling in the future.

Funding

Youth Project of Peking University Civil Aviation Clinical Medical College (Project No.: 202427); Civil Aviation Medical Center of the Civil Aviation Administration of China (Project No.: 2025-L-K-064).

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Li Y, Teng D, Shi X, et al., 2020, Prevalence of Diabetes Recorded in Mainland China Using 2018 Diagnostic Criteria from the American Diabetes Association: National Cross-Sectional Study. *BMJ*, 369: m997.
- [2] Deng J, Yin K, Wang Y, et al., 2025, Meta-Analysis of Influencing Factors for Amputation in Diabetic Foot. *Chinese Journal of Gerontology*, 45(15): 3634–3640.
- [3] Chinese Diabetes Society, Chinese Society of Infectious Diseases, Chinese Society for Tissue Repair and Regeneration, 2019, Guidelines for the Prevention and Treatment of Diabetic Foot in China (2019 Edition) (II). *Chinese Journal of Diabetes*, 11(3): 161–189.
- [4] Qi A, Yu Y, Zheng J, et al., 2025, Risk Factors for Amputation in Patients with Diabetic Foot. *Journal of Vascular and Endovascular Surgery*, 11(06): 789–793.
- [5] Yusuf S, Ibrahim S, Musa A, et al., 2024, Risk Factors for Lower Extremity Amputation among Diabetic Patients with Diabetic Foot Gangrene in ATBUTH, Bauchi. *Open Journal of Orthopedics*, 14(09): 391–403.
- [6] Liu N, 2025, Construction and Initial Validation of a Risk Prediction Model for Diabetic Foot, thesis, Xi'an Medical University.
- [7] Zhang X, Li Q, Zhou X, et al., 2024, Risk Factors for Amputation in Diabetic Foot Ulcers: A Retrospective Analysis. *International Wound Journal*, 21(4): e14832–e14832.
- [8] Karaca B, Kiris T, Ormen B, et al., 2024, Letter: Predictive Value of C-Reactive Protein to Albumin Ratio for Amputation Risk in Diabetic Foot Infection: Reply. *Angiology*, 76(4): 33197241245495–33197241245495.
- [9] Lin Q, Yu K, Qin Y, et al., 2024, Systematic Evaluation of Risk Prediction Models for Amputation in Patients with Diabetic Foot. *China Medical Herald*, 21(35): 114–120.
- [10] Burak Y, Bugra Z, Yildirim I, et al., 2023, An Overview of Risk Factors for Diabetic Foot Amputation: An Observational,

Single-Centre, Retrospective Cohort Study. *TouchREVIEWS in Endocrinology*, 19(1): 85–93.

- [11] Xu T, Hu L, Xie B, et al., 2024, Analysis of Clinical Characteristics in Patients with Diabetic Foot Ulcers Undergoing Amputation and Establishment of a Nomogram Prediction Model. *Scientific Reports*, 14(1): 27934–27934.
- [12] Ye Y, Wang H, Li N, et al., 2023, Research Progress on Influencing Factors and Comprehensive Treatment Management of Amputation in Patients with Diabetic Foot. *Electronic Journal of Foot and Ankle Surgery*, 10(02): 101–106.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Optimization and Practice of the Emergency Response Mechanism of Primary Healthcare Institutions in Plague Prevention and Control

Yanhua Liu*

Chifeng City Center for Disease Control and Prevention, Chifeng 024000, Inner Mongolia, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: As a Class A infectious disease legally stipulated in China, plague is characterized by rapid transmission and high fatality rate, and its prevention and control effectiveness is directly related to public health security and social stability. As the “first line of defense” in the infectious disease prevention and control system, primary healthcare institutions play a key role in the early detection, timely reporting, and preliminary handling of plague outbreaks. This paper systematically analyzes the existing problems in the emergency response mechanism of primary healthcare institutions in the context of China’s plague prevention and control efforts and proposes targeted optimization strategies. Through analysis, it aims to provide references for improving the emergency response system for plague prevention and control in primary healthcare institutions, comprehensively enhancing the emergency response capabilities of primary public health institutions, and strengthening the grassroots defense against plague.

Keywords: Plague prevention and control; Primary healthcare institutions; Emergency response mechanism; Optimization strategies; Public health

Online publication: September 26, 2025

1. Introduction

China is a country with a history of plague endemics, and currently, there are still natural plague foci in 19 provinces (autonomous regions), including Inner Mongolia, Qinghai, Tibet, and Gansu. The total area of these foci accounts for over 10% of the country’s land area, making plague prevention and control a long-term and complex task ^[1]. In recent years, influenced by factors such as ecological environmental changes, increased population mobility, and more frequent field operations, the risk of plague transmission from endemic to non-endemic areas has continued to rise, posing a potential threat to public health security ^[2]. Primary healthcare institutions serve as the “last mile” connecting the public health system with residents, and their emergency response capabilities directly determine whether plague outbreaks can be detected, reported, isolated, and treated early. However, constrained by factors such as uneven allocation of primary public health resources, limited professional capabilities of medical personnel, and inadequate coordination mechanisms, some primary healthcare institutions face issues such as low response efficiency, difficulty in case identification, and weak handling capabilities in plague prevention and control emergency responses. Therefore, optimizing the emergency

response mechanism for plague prevention and control in primary-level medical institutions is not only a key measure to enhance the overall effectiveness of plague prevention and control but also an important practice to fulfill the requirement of “strengthening primary-level public health services” outlined in the “Healthy China 2030” Plan Outline. It holds significant importance for constructing a modern public health emergency response system.

2. Current status and issues of the emergency response mechanism for plague prevention and control in primary-level medical institutions

2.1. Inadequate organizational structure and insufficient implementation of responsibilities

Some primary-level medical institutions have not established dedicated emergency response teams for plague prevention and control, with routine prevention and control efforts often being handled on a part-time basis by the public health department. This results in a lack of targeted and systematic prevention and control measures. Even in primary-level medical institutions located in plague-endemic areas, emergency response teams are often formed on an ad-hoc basis, with members solely from the public health department, excluding key personnel from clinical departments, pharmacies, logistics, and other essential sectors. This leads to issues of poor coordination, overlapping responsibilities, or gaps in responsibilities among departments during emergency responses. Additionally, the “Emergency Plan for Plague Prevention and Control” in some primary-level medical institutions simply replicates content from higher-level documents without tailoring responsibilities to local conditions, such as the distribution of plague foci, population structure, and transportation conditions. Specific tasks, such as “who is responsible for reporting cases,” “who is responsible for environmental disinfection,” and “who is responsible for contacting higher-level authorities,” are not clearly defined, resulting in buck-passing and a lack of leadership during emergency responses, severely impacting response efficiency.

2.2. Weak monitoring and early warning capabilities make early identification difficult

The professional capacity of medical personnel in primary-level medical institutions for plague prevention and control is generally inadequate. Due to the low incidence of plague, most medical personnel lack clinical practical experience and have a poor grasp of the typical symptoms, transmission routes, and identification criteria for high-risk groups of plague, making it difficult to accurately distinguish suspected plague cases from common infectious diseases. Some medical personnel in primary-level medical institutions located in non-endemic areas even have a complete lack of knowledge about plague prevention and control, rendering them unable to conduct effective preliminary screenings^[3]. Furthermore, the monitoring methods employed by primary-level medical institutions are relatively limited. Most institutions do not have rapid plague detection equipment and can only conduct preliminary monitoring through symptom observation, without the ability to quickly confirm cases through laboratory testing. This results in difficulty distinguishing suspected plague cases from common cases, leading to potential issues of “false negatives” or “false positives.” In addition, some primary-level medical institutions have not strictly implemented the reporting system for Category A infectious diseases. There have been irregularities such as seeking approval from the hospital director before reporting, using oral reports instead of systematic reports, and incomplete report content. These issues have led to delayed reporting or missing information, which in turn affects the timely assessment and response to the epidemic situation by higher-level departments.

2.3. Insufficient resource support and lack of emergency response support

In terms of material support, some primary-level medical institutions have not established a special reserve for plague prevention and control materials. They only make temporary purchases of a small quantity of materials before inspections by superior authorities. Moreover, the types of materials are incomplete, and the quantities are insufficient, lacking key materials such as N95 masks, protective suits, rapid detection reagents for plague, and emergency medicines. Even if some institutions have stockpiled materials, they have not established a dynamic management mechanism, leading to frequent occurrences of expired and damaged materials that cannot meet the needs of emergency response. In terms of

human resources, the number of public health personnel in primary-level medical institutions is generally insufficient. Most township health centers are only equipped with 1–2 public health personnel who are simultaneously responsible for multiple tasks, including chronic disease management, vaccination, infectious disease prevention and control, etc. The workload is heavy, making it difficult for them to focus on plague prevention and control. Additionally, the high turnover rate of medical staff at the grassroots level results in poor stability of the workforce, making it difficult to ensure the continuity of prevention and control work. Furthermore, plague prevention and control training in primary-level medical institutions is mostly conducted through short-term online training, with a focus on theoretical knowledge and a lack of practical drills. As a result, medical personnel have weak practical emergency response capabilities and are prone to panic and non-standard operations when facing sudden outbreaks. In terms of funding support, the plague prevention and control funds of primary-level medical institutions mainly rely on basic public health service funds. However, these funds need to be allocated for multiple public health tasks, and the proportion allocated to plague prevention and control is low, making it difficult to support the regular implementation of material reserves, training drills, health education, and other work. This results in a lack of resource support for prevention and control work.

2.4. Inefficient collaboration and barriers to information sharing

Some primary-level medical institutions have issues with an inadequate linkage mechanism with county-level CDCs. There is a lack of regular communication channels, and contact is only made temporarily after suspected cases emerge. This results in the county-level CDC being unable to promptly provide primary-level medical institutions with key information, such as monitoring data on epidemic sources and updates on prevention and control policies. Similarly, primary-level medical institutions cannot promptly provide feedback on suspected case leads and prevention and control difficulties within their jurisdictions. The delayed information transmission between both parties affects the coordination of prevention and control work. Meanwhile, primary-level medical institutions have not established a “green channel” with superior designated hospitals for plague treatment. When referring suspected cases, they need to arrange vehicles and go through cumbersome procedures on their own, and there is a lack of dedicated personnel for coordination. This results in delayed referrals and affects the efficiency of patient treatment ^[4]. Additionally, primary-level medical institutions have not fully collaborated with township governments, village (neighborhood) committees, grid staff, and other grassroots governance forces, failing to promptly obtain key information such as the “dynamics of outdoor workers,” “history of contact with wild animals,” and “situation of the floating population” within their jurisdictions. This leads to “blind spots” in the monitoring of high-risk populations and prevents the realization of “proactive detection and precise prevention and control” ^[5].

3. Optimization strategies for the emergency response mechanism of plague prevention and control in primary-level medical institutions

3.1. Optimizing organizational structure and responsibility system, clarifying division of responsibilities

3.1.1. Establishing a hierarchical organizational structure

Construct a three-tier emergency response organization system for plague prevention and control, involving “county-level health departments - primary-level medical institutions - village clinics.” The county-level health department should establish an emergency response command group for plague prevention and control, headed by the director, with the deputy director serving as the deputy head. The group members include the heads of departments such as disease control, medical administration, and primary healthcare, responsible for coordinating the emergency response work of primary-level medical institutions and conducting regular supervision and inspections. Primary-level medical institutions should establish an emergency response working group for plague prevention and control, headed by the hospital director, with the director of the public health department serving as the deputy head. The group members include clinical doctors, nurses, the heads of the pharmacy and logistics departments, ensuring that all key departments participate in the emergency

response. Village clinics should designate village doctors as the primary responsible persons for plague prevention and control and appoint a member of the village (neighborhood) committee to assist in the work, responsible for preliminary screening of suspected cases, information reporting, health education, and other basic tasks within their jurisdiction.

3.1.2. Refining the responsibility list

Primary-level medical institutions should develop a “Responsibility List for Emergency Response to Plague Prevention and Control” based on local conditions, clarifying the specific responsibilities and workflows of each position ^[6]. Outpatient doctors are responsible for admitting patients with fever, immediately implementing isolation measures for patients who meet the criteria for suspected cases, filling out the “Suspected Plague Case Registration Form,” and notifying the Public Health Department. Upon receiving the notification, personnel from the Public Health Department must complete the reporting of suspected cases through the “China Disease Prevention and Control Information System” within 10 minutes, while simultaneously reporting by phone to the County-level CDC. They also assist in identifying and registering close contacts and establish a “Close Contact Ledger.” The person in charge of the pharmacy is responsible for the daily management and allocation of plague prevention and control supplies, ensuring rapid availability of emergency supplies. Upon receiving the isolation notification, the person in charge of logistics must conduct initial disinfection of the patient contact area within 30 minutes, using chlorine-containing disinfectants to wipe surfaces and ventilate the area to ensure environmental safety.

3.2. Strengthen monitoring and early warning capacity building to enhance early identification efficiency

3.2.1. Conduct differentiated training to enhance the professional capabilities of medical personnel

Develop differentiated training programs for primary healthcare institutions in plague-endemic and non-endemic areas. In plague-endemic areas, conduct specialized training once every quarter, while in non-endemic areas, conduct training once every six months. The training content covers plague epidemiology, symptom identification, case management, personal protection, and reporting standards. Additionally, incorporate domestic typical cases into the teaching and organize practical drills on “identifying and managing suspected cases,” simulating scenarios such as “admitting patients with fever and swollen lymph nodes” and practicing the entire process of “isolation-reporting-disinfection-referral.” County-level CDCs regularly send experts to provide on-site guidance at primary healthcare institutions, answering questions to enhance training effectiveness ^[7].

3.2.2. Improve the monitoring network and diversify monitoring methods

Establish a three-dimensional monitoring network consisting of “symptom monitoring + high-risk population monitoring + plague-endemic area information monitoring” [8]. Symptom monitoring is conducted through outpatient consultations, village doctor visits, and family doctor services, with a focus on patients with fever accompanied by swollen lymph nodes or respiratory symptoms. High-risk population monitoring targets farmers, herders, and field workers, conducting monthly follow-ups to record contact history and health status. Plague-endemic area information monitoring involves real-time collaboration with county-level CDCs to obtain data on rodent density and flea indices. At the same time, equip key institutions in both plague foci and non-plague foci with rapid plague detection reagents to enable on-site preliminary screening of suspected cases and shorten confirmation time.

3.2.3. Standardize reporting procedures to ensure timely and accurate information

Clarify that the first-attending physician is the primary responsible person for reporting. Upon discovering suspected cases, they can first report through the information system and then notify the hospital dean, streamlining the process to avoid delays. County-level health departments should open a green channel for reporting, and county-level CDCs should respond and provide guidance within one hour of receiving reports. Additionally, establish a supervision mechanism where county-

level health departments inspect the timeliness, completeness, and accuracy of reports every month, publicly criticize institutions and individuals for delays, omissions, or misreports, and incorporate reporting performance into grassroots performance evaluations to strengthen accountability.

3.3. Strengthen resource support to lay a solid foundation for emergency response

3.3.1. Establish a standardized material reserve system

Develop the “Standards for Material Reserves for Plague Prevention and Control in Grassroots Medical Institutions,” specifying the types, quantities, and expiration dates of material reserves for township health centers and village clinics in both plague foci and non-plague foci. For example, township health centers in plague foci are required to have 500 N95 masks and 30 sets of protective suits, while village clinics should have 50 N95 masks and 5 sets of protective suits. Establish a dynamic material management mechanism where designated personnel at the grassroots level conduct monthly inventories to promptly replenish shortages and replace expired materials; county-level health departments should conduct regular inspections and order rectifications for institutions that fail to meet standards ^[9].

3.3.2. Strengthen human resource development

Implement policies such as targeted recruitment, on-the-job training, and preferential professional title assessments to bolster staffing, ensuring that each township health center has at least two full-time public health professionals responsible for plague prevention and control. Incorporate plague prevention and control knowledge into the continuing education of medical personnel, and regularly conduct online theoretical training and offline practical drills. Establish a “county-township collaboration” support mechanism, where county-level hospitals and Centers for Disease Control and Prevention (CDC) dispatch experts to provide on-site guidance, enhancing the quality of the grassroots workforce.

3.3.3. Ensure dedicated funding

County-level finance should allocate special funds for plague prevention and control, clarifying their sources and uses. These funds should be exclusively used for material reserves, training drills, and other purposes, and not be mixed with other funds. A dynamic adjustment mechanism for funding should be established, with annual adjustments based on changes in plague foci, price levels, and other factors. County-level health departments should strengthen supervision and conduct regular audits to ensure that funds are used for their designated purposes.

3.4. Improve the collaborative and linkage mechanism, break down barriers to information sharing

3.4.1. Strengthen linkage with county-level CDCs

Establish a regular communication mechanism between “primary healthcare institutions and county-level CDCs,” with weekly online meetings. Primary healthcare institutions provide feedback on surveillance situations, suspected case leads, and prevention and control challenges, while CDCs share data on plague foci, policy updates, and technical guidelines, enabling real-time information sharing. The CDC should establish a technical guidance team to visit primary healthcare institutions monthly to guide the improvement of contingency plans, standardize procedures, and enhance capabilities. Additionally, a 24-hour emergency response mechanism should be established to ensure that primary healthcare institutions receive professional support promptly in case of emergencies.

3.4.2. Improve coordination with higher-level designated hospitals

Both parties should establish a green channel for the referral of suspected cases, signing agreements that clearly outline the process, division of responsibilities, and contact information, with designated personnel for coordination. Primary healthcare institutions can directly call a dedicated phone number upon discovering suspected cases, and the hospital should arrange an ambulance and medical staff within one hour, making necessary preparations for admission to achieve “seamless connection.” Simultaneously, an information-sharing mechanism should be established, with primary healthcare

institutions providing preliminary diagnoses and contact histories of patients, and hospitals providing feedback on confirmed results and treatment progress to inform prevention and control efforts.

3.4.3. Strengthen linkage with grassroots governance forces

Primary healthcare institutions should establish a collaborative prevention and control mechanism with township governments, village (neighborhood) committees, and grid staff, integrating plague prevention and control into grassroots governance and clarifying the responsibilities of all parties. Village (neighborhood) committees and grid staff should assist in conducting screenings of high-risk populations, health education, and environmental disinfection, providing information on the dynamics of outdoor workers, wildlife contact histories, and floating population data to eliminate surveillance blind spots. Additionally, an information-sharing platform should be established to facilitate information exchange and coordinated actions among all parties, thereby forming a joint force for prevention and control.

3.5. Improve plan management and drills to enhance emergency response capabilities

Primary-level medical institutions should regularly revise their “Emergency Response Plan for Plague Prevention and Control” based on local conditions. Each year, the plan should be optimized and updated based on factors such as changes in epidemic foci, policy adjustments, and resource availability to ensure its scientificity, relevance, and operability^[10]. At the same time, a regular drill mechanism should be established. Primary-level medical institutions should conduct quarterly emergency drills for plague prevention and control, covering the entire process from identifying, isolating, reporting, and transferring suspected cases to environmental disinfection and close contact tracing. Drills should take various forms, including tabletop exercises and live-action drills, and should be conducted with on-site guidance from experts from county-level health departments, CDCs, and designated hospitals. After drills, problems should be promptly summarized, and processes optimized to continuously improve the practicality of the emergency plan and emergency response capabilities. Additionally, primary-level medical institutions should establish an emergency response evaluation mechanism. After each emergency response or drill, evaluations should be conducted from dimensions such as “response speed, handling standards, coordination efficiency, and resource support,” and evaluation reports should be formed. Based on identified issues, corrective measures should be developed to continuously optimize the emergency response mechanism and ensure a steady improvement in emergency response capabilities.

4. Conclusion

As the “first line of defense” in plague prevention and control, the completeness of the emergency response mechanism of primary-level medical institutions directly determines the effectiveness of plague prevention and control efforts. In the future, with the continuous advancement of China’s public health system construction, the emergency response mechanism for plague prevention and control in primary-level medical institutions needs to further develop towards “intelligence, precision, and regularity.” By introducing technologies such as big data and artificial intelligence, an intelligent monitoring and early warning system can be constructed to achieve automatic identification of suspected cases, precise location of at-risk populations, and intelligent allocation of prevention and control resources. Through deepening the integration of medical treatment and prevention reforms, primary-level medical institutions and public health institutions can be promoted to collaborate deeply, transforming prevention and control efforts from “passive response” to “active prevention.” By strengthening regional coordination and international cooperation, the overall effectiveness of plague prevention and control can be enhanced, providing solid support for safeguarding the health of the people and public health security.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Xiang S, Sun X, Wu Z, 2020, Progress in the Epidemic Situation and Prevention and Control of Plague in China. *China Tropical Medicine*, 20(05): 486–490.
- [2] Song C, Zhang W, Zhou X, 2024, Current Situation and Prevention and Control Status of Human Plague in China. *Chinese Journal of Endemic Disease Prevention and Control*, 39(04): 286–287 + 329.
- [3] Hao J, Gui Y, Luo Y, et al., 2022, Investigation and Analysis of Plague Knowledge Awareness Among Grassroots Medical Personnel in Xinjiang. *Chinese Journal of Hygiene and Insecticides & Equipment*, 28(05): 460–462.
- [4] Zhang X, Lang S, Gao Y, 2022, Investigation on the Awareness of Plague Prevention and Control Knowledge Among Grassroots Medical Personnel in Etuo Banner, Inner Mongolia Autonomous Region in 2019. *Chinese Journal of Primary Health Care*, 36(3): 108–110.
- [5] Shi M, Gao C, 2021, Research on Emergency Management of Public Health Emergencies in Ethnic Regions Under the 4R Model: Taking the Plague in Xilingol League as an Example. *Popular Standardization*, 2021(10): 187–189.
- [6] Cao L, Jin F, Li D, 2022, Comprehensive Prevention and Control of Plague in Yumen City, a Plague Focus of Himalayan Marmot. *Qinghai Journal of Animal and Veterinary Sciences*, 52(06): 52–54.
- [7] Lei H, Yue J, Li J, et al., 2020, Reflections on the Current Situation and Prevention and Control of Plague in Gansu Province. *Chinese Journal of Endemic Disease Prevention and Control*, 35(05): 514–515 + 519–520.
- [8] Yang Z, Zhang G, Zhu P, 2022, Analysis of Prevention and Control Strategies for Plague and Cholera, Class A Infectious Diseases, in Pre-hospital Medical Institutions. *Chinese Journal of Endemic Disease Prevention and Control*, 37(02): 107–108.
- [9] Meng H, 2015, Analysis of Emergency Response to Public Health Emergencies. *Health for Everyone (Academic Edition)*, 9(16): 29.
- [10] Zhao Q, Yin J, 2016, Analysis of the Epidemic Situation of Plague in China and Discussion on Its Prevention and Control Strategies. *China Tropical Medicine*, 16(07): 733–735.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Application of CT Whole Brain Perfusion Combined with CT Angiography in The Diagnosis of Acute Cerebral Infarction

Zhengwei Chen*

Yancheng Traditional Chinese Medicine Hospital, Yancheng 224000, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the application effect of CT whole brain perfusion (CTP)+CT angiography (CTA) in the diagnosis of acute cerebral infarction. *Method:* Study period: January 2023 to January 2025, reference subjects: 50 patients with acute cerebral infarction. All patients underwent CTA and CTP examinations, with whole-brain angiography (DSA) as the gold standard, and the results of the combined diagnosis of CTP and CTA were analyzed. *Result:* DSA examination detected 44 positive cases and 6 negative cases, and combined examination detected 44 positive cases and 6 negative cases. The diagnostic efficacy of CTA, CTP, and combined examination was compared with $P > 0.05$. One false positive case of combined examination was due to vascular hyperplasia in Moyamoya disease, and one false negative case was due to occlusion of the perforating artery; Two cases of false positive CTA were vascular spasm, and four cases of false negative CTA included two cases of distal branch occlusion and two cases of mild stenosis; Three cases of false positive CTP were blood flow changes during migraine attacks, and six cases of false negative CTP were small infarcts in the posterior circulation. The consistency between the combined examination and DSA was the highest ($\text{Kappa} = 0.896$). *Conclusion:* CTA combined with CTP for diagnostic examination can greatly improve the accuracy of early diagnosis of acute cerebral infarction through complementary integration of structural and functional information, providing a more reliable imaging basis for clinical treatment decisions.

Keywords: CT whole brain perfusion; CT vascular imaging; Acute cerebral infarction; diagnostic efficiency

Online publication: September 26, 2025

1. Introduction

Acute cerebral infarction, as a neurological emergency, causes irreversible damage to approximately 1.9 million neurons every minute after onset. Accurate assessment within the time window during clinical diagnosis and treatment can directly affect the effectiveness of key treatment measures such as intravenous thrombolysis and endovascular thrombectomy. Although traditional CT plain scan can quickly rule out cerebral hemorrhage, it has significant limitations in identifying early cerebral ischemic changes, with about 60% of cases having difficulty displaying clear infarction foci within 6 hours of onset^[1]. The vascular imaging technology (CTA) achieved by spiral CT with 128 or more rows, through intravenous injection

of iodine contrast agent and intelligent triggering scanning, can clearly present the morphology of cerebral blood vessels from the aortic arch to the Willis ring. This examination method is particularly helpful in discovering the degree of stenosis, occlusion site, and establishment of collateral circulation of responsible blood vessels. For patients considering endovascular treatment, preoperative understanding of the pathological characteristics of large blood vessels such as the internal carotid artery and middle cerebral artery is of decisive significance. CT whole brain perfusion (CTP) can quantitatively analyze the microcirculation status of brain tissue by dynamically monitoring the first pass effect of contrast agents. Research has shown that combining vascular morphology with hemodynamic information can provide more comprehensive diagnostic information^[2]. Therefore, this study uses whole brain angiography (DSA) as the gold standard to explore the diagnostic value of CTA combined with CTP. The summary is as follows:

2. Data and methods

2.1. General information

Research period: January 2023 to January 2025, reference subjects: 50 patients with acute cerebral infarction. 28 male and 22 female patients were counted; The age is 60 to 78 years old, with a mean of (68.52 ± 5.63) years old. The time from onset to examination is 2–8 hours, with a mean of (4.82 ± 1.35) hours. Complicated diseases: 38 cases of hypertension, accounting for 76.00%, 25 cases of diabetes, accounting for 25.00%, and 32 cases of hyperlipidemia, accounting for 64.00%.

Inclusion criteria: (1) Age above 60 years old; (2) The clinical diagnosis is acute cerebral infarction; (3) The onset time is ≤ 8 hours; (4) Simultaneously complete CTA, CTP, and DSA examinations.

Exclusion criteria: (1) Previous history of cerebral hemorrhage or major cranial surgery; (2) Allergic to iodine contrast agents; (3) Can cooperate to complete the inspection; (4) The imaging data are missing.

2.2. Method

CTA examination: The dual-source Force spiral CT equipment produced by Siemens AG in Germany is used for examination, which has a high spatial resolution detector and can achieve rapid volumetric scanning. Standardize and calibrate the equipment before inspection to ensure stable and reliable image quality. During the examination, the patient is placed in a supine position with the head advanced and the jaw slightly retracted. A specialized head support is used to fix the position of the head, and the scanning baseline is parallel to the canthus line, ranging from the skull base to the skull top. Scanning parameter settings: Based on clinical practice experience and equipment performance, determine a tube voltage of 120 kV and a tube current of 200 mAs. Adopting spiral scanning mode, the detector is collimated at 64×0.6 mm, with a scanning layer thickness of 0.625 mm, a pitch of 0.8, and a rotation time of 0.28/s per turn. The reconstruction algorithm selected is the standard brain tissue algorithm, with a matrix of 512×512 and a field of view of $220 \text{ mm} \times 220 \text{ mm}$. The contrast agent used is iodixanol (350 mgI/mL), and the total amount is calculated based on 1.5 mL/kg body weight. A double tube high-pressure injector is used to inject through the anterior elbow vein at a rate of 4.0 mL/s. Immediately after injection, 20 mL of physiological saline is added at the same rate to flush the tube. After the start of contrast agent injection, intelligent triggering technology is used to monitor changes in CT values at the aortic arch level. When the CT value reaches the preset threshold of 100 HU, the scan is automatically initiated with a delay time of about 18–22 seconds. The image post-processing is performed on a workstation using three reconstruction techniques: Maximum Intensity Projection (MIP): layer thickness of 10mm, spacing of 5 mm, and rotation angle of 10° . Multiplanar reconstruction (MPR): coronal, sagittal, and arbitrary oblique plane reconstruction with a layer thickness of 2 mm; volume rendering (VR): transparency setting of 40–60% to optimize the comparison between blood vessels and surrounding tissues.

CTP examination: Using the same CT equipment, the scanning range covers the entire brain, from the skull base to the skull top, and the patient's position is maintained consistent with CTA examination; Adopting dynamic sequence scanning mode, image data of 20 time phases are continuously acquired within 40 seconds, with a scanning interval of 2 seconds and

a scanning time of 1.5 seconds for each time phase, ensuring sufficient time resolution. The contrast agent used was the same iodixanol (350 mgI/mL) as CTA, with a fixed dose of 50 mL. It was injected into the contralateral elbow vein at a rate of 5.0 mL/s, and scanning began 5 seconds before injection to obtain basic images. Scanning parameters: tube voltage of 80 kV, tube current of 150 mAs, detector collimation of 32×1.2 mm, layer thickness of 5mm. Image processing is performed using the Infusion CT specialized software provided by Siemens. Process flow: First, perform motion correction to eliminate artifacts caused by slight patient movements. Vascular recognition uses automatic labeling of input arteries and draining veins; The deconvolution algorithm calculates perfusion parameters: cerebral blood flow (CBF) in mL/100 g/min, cerebral blood volume (CBV) in mL/100 g, mean transit time (MTT) in seconds, and time to peak (TTP) in seconds; Parameter graph generation: Pseudo color encoding displays the spatial distribution of each parameter; The software automatically generates bilateral hemisphere mirrored ROIs and compares the perfusion differences between the healthy and affected sides; The abnormal threshold is set as follows: CBF decreases by more than 30%, CBV decreases by more than 25%, MTT prolongs by more than 40%, TTP prolongs by more than 20%. All parameter maps are independently analyzed by two neuroimaging physicians with more than 5 years of experience, and consensus is reached through negotiation in case of disagreement.

DSA cerebral angiography examination: The examination uses the Philips Allura Xper FD20 digital subtraction angiography system, equipped with a 20-inch flat panel detector, with a spatial resolution of 2.5 line pairs/mm, which can meet the imaging requirements of fine neural and vascular structures; During the examination, the patient was placed in a supine position with their head fixed on a specialized headband. After disinfection and drape, the improved Seldinger technique was used to puncture the right femoral artery, and a 5F arterial sheath was inserted. The catheter was either a 5F vertebral artery catheter or a Simmons catheter, and under the guidance of a guidewire, it was sequentially selected to reach the openings of the bilateral common carotid arteries, internal carotid arteries, and vertebral arteries. The contrast parameters are set as follows: contrast agent iodoprolol (370 mgI/mL), internal carotid artery injection dose of 8–10 mL, flow rate of 4–5 mL/s; Vertebral artery dose 6–8 mL, flow rate 3–4 mL/s; Use a high-pressure injector to inject contrast agent, with a pressure limit of 300 psi, an image acquisition frame rate of 3–4 frames per second, exposure conditions of 70–80 kV, 200–250 mA, and at least arterial, capillary, and venous phase images should be collected at each vascular location.

Standard projection position: upright position: align the centerline of the ray with the upper edge of the eye socket; Lateral position: Align the centerline of the ray 2 cm in front of the external ear canal; Oblique position: Rotate 30° to the same side to better display the siphon segment of the internal carotid artery; Special position: If necessary, use the Townes position to observe the vertebral basilar artery system. The image post-processing application uses digital subtraction technology to optimize blood vessel display through mask selection. The workstation provides real-time magnification, window width and level adjustment, and path map functions to assist diagnosis. After all images are anonymously processed, they are independently reviewed by two deputy chief physicians who have been engaged in nerve intervention work for more than 10 years. If there is a disagreement on the diagnosis, a double-blind reassessment is conducted and a consensus is reached through negotiation. After the examination is completed, the arterial sheath is removed, the puncture point is compressed for 15 minutes to stop bleeding, the elastic bandage is compressed and wrapped, and the lower limb is immobilized for 24 hours.

2.3. Observation indicators

Using DSA examination results as the gold standard, calculate the results of CTP, CTA, and combined examinations, and assess diagnostic efficacy; DSA gold standard: Positive: vascular stenosis $\geq 50\%$ or complete occlusion; Negative: Vascular stenosis $< 50\%$ or no stenosis. CTA evaluation criteria: Positive: vascular stenosis $\geq 50\%$ or complete occlusion; Negative: Vascular stenosis $< 50\%$ or no stenosis. CTP evaluation criteria: Positive: CBF reduction $> 30\%$ and/or MTT prolongation $> 40\%$; Negative: The perfusion parameters are within the normal range.

2.4. Statistical methods

Use SPSS 26.0 software to process the data involved in the study, using mean \pm standard deviation (SD) to represent the

quantitative data, and conduct tests using “t”; The count data is represented by n(%), and the consistency is checked using the McNemar test. A $P < 0.05$ indicates a significant difference.

3. Results

3.1. Analysis of diagnostic results

DSA examination detected 44 positive cases and 6 negative cases, while the combined examination detected 44 positive cases and 6 negative cases (Table 1).

Table 1. Analysis of CTA, CTP, DSA inspection results

Inspection method	Inspection results	DSA examination		Total
		Positive	Negative	
CTA examination	Positive	40	2	42
	Negative	4	4	8
	Total	44	6	50
CTP inspection	Positive	38	3	41
	Negative	6	3	9
	Total	44	6	50
Joint inspection	Positive	43	1	44
	Negative	1	5	6
	Total	44	6	50

3.2. Diagnostic efficacy of different examination methods

The diagnostic efficacy of CTA, CTP, and combined examination was compared with $P > 0.05$. One false positive case of combined examination was due to vascular hyperplasia in Moyamoya disease, and one false negative case was due to occlusion of the perforating artery. Two cases of false positive CTA were vascular spasm, and four cases of false negative CTA included two cases of distal branch occlusion and two cases of mild stenosis; Three cases of CTP false positives were blood flow changes during migraine attacks, and six cases of false negatives were small infarcts in the posterior circulation. The consistency between combined examination and DSA was the highest (Kappa = 0.896) (Table 2).

Table 2. Diagnostic efficacy of different examination methods [n (%)]

Group	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
CTA examination	90.91 (40/44)	66.67 (4/6)	80.00 (44/50)	95.24 (40/42)	50.00 (4/8)
CTP inspection	86.36 (38/44)	50.00 (3/6)	82.00 (41/50)	92.68 (38/41)	33.33 (3/9)
Joint inspection	97.73 (43/44)	83.33 (5/6)	96.00 (48/50)	97.73 (43/44)	83.33 (5/6)
χ^2	3.769	1.500	4.909	1.200	3.630
P	0.152	0.472	0.056	0.549	0.163

4. Discussions

Acute cerebral infarction is mainly caused by the sudden occlusion of cerebral blood vessels, leading to ischemic necrosis of brain tissue and high disability and mortality rates. Due to the extreme sensitivity of neurons to ischemia, about 1.9

million neurons die per minute. Therefore, early and accurate diagnosis is directly related to the implementation of key treatments such as intravenous thrombolysis and endovascular thrombectomy. Although traditional CT plain scan can quickly exclude cerebral hemorrhage, its sensitivity to early ischemic lesions is insufficient. About 60% of patients cannot clearly display the infarct size within 6 hours of onset, which can delay treatment decisions. Moreover, relying solely on clinical symptoms or routine imaging can easily overlook responsible vascular lesions and microcirculation disorders, leading to incomplete treatment or excessive intervention. Therefore, exploring a diagnostic method that can simultaneously evaluate vascular morphology and hemodynamics is significant for providing a more comprehensive decision-making basis for clinical practice^[3]. CTA examination is based on spiral CT rapid volume scanning technology, which uses intravenous injection of iodine contrast agent and intelligent triggering to capture arterial phase vascular imaging, reconstructing three-dimensional vascular images from the aortic arch to the Willis ring. This examination can intuitively display the location of vascular stenosis, occlusion, and collateral circulation status, especially for the localization of large vessel lesions such as the internal carotid artery and middle cerebral artery, which is invaluable.

CTP examination mainly relies on dynamic monitoring of the first pass effect of contrast agents and quantitative analysis of brain tissue perfusion parameters (CBF, CBV, MTT, TTP), which can reveal the range of ischemic penumbra and salvageable brain tissue^[4]. Two examination techniques provide complementary information from macroscopic vascular morphology and microscopic blood flow perfusion levels. CTA can solve the problem of where blood vessels are blocked, while CTP solves the problem of how severe ischemia is. This study shows that the sensitivity (97.73%) and negative predictive value (83.33%) of the combined examination are significantly higher than those of single examination. The reason for this is that although CTA can accurately locate large vascular lesions, it is prone to missed diagnosis of perforating artery occlusion or mild stenosis, which is also an important reason for the four false negatives in this group; Although CTP can sensitively capture perfusion abnormalities, it is susceptible to non-infarct blood flow interference such as migraine^[5], resulting in 3 false positives. After joint examination, the vascular localization information of CTA can assist CTP in excluding perfusion abnormalities in non-responsible vascular areas, and the perfusion parameters of CTP can correct stenosis with unclear hemodynamic significance of CTA. Through the dual verification mechanism of structure function, the consistency between joint diagnosis and gold standard DSA can reach 0.896, especially for the detection of small infarcts in the posterior circulation and perforating artery lesions^[6].

5. Conclusion

In summary, the combination of CTA and CTP for diagnostic examination, through the complementary integration of structural and functional information, can greatly improve the accuracy of early diagnosis of acute cerebral infarction and provide more reliable imaging basis for clinical treatment decisions.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Chen B, Yang A, Pang X, 2023, The Application Value of CT Whole Brain Perfusion Combined with CT Angiography in the Diagnosis of Acute Cerebral Infarction. *Zhejiang Practical Medicine*, 28(2): 124–126.
- [2] Yu X, Jin P, 2024, The Prognostic Value of CT Perfusion Imaging in Patients with Acute Cerebral Infarction, thesis, Bengbu Medical College.
- [3] Sun R, Qian X, 2024, Analysis of the Efficacy of Early Diagnosis of Cerebral Infarction Using Head CT Angiography

Combined with Whole Brain CT Perfusion Imaging. *Imaging Research and Medical Applications*, 8(22): 173–175.

- [4] Hu G, Bai X, 2024, Analysis of the Application Value of CT Angiography (CTA) Combined with CT Perfusion Imaging (CTP) in the Diagnosis and Treatment of Acute Cerebral Infarction. *Modern Medical Imaging*, 33(9): 1597–1599 + 1603.
- [5] Wang L, Li J, Wang Q, et al., 2024, The Application Value of CT Cerebral Perfusion Imaging (CTP) Combined with Head and Neck CT Angiography (CTA) in the Early Diagnosis of Acute Cerebral Infarction. *Modern Medical Imaging*, 33(5): 819–822 + 829.
- [6] Jiang H, Tian W, Wang S, et al., 2024, Analysis of the Diagnostic Effect of Multi-Slice CT Whole Brain Perfusion Imaging Technology on Acute Cerebral Infarction. *Journal of Practical Medical Imaging*, 25(2): 94–98.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Observation of Dachaihu Decoction in the Treatment of Bile Reflux Gastritis

Hao Zhou*

Xuzhou Tongshan Maternal and Child Health Hospital, Xuzhou 221100, Jiangsu, China

*Author to whom correspondence should be addressed.

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the effect of Dachaihu decoction in the treatment of bile reflux gastritis. *Methods:* A total of 70 patients with bile reflux gastritis were selected for data analysis in this experiment. The selected time was from June 2024 to May 2025. 35 patients in each group were divided into two groups by lot. The study group was treated with conventional Western medicine + Dachaihu decoction, and the control group was treated with conventional Western medicine. The data of the two groups were compared. *Results:* Compared with the control group, the total effective rate of the study group was significantly higher, the TCM syndrome score after treatment was significantly lower, the number of bile reflux after treatment was significantly less, and the time of bile reflux after treatment was significantly shorter, $P < 0.05$; The TCM syndrome score, bile reflux times and bile reflux time before treatment were compared between the two groups, $P > 0.05$. *Conclusion:* The effect of Dachaihu decoction in the treatment of bile reflux gastritis is ideal.

Keywords: Dachaihu decoction; Bile reflux gastritis; Therapeutic effect

Online publication: September 26, 2025

1. Introduction

The incidence of bile reflux gastritis is relatively high. Clinical research on its etiology and treatment options has been given great attention, and a large number of studies have been carried out. In recent years, with the interference of factors such as the change of people's dietary structure and the increase in life pressure, the incidence of this disease has increased year by year. The main clinical symptoms are epigastric pain, abdominal distension, acid regurgitation, bitter mouth, etc. ^[1] The repeated attacks of the disease will lead to adverse outcomes and seriously affect the quality of life of patients. During the treatment of patients with Western medicine, acid suppressants, gastric mucosal protectors, and gastrointestinal motility-promoting drugs are mainly used ^[2]. The curative effect of long-term treatment of patients is not good, drug dependence is easy to occur, and patients have adverse reactions, such as gastrointestinal flora imbalance. Bile reflux gastritis in the theoretical system of traditional Chinese medicine belongs to the categories of "epigastric pain," "fullness of the stomach," "acid swallowing," etc., including liver and gallbladder stagnation, stomach qi inversion, and patients with damp heat or food accumulation, patients should be given the implementation of soothing the liver and gallbladder, and stomach depression ^[3]. In the Treatise on febrile diseases, Dachaihu Decoction contains bupleurum, *Scutellaria baicalensis*, *Pinellia ternata*, *Fructus aurantii Immaturus*, rhubarb, *Radix Paeoniae Alba* and other drugs. Its

efficacy is to reconcile Shaoyang and internal diarrhea heat knot. It is applied to the treatment of patients with bile reflux gastritis, which conforms to the characteristics of pathogenesis. In recent years, there have been clinical reports suggesting that Dachaihu decoction can help patients improve bile reflux symptoms and effectively repair gastric mucosal damage in patients^[4]. In this paper, 70 patients with bile reflux gastritis were selected to explore the effect of Dachaihu decoction.

2.1. Data

In this experiment, a total of 70 patients with bile reflux gastritis were selected for data analysis. The selected time was from June 2024 to May 2025, with 35 patients in each group. The study group had 20 men and 15 women, aged 27–69 (44.54 ± 5.36) years old, and the control group had 21 men and 14 women, aged 25–67 (44.55 ± 5.34) years old. The comparison of the two groups of data showed that $P > 0.05$.

Inclusion criteria: (1) In line with the disease diagnostic criteria, gastroscopy suggested gastric mucosal lesions and bile reflux; (2) Chief complaint: burning sensation, epigastric pain, bitter mouth, dry mouth, etc; (3) The onset was relatively slow and recurrent within 2 months.

Exclusion criteria: (1) Severe gastrointestinal bleeding and esophageal stenosis; (2) In lactation or pregnancy; (3) Mental disorders, language dysfunction, etc.

2.2. Method

The control group was treated with conventional Western medicine, oral Domperidone Tablets, 10 mg/time, 3–4 times/D, chewing hydrotalcite tablets, 10 mg/time, 4 times/D, for 4 weeks.

The study group was treated with conventional Western medicine plus Dachaihu decoction. Based on the treatment in the control group, the following were added: *Radix bupleuri* 10 g, *Radix scutellariae* 10 g, fried *Radix paeoniae alba* 10 g, *Radix et rhizoma rhei* 6 g, *Radix curcumae* 10 g, *Rhizoma pinelliae* 10 g, fried *Fructus aurantii* 6 g, ocher 30 g and licorice 3 g. The gallbladder wall of patients with cholecystitis was rough, so it was necessary to add *Lysimachia christinae* 30 g and *Artemisia scopariae* 15 g. If the patients had severe pain, it was necessary to increase *Rhizoma corydalis* 10 g and *Rhizoma curcumae* 10 g. If the patients had obvious acid regurgitation, it was necessary to increase *Rhizoma coptidis* 9 g and *Fructus evodiae* 1.5 g. If the 30 g, 10 g of bitter almond, 1 dose per day for the patient, 300 mL of drug solution obtained by boiling, morning and evening medication, continuous treatment for 8 weeks.

2.3. Observation indexes

- (1) The total effective rate of the two groups was compared. After treatment, the symptoms disappeared completely, gastroscopy showed that the lesion of gastric mucosa was basically disappeared, and the gastric mucosa was well repaired, which was judged to be effective; After treatment, the symptoms were improved, and gastroscopy showed that the lesion of gastric mucosa was reduced by 50% or more, which was judged to be effective; In other cases, the judgment is invalid. Total effective rate = 100% - ineffective rate.
- (2) The TCM syndrome scores of the two groups were compared.
- (3) The times and frequency of bile reflux were compared between the two groups.

2.4. Data statistics

Statistical SPSS 28.0 software was used to complete the data calculation. The measurement data were described by mean \pm standard deviation (SD), t -test, and count data were described by % and χ^2 test, $P < 0.05$, there was statistical significance.

3. Results

Compared with the control group, the total effective rate of the study group was significantly higher, the TCM syndrome score after treatment was significantly lower (**Table 1**), the number of bile reflux after treatment was significantly less, and the bile

reflux time after treatment was significantly shorter, $P < 0.05$ (Table 2). The TCM syndrome score, bile reflux times and bile reflux time before treatment were compared between the two groups, $P > 0.05$ (Table 3).

Table 1. Comparison of total effective rate between the two groups (%)

Group	Markedly effective	Effective	Invalid	Total effective rate
Research group ($n = 35$)	30 (85.71)	4 (11.43)	1 (2.86)	97.14
Control group ($n = 35$)	14 (40.00)	13 (37.14)	8 (22.86)	77.14
χ^2				6.2477
P				< 0.05

Table 2. Comparison of TCM syndrome scores between the two groups

Group	Epigastric pain		Abdominal distension and fullness		Dry mouth and bitter mouth		Heartburn and noise	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group ($n = 35$)	4.22 \pm 1.35	1.21 \pm 0.21	4.08 \pm 1.22	1.16 \pm 0.15	3.80 \pm 1.66	1.06 \pm 0.47	3.61 \pm 1.71	1.18 \pm 0.36
Control group ($n = 35$)	4.25 \pm 1.41	2.36 \pm 1.87	4.10 \pm 1.28	2.22 \pm 1.21	3.92 \pm 1.65	2.38 \pm 1.22	3.58 \pm 1.85	2.46 \pm 1.84
t	0.0909	3.6155	0.0669	5.1433	0.3033	5.9731	0.0705	4.0390
P	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Table 3. Comparison of bile reflux times and bile reflux time between the two groups

Group	Bile reflux times (times/d)		Bile reflux time (min/time)	
	Before treatment	After treatment	Before treatment	After treatment
Research group ($n = 35$)	7.12 \pm 0.48	2.05 \pm 0.26	7.62 \pm 0.51	2.02 \pm 0.47
Control group ($n = 35$)	7.09 \pm 0.52	3.07 \pm 0.36	7.51 \pm 0.47	3.23 \pm 0.52
t	0.2508	13.5888	0.9383	10.2128
P	> 0.05	< 0.05	> 0.05	< 0.05

4. Discussion

Bile reflux gastritis is a common disease in the clinic. The incidence of patients is high, and there is a clinical treatment dilemma. How to solve it is explored and analyzed in the clinic. Epidemiological data show that in patients with chronic gastritis accounts for 10% to 20% [5]. Affected by factors such as refined diet, irregular work and rest, and a sharp increase in mental pressure in modern society, the incidence of chronic gastritis increases by 3–5% every year. The number of young and middle-aged patients has also increased in recent years. From the perspective of pathological mechanism, the core contradiction of bile reflux gastritis is gastroduodenal motility disorder or pyloric sphincter dysfunction. The duodenal contents of patients reflux to the stomach, which contains bile salt and trypsin. The former can directly damage the phospholipid bilayer structure of the patient's gastric mucosa. Patients are prone to gastric mucosal barrier function,

resulting in mucosal congestion, edema, erosion, and long-term repeated attacks ^[6], which will lead to gastric mucosal atrophy, intestinal metaplasia, and significantly increase the risk of precancerous lesions such as dysplasia. The health and quality of life of patients' digestive systems are seriously threatened.

The experimental results of this group are: compared with the control group, the total effective rate of the study group is significantly higher, the TCM syndrome score is significantly lower after treatment, the number of bile reflux after treatment is significantly less, and the bile reflux time after treatment is significantly shorter, $P < 0.05$; The TCM syndrome score, bile reflux times and bile reflux time before treatment were compared between the two groups, $P > 0.05$.

Detailed analysis of the causes of the results:

- (1) The efficacy of *Radix bupleuri* is to soothe the liver and relieve depression, regulate Qi, effectively restore the liver drainage function of patients, and significantly improve the poor bile excretion of patients. *Radix scutellariae* is bitter, cold and clear heat, which can directly remove the heat of the liver and gallbladder of patients with Shaoyang. After compatibility, it can help patients "reconcile Shaoyang" and effectively alleviate the pathological basis of patients with "liver and gallbladder stagnation heat" from the root.
- (2) Fried *Radix paeoniae alba* with herbal medicine can soften the liver, relieve pain, assist *Radix bupleuri* to soothe the liver, and effectively relieve the pain caused by epigastric spasm caused by liver Qi inversion. The effect of rhubarb is to relieve cold and cold, help patients to clear the bowels and relieve heat, and effectively remove the gastrointestinal heat of patients. Through "clearing the bowels," it can improve the gastrointestinal motility of patients, reduce bile reflux, and use *Rhizoma pinelliae* ginger for patients, which can promote the patients' pungent temperature and reduce adverse reactions, dry dampness and remove phlegm, significantly enhance the ability of stomach Qi to reduce turbidity, and effectively relieve the symptoms of acid reflux and heartburn caused by stomach Qi inversion. The function of Yujin is to relieve Qi depression, promote the gallbladder and eliminate jaundice, and soothe the liver and benefit patients. The bile effect was further strengthened and bile excretion was significantly improved.
- (3) The effect of fried *Fructus aurantii immaturus* with adjuvant is to regulate Qi and relieve stagnation and distension. It can effectively relieve the symptoms of abdominal distension and fullness. It can replace the heavy deposition of ochre. It can help patients reduce adverse reactions and stop vomiting. The downward force of stomach Qi is effectively enhanced, and bile reflux is directly reduced. The role of licorice is to reconcile various drugs. The bitter cold nature of rhubarb and *Scutellaria baicalensis* can be alleviated, which can effectively prevent patients from damaging the Yang Qi of spleen and stomach ^[7].
- (4) This study combined with the syndrome differentiation and subtraction of patients. Rough gallbladder wall, cholecystitis plus *Lysimachiae* and *Artemisiae capillaris* can help patients clear away heat and dampness, promote gallbladder and reduce jaundice. Severe pain plus *Rhizoma corydalis* and *Rhizoma curcumae* can significantly strengthen the effect of promoting Qi and activating blood circulation, removing blood stasis and relieving pain in patients. *Coptis rutaecarpa* and *Evodia rutaecarpa* can help patients clear liver and fire, soothe the stomach and stop acid, and add *Atractylodis macrocephalae* and bitter almond for constipation. Patients can effectively strengthen the spleen and intestines, and the pertinence and efficacy of prescriptions are significantly improved ^[8].

From the perspective of modern pharmacological mechanism, Dachaihu Decoction plays a therapeutic role through multiple targets and channels. For example, saikosaponin in *Bupleurum* can effectively regulate the level of gastrointestinal hormones in patients, improve gastrointestinal motility, enhance the tension of the pyloric sphincter, and reduce bile reflux; Baicalin in *Scutellaria baicalensis georgi* can help patients with anti-inflammatory and anti-oxidation, inhibit the release of inflammatory factors in gastric mucosa, and reduce mucosal damage. Paeoniflorin in *Radix paeoniae alba* can effectively inhibit the spasm of gastrointestinal smooth muscle, relieve epigastric pain, and enhance the function of the gastric mucosal barrier in patients with good mucosal repair. Emodin in Rhubarb can effectively regulate the balance of intestinal flora in patients, improve intestinal peristalsis function, reduce retention of duodenal contents by "dredging the bowels," and effectively reduce the risk of reflux in patients. Alkaloids in *Pinellia ternata* can inhibit the vomiting center of patients,

and reduce gastric Qi upwardness. Iron oxide, silicon dioxide and other components in ochre can neutralize gastric acid and protect the gastric mucosa. The pharmacological effect of “heavy falling and downwardness” can effectively delay gastric emptying speed and reduce bile reflux.

5. Conclusion

The effect of Dachaihu Decoction in the treatment of bile reflux gastritis is ideal; the TCM syndrome score of patients after treatment is significantly lower, the number of bile reflux episodes after treatment is significantly less, and the time of bile reflux after treatment is significantly shorter, which is worthy of clinical use and promotion.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Chen Q, Wu P, 2024, Clinical Observation of Banxia Xiexin Decoction Combined with Zuojin Pill in the Treatment of Bile Reflux Gastritis. *Journal of Practical Traditional Chinese Medicine*, 40(4): 626–627.
- [2] Chen Y, Cao C, 2024, Effect and Pharmacological Mechanism of Xiaochaihu Decoction Combined with Western Medicine in the Treatment of Bile Reflux Gastritis. *Clinical Rational Drug Use*, 17(27): 70–73.
- [3] Liu J, Zhang Z, Sun Y, et al., 2024, Observation on the Effect of Chaihu Guizhi Ganjiang Decoction Plus Acupuncture in the Treatment of Bile Reflux Gastritis. *Chinese Prescription Drug*, 22(8): 157–160.
- [4] Yang H, Liu Y, 2024, Clinical Efficacy of Shugan Jiangni Decoction in the Treatment of Bile Reflux Gastritis of Liver Stomach Stagnation Heat Type. *Shenzhen Journal of Integrated Traditional Chinese and Western Medicine*, 34(13): 46–49.
- [5] Hong Y, 2024, Shugan Jiangni Decoction in the Treatment of 30 Cases of Bile Reflux Gastritis of Liver Stomach Stagnation Heat Type. *Guangming Traditional Chinese Medicine*, 39(10): 1993–1996.
- [6] Zhan Q, 2023, Clinical Effect of Chaihu Xianxiong Decoction Combined with Haoqin Qingdan Decoction in the Treatment of Bile Reflux Gastritis After Cancer Radiotherapy. *Chinese and Foreign Medical Research*, 21(21): 157–160.
- [7] Zheng Z, 2023, Clinical Observation of Dachaihu Decoction in the Treatment of Bile Reflux Gastritis. *Journal of Practical Traditional Chinese Medicine*, 39(10): 1946–1947.
- [8] Bai T, 2022, Clinical Efficacy of Modified Dachaihu Decoction in the Treatment of Bile Reflux Gastritis. *Inner Mongolia Traditional Chinese Medicine*, 41(5): 13–14.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Observation of Minimally Invasive Puncture Drainage Assisted by Robot Navigation for the Treatment of Hypertensive Cerebral Hemorrhage

Shichen Jiang, Hongbo Xiao*

Rugao People's Hospital, Nantong 226500, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To study the clinical effect of robot navigation-assisted minimally invasive puncture drainage treatment for hypertensive intracerebral hemorrhage. *Method:* 80 patients with hypertensive intracerebral hemorrhage who received treatment in our hospital from February 2024 to February 2025 were selected and randomly divided into two groups using a random number table, with 40 patients in each group. The conventional puncture group received traditional minimally invasive puncture drainage treatment, while the robot navigation group received minimally invasive puncture drainage treatment with the assistance of robot navigation. The treatment effects of the two groups were compared. *Result:* The robot navigation group had better surgical-related indicators, lower neurological deficit scores, and fewer complications ($P < 0.05$). *Conclusion:* The application of robot navigation-assisted minimally invasive puncture drainage therapy for hypertensive intracerebral hemorrhage can optimize surgical indicators, improve neurological function, and reduce the probability of complications.

Keywords: Robot navigation; Hypertensive cerebral hemorrhage; Minimally invasive puncture drainage; Neurological function; complication

Online publication: September 26, 2025

1. Introduction

Hypertensive intracerebral hemorrhage is a common and critical condition in clinical practice, mainly caused by long-term hypertension leading to hyalinization and fibrinoid necrosis of small cerebral arteries. When blood pressure suddenly rises sharply, these diseased blood vessels are prone to rupture and bleed, leading to the formation of intracranial hematomas^[1]. The onset of this disease is extremely rapid, usually taking only a few minutes to a few hours from the onset to the appearance of significant symptoms, and the condition progresses rapidly, which may lead to serious symptoms such as consciousness disorders and limb paralysis in a short period of time. If effective treatment measures are not taken promptly, it will not only leave serious neurological sequelae for patients, but may even directly endanger their life safety. At present, the core goal of treating hypertensive intracerebral hemorrhage in clinical practice is to clear the intracranial hematoma as soon as possible, reduce the pressure of the hematoma on surrounding brain tissue, lower intracranial pressure, thereby reducing ischemic and hypoxic damage to brain tissue, and create favorable conditions for the recovery of neurological

function.

Among the various methods for treating hypertensive intracerebral hemorrhage, minimally invasive puncture drainage has become a commonly used treatment method due to its advantages of minimal trauma, relatively simple operation, and minimal impact on the patient's overall condition. Especially for elderly patients with poor physical condition who cannot afford craniotomy surgery, it is the preferred option. However, traditional minimally invasive puncture drainage surgery mainly relies on doctors to determine the location and size of the hematoma based on the patient's head CT image, and then determine the puncture point and path based on their own clinical experience. The entire operation process is not accurately guided, so it is easy to cause inaccurate puncture due to factors such as insufficient doctor experience, deviation in hematoma location judgment, or slight movement of the patient's head. With the continuous development of medical technology, robot navigation technology is gradually being used in neurosurgery. This technology relies on advanced imaging and computer processing systems to perform three-dimensional reconstruction of the patient's intracranial structure, helping doctors to more intuitively and accurately understand the location of the hematoma and the distribution of important nerves and blood vessels around it. It can also guide surgical operations in real time to allow the puncture needle to accurately reach the hematoma site according to the pre-set optimal path. Based on this background, this study mainly observes the clinical role of robot navigation-assisted minimally invasive puncture and drainage treatment for hypertensive intracerebral hemorrhage.

2. Data and methods

2.1. General information

Eighty patients with hypertensive intracerebral hemorrhage who received treatment in our hospital from February 2024 to February 2025 were randomly divided into a conventional puncture group and a robot navigation group using a random number table method, with 40 patients in each group. There were 22 males and 18 females in the routine puncture group, with ages ranging from 45 to 78 (58.62 ± 5.34) years old; There were 21 males and 19 females in the robot navigation group, aged 46–79 (59.05 ± 5.28) years old. Two groups are comparable, $P > 0.05$. Inclusion criteria: (1) Meet the diagnostic criteria for hypertensive intracerebral hemorrhage; (2) The time from onset to admission is less than 24 hours; (3) Patients and their families give informed consent. Exclusion criteria: (1) Combination of severe liver, liver, and kidney diseases; (2) Coagulation dysfunction; (3) Patients with brainstem hemorrhage.

2.2. Method

The conventional puncture group adopts traditional minimally invasive puncture drainage treatment. The doctor determines the puncture point and puncture path based on the imaging examination results. After local anesthesia, the puncture operation is carried out, and a drainage tube is inserted and connected to the drainage device. After surgery, the drainage speed is adjusted according to the patient's condition, and regular head CT scans are conducted to observe the clearance of the hematoma.

The robot navigation group carries out minimally invasive puncture and drainage treatment with the assistance of robot navigation. Before surgery, the patient's head CT scan is performed, and the image data is imported into the robot navigation system. The system constructs a three-dimensional model based on the data and plans the optimal puncture path. During the operation, the robot navigation system guides the doctor in real-time to ensure that the puncture needle accurately reaches the hematoma site. The subsequent drainage operation is consistent with the conventional puncture group.

2.3. Observation indicators

Compare the surgical time, intraoperative blood loss, hematoma clearance rate, NIHSS score before and after intervention, and the probability of complications between the two groups.

2.4. Statistical methods

Use SPSS 24.0 to analyze the data. Measurement data *t*-test; Count data chi-square test. $P < 0.05$ represents a significant difference.

3. Results

3.1. Comparison of surgical-related indicators between the two groups

The robot navigation group had shorter surgical time, less intraoperative bleeding, and higher hematoma clearance rate ($P < 0.05$), as shown in Table 1.

3.2. Comparison of NIHSS scores between two groups before and after intervention

After intervention, the scores of the robot navigation group were lower than those of the conventional puncture group ($P < 0.05$), as shown in Table 2.

3.3. Comparison of the incidence of complications between the two groups

The probability of complications in the robot navigation group was lower than that in the conventional puncture group ($P < 0.05$), as shown in Table 3.

Table 1. Comparison of surgical-related indicators between two groups (mean \pm SD)

Group	Operation time (min)	Intraoperative blood loss (mL)	Hematoma clearance rate (%)
Conventional puncture group ($n = 40$)	58.45 ± 8.62	42.36 ± 7.58	72.58 ± 6.34
Robot navigation team ($n = 40$)	35.28 ± 6.15	21.45 ± 5.26	89.63 ± 5.72
<i>t</i>	13.839	14.334	12.628
<i>P</i>	0.000	0.000	0.000

Table 2. Comparison of NIHSS scores between the two groups before and after intervention (mean \pm SD, points)

Group	Pre-intervention evaluation	Post-intervention score
Conventional puncture group ($n = 40$)	18.65 ± 3.24	10.82 ± 2.56
Robot navigation team ($n = 40$)	18.72 ± 3.18	6.35 ± 2.14
<i>t</i>	0.098	8.473
<i>P</i>	0.923	0.000

Table 3. Comparison of incidence of complications between two groups [$n(\%)$]

Group	Intracranial rebleeding	Infection	Nerve injury	Overall incidence rate [$n(\%)$]
Conventional puncture group ($n = 40$)	3 (7.50)	3 (7.50)	2 (5.00)	8 (20.00)
Robot navigation team ($n = 40$)	0 (0.00)	1 (2.50)	0 (0.00)	1 (2.50)
χ^2				4.507
<i>P</i>				0.034

4. Discussions

Hypertensive intracerebral hemorrhage, as one of the most serious complications of hypertension patients, has an extremely complex pathophysiological process and involves multidimensional mechanisms of damage to brain tissue. The intracranial hematoma formed after the rupture and bleeding of cerebral blood vessels will exert mechanical compression on surrounding brain tissue in a short period of time. This compression directly leads to a decrease in local cerebral blood perfusion, triggering ischemia and hypoxia reactions. At the same time, during the process of hematoma decomposition, a large amount of harmful substances, such as iron ions and various inflammatory factors produced by hemoglobin decomposition, will be released, which will further exacerbate the inflammatory response and oxidative stress damage of brain tissue, thereby inducing neuronal apoptosis and brain tissue edema. Brain edema will aggravate the increase of intracranial pressure, ultimately forming a vicious cycle of “hematoma compression ischemia hypoxia brain edema intracranial pressure increase”. If this cycle is not broken in a timely manner, the extent of brain tissue damage will continue to expand, and neurological dysfunction will further deteriorate. Therefore, the prompt and safe removal of intracranial hematoma in the treatment of hypertensive intracerebral hemorrhage is the core link to block the progression of pathological damage and improve patient prognosis. Minimally invasive puncture and drainage surgery is a treatment technology developed around this critical need. However, the long-standing problem of insufficient precision in traditional minimally invasive puncture and drainage surgery has always been an important factor restricting its therapeutic effect.

The results of this study showed that the surgical time of the robot navigation group was significantly shorter than that of the conventional puncture group, and the intraoperative blood loss was also significantly less than that of the conventional puncture group. This data fully demonstrates the outstanding advantages of robot navigation technology in improving surgical efficiency and safety. From the analysis of the surgical operation process, it can be seen that traditional minimally invasive puncture surgery requires doctors to repeatedly read the patient's head CT images and construct the hematoma spatial position in their mind, and then determine the puncture point and depth based on clinical experience. During this process, doctors often need to adjust the puncture angle and direction multiple times to approach the ideal puncture position, which not only prolongs the surgical time but also easily leads to damage to surrounding brain tissue and small blood vessels by the puncture needle, thereby increasing the risk of intraoperative bleeding. The robot navigation team performed a cranial CT scan before surgery. After scanning and obtaining detailed data of the patient's intracranial structure, the navigation system can automatically process this data and construct a clear 3D image model. Doctors can intuitively observe the size, shape, and relative position relationship of the hematoma with surrounding important nerves and blood vessels on the model, and then accurately plan the optimal puncture path, including the specific coordinates of the puncture point, puncture angle, and puncture depth based on this information. During the surgical operation, the navigation system will track the position of the puncture needle in real time and compare it with the preset puncture path, provide timely feedback on deviation information to the doctor, and guide adjustment, ensuring that the puncture needle reaches the center of the hematoma accurately at once without repeated adjustment. This not only greatly shortens the surgical time but also avoids unnecessary damage to surrounding normal tissues caused by puncture, thereby reducing intraoperative bleeding.

In terms of hematoma clearance rate, the robot navigation group was significantly higher than the conventional puncture group, which is of great significance for patient prognosis. The core reason for the difference in hematoma clearance rate between the two groups is the difference in puncture accuracy. Traditional minimally invasive puncture surgery may not reach the central area of the hematoma due to insufficient puncture accuracy, and the puncture needle may only be able to drain the surrounding blood of the hematoma, making it difficult to effectively remove the coagulation block in the hematoma center, resulting in incomplete hematoma removal. At the same time, the deviation of puncture position may also cause the drainage tube side hole to not be completely placed inside the hematoma, and some side holes may be exposed to normal brain tissue areas, thereby weakening the drainage effect and further affecting the hematoma removal rate; The puncture operation assisted by robot navigation can ensure that the puncture needle accurately reaches the center of the hematoma and the drainage tube side hole can be completely placed inside the hematoma, maximizing

the drainage efficiency to fully discharge the blood and clots inside the hematoma. At the same time, based on the precise puncture position, doctors can adjust the drainage speed and time more reasonably according to the specific situation of the hematoma, avoiding new injuries caused by rapid drainage, leading to a sudden drop in intracranial pressure or affecting the hematoma clearance effect due to slow drainage. A more thorough removal of hematoma can effectively reduce the pressure on surrounding brain tissue, alleviate the increase in intracranial pressure to create favorable conditions for the recovery of cerebral blood perfusion, shorten the time of cerebral ischemia and hypoxia, and thus reduce the degree of cerebral tissue damage. This also lays a solid foundation for the subsequent recovery of neurological function in patients ^[2].

In this study, there was no significant difference in NIHSS scores between the two groups of patients before intervention, indicating that the degree of neurological damage before treatment was basically the same and comparable between the two groups of patients; After intervention, the NIHSS score of the robot navigation group was significantly lower than that of the conventional puncture group, indicating that minimally invasive puncture drainage treatment assisted by robot navigation has a more significant role in promoting the recovery of patients' neurological function. Analyzing its mechanism, firstly, the higher hematoma clearance rate of the robot navigation group can effectively relieve the compression of hematoma on nerve tissue, improve the blood and oxygen supply of nerve tissue to provide a good recovery environment for damaged nerve cells, and reduce the number of nerve cell apoptosis. Secondly, the application of robot navigation technology reduces the damage to the surrounding normal nerve tissue during surgical operations. Traditional puncture techniques may damage the nerve fiber bundles around hematomas and cause new nerve dysfunction due to insufficient accuracy. However, precise puncture assisted by robot navigation can minimize this problem and protect normal nerve function, allowing patients to better recover their nerve function to the original state. In addition, the robot navigation group has less intraoperative bleeding, shorter surgical time, and faster postoperative recovery for patients, allowing for earlier rehabilitation training. Early rehabilitation training can activate brain compensation mechanisms, promote the remodeling of damaged neural pathways, and further improve neurological function ^[3,4].

In terms of complications, the overall incidence rate of the robot navigation group was significantly lower than that of the conventional puncture group, with zero incidence of intracranial rebleeding and nerve injury, and a lower incidence of infection compared to the conventional puncture group. This fully confirms the higher safety of robot navigation-assisted therapy. Intracranial rebleeding, as one of the most serious complications after hypertensive intracerebral hemorrhage surgery, often leads to a rapid deterioration of the patient's condition and even endangers their life. Traditional puncture surgery is prone to intracranial rebleeding. On the one hand, due to insufficient puncture accuracy, the puncture needle may damage the surrounding blood vessels and cause vascular rupture and bleeding. On the other hand, incomplete hematoma removal may cause residual hematoma to continue to compress the surrounding blood vessels or their decomposition products to damage the blood vessel wall, leading to new bleeding ^[5,6]. The precise puncture assisted by robot navigation can effectively avoid damage to blood vessels caused by puncture, and more thorough hematoma removal also reduces the adverse effects of residual hematoma on blood vessels, thereby reducing the risk of intracranial rebleeding. The occurrence of nerve injury is mainly due to accidental injury of the surrounding nerve tissue during the puncture operation. The robot navigation system can clearly display the location of nerve tissue and guide doctors to avoid these important structures, thus significantly reducing the incidence of nerve injury. The occurrence of infection is related to factors such as surgical time and sterile operation during surgery. The robot navigation group has a shorter surgical time, which can reduce the chance of bacterial contamination during the surgical process. At the same time, precise puncture can reduce tissue damage to reduce susceptibility to infection, resulting in a relatively lower incidence of infection ^[7,8].

5. Conclusion

In summary, the application of robot navigation assistance in minimally invasive puncture and drainage treatment for hypertensive intracerebral hemorrhage can significantly optimize surgical indicators, promote neurological function recovery, and reduce the probability of complications. It provides a safer and more efficient treatment option for

hypertensive intracerebral hemorrhage patients and has important clinical promotion value. In future clinical practice, personalized adjustments can be made to navigation system parameters and puncture plans based on individual patient differences (such as hematoma type, location, underlying disease, etc.) to further improve treatment efficacy and long-term patient prognosis.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Li X, Yan Y, Kong F, 2024, Clinical Effect Analysis of Robot Navigation-assisted Deep Brain Hematoma Puncture Drainage for the Treatment of Hypertensive Intracerebral Hemorrhage. *Medical Clinical Research*, 41(9): 1361–1364.
- [2] Wei G, Tan S, Zhang Q, et al., 2024, Clinical Study on Robot-Assisted Minimally Invasive Puncture Surgery and Conservative Treatment for Moderate to Moderate Hypertensive Intracerebral Hemorrhage. *Jilin Medical Journal*, 45(7): 1558–1562.
- [3] Ma H, Jin H, Lei W, et al., 2024, Clinical Efficacy of Robot-Assisted Intracranial Hematoma Drilling and Drainage in the Treatment of Hypertensive Intracerebral Hemorrhage. *Journal of Clinical Medical Medicine*, 52(7): 747–750.
- [4] Qiu Q, Yan H, Zhang G, et al., 2024, Clinical Study on Robot Guided Puncture Drainage of 10–30 mL Intracerebral Hematoma. *Chinese Journal of Modern Surgery*, 28(2): 115–119.
- [5] Ding J, Zhang Y, Yu H, et al., 2024, Comparison of the Therapeutic Effects of Robot-Assisted Stereotactic Puncture and Craniotomy Hematoma Clearance in the Treatment of Hypertensive Intracerebral Hemorrhage. *Journal of Lanzhou University (Medical Edition)*, 50(4): 36–40.
- [6] Li X, Hu H, Wang L, et al., 2024, Robot-Assisted Intracranial Hematoma Puncture and Drainage for HICH Patients. *Bachu Medical*, 7(1): 28–30.
- [7] Wang H, Hu F, Chen J, et al., 2024, Clinical Application of Neurosurgical Robots in Hypertensive Intracerebral Hemorrhage Surgery (Analysis of 54 Cases). *Chinese Journal of Minimally Invasive Neurosurgery*, 28(2): 90–93.
- [8] Lai W, Zhao Z, Zhang C, 2023, Analysis of the Therapeutic Effect of Robot-Assisted Therapy for Small Amounts of Hypertensive Intracerebral Hemorrhage. *Journal of Stereotactic and Functional Neurosurgery*, 36(5): 299–303.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Exploring and Analyzing the Application Value of Endoscopic Nasal Septum Deviation Correction Combined with Low-Temperature Plasma Radiofrequency Ablation in the Treatment of Chronic Sinusitis

Chao Chen¹, Rui Wu²

¹Department of Otolaryngology, Head and Neck Surgery, The First Clinical Medical College of China Three Gorges University & Yichang Central People's Hospital, Yichang 443003, Hubei, China

²Department of Operating room, The First Clinical Medical College of China Three Gorges University & Yichang Central People's Hospital, Yichang 443003, Hubei, China

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical efficacy and application value of endoscopic nasal septum deviation correction combined with low-temperature plasma radiofrequency ablation in the treatment of chronic sinusitis. *Methods:* Among the patients with chronic sinusitis admitted to our hospital, 70 patients admitted from January 2023 to January 2025 were selected as the observation subjects. All patients underwent endoscopic nasal septum deviation correction surgery and were divided into two groups based on the order of admission. The first 35 patients admitted were designated as the control group and underwent combined endoscopic sinus surgery. The latter 35 patients admitted were designated as the observation group and underwent combined low-temperature plasma radiofrequency ablation. The postoperative nasal mucosal function, olfactory function, airway reactivity, and occurrence of complications were observed in both groups to evaluate the therapeutic efficacy. *Results:* (1) Nasal mucosal function. The observation group had a shorter postoperative saccharin clearance time compared to the control group ($P < 0.05$). The nasal mucociliary clearance rate was higher in the observation group than in the control group ($P < 0.05$). (2) Olfactory function. The olfactory function grading in the observation group was superior to that in the control group ($P < 0.05$). (3) Airway reactivity. The observation group exhibited lower postoperative airway resistance at 5 Hz and 20 Hz compared to the control group ($P < 0.05$). Additionally, the resonance frequency was lower in the observation group than in the control group ($P < 0.05$). (4) The incidence of complications was similar between the two groups ($P > 0.05$). (5) The total therapeutic efficacy rate in the observation group was superior to that in the control group ($P < 0.05$). *Conclusion:* Endoscopic nasal septum deviation correction combined with low-temperature plasma radiofrequency ablation in the treatment of patients with chronic sinusitis can promote the recovery of nasal mucosal function, improve olfactory function, alleviate airway reactivity, and demonstrate good safety and significant therapeutic efficacy.

Keywords: Endoscopic correction of nasal septum deviation; Low-temperature plasma radiofrequency ablation; Chronic sinusitis; Clinical efficacy

Online publication: September 26, 2025

1. Introduction

Chronic sinusitis is a common nasal disease in clinical practice, commonly known as rhinitis. After its onset, it can affect the patient's nasal cavity condition and olfactory function. From a pathological perspective, it is a chronic inflammatory lesion with strong heterogeneity. Moreover, most cases of chronic sinusitis are accompanied by nasal septum deviation. When both conditions coexist, they interact with each other, exacerbating the severity of the illness. Currently, the primary treatment for chronic sinusitis is medication control, which only addresses the symptoms rather than the root cause. As the condition recurs, it can have a significant negative impact on the patient's physical and psychological well-being. Under such circumstances, clinical practice advocates for the treatment of chronic sinusitis accompanied by nasal septum deviation using endoscopic nasal surgery. Among these, nasal septum correction combined with sinus surgery is relatively common and yields acceptable results. During surgery, measures such as cryotherapy, laser, microwave, and electrocautery may be employed to shape the inferior turbinate. Different treatment measures result in varying degrees of trauma to the patient. If an inappropriate approach is chosen, it may lead to larger wounds, hindering the recovery of nasal mucosal function and increasing the likelihood of complications. With the continuous advancement of medical technology, low-temperature plasma radiofrequency ablation has also become increasingly mature. As a minimally invasive procedure, it can minimize trauma to the patient's nasal cavity while treating the diseased tissue, thereby preventing postoperative complications. Its principle involves using radiofrequency energy to vaporize and ablate the diseased tissue under low-temperature conditions to achieve therapeutic goals. This study observed 70 patients who underwent endoscopic correction of nasal septum deviation surgery at our hospital from January 2023 to January 2025, exploring the efficacy of combining it with low-temperature plasma radiofrequency ablation. The report is as follows.

2. General information and methods

2.1. General information

Among the patients with chronic sinusitis admitted to the hospital, 70 cases admitted from January 2023 to January 2025 were selected as the observation subjects. All patients underwent nasal endoscopic surgery for the correction of a deviated nasal septum. Based on the order of admission, they were divided into two groups.

The first 35 patients admitted constituted the control group, consisting of 19 males and 16 females, aged between 24 and 62 years old, with an average age of (45.29 ± 7.12) years old. The disease grading was as follows: 16 cases of Type I, 12 cases of Type II, and 7 cases of Type III. Among the 35 patients admitted later, serving as the control group, there were 18 males and 17 females, aged between 23 and 65 years old, with an average age of (45.72 ± 7.41) years old. The lesion grading was as follows: 15 cases of Type I, 13 cases of Type II, and 7 cases of Type III. A comparison of the basic data of the two groups of patients determined that $P > 0.05$.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Meeting the diagnostic criteria for chronic sinusitis upon examination^[1]; (2) Meeting the criteria for surgical treatment; (3) Having undergone conservative treatment for more than 6 months with poor efficacy; (4) Patients and their families have signed an informed consent form.

Exclusion criteria: (1) Presence of other infectious diseases or coagulopathy; (2) Previous nasal surgery; (3) Presence of other nasal pathologies; (4) Presence of malignant tumors or organic defects.

2.3. Methodology

After determining the surgical schedule, the patient's nasal cavity was cleaned preoperatively, including routine trimming of nasal hair and nasal cleansing.

Control group: Nasal endoscopic surgery for the correction of deviated nasal septum + nasal endoscopic sinus surgery. Tracheal intubation was performed under general anesthesia. A 1% tetracaine cotton pad (containing 1%

epinephrine) was inserted into the top, bottom, and middle meatus of the nasal cavity to constrict the nasal mucosa. Under nasal endoscopy, an L-shaped incision was made, the left mucoperichondrium and mucoperiosteum were dissected, and then the nasal septum cartilage was incised. The procedure is performed on the right side, where the connection between the cartilage and the perpendicular plate of the ethmoid bone is severed, and the cartilage is incised. The deviated tissue is then bitten off to observe the correction status. If satisfactory, the mucosa can be repositioned and sutured. After correcting the deviation, endoscopic sinus surgery, specifically bilateral inferior turbinate fracture and lateralization, is performed. A nasal septum scissor is used to remove a portion of the inferior turbinate, not exceeding one-third, followed by bipolar electrocoagulation for hemostasis. Gauze is applied to the wound surface of the inferior turbinate to achieve hemostasis. Postoperatively, the patient's middle meatus is symmetrically packed with highly expansive sponges.

Observation group: Endoscopic nasal septoplasty combined with low-temperature plasma radiofrequency ablation. The endoscopic nasal septoplasty procedure is essentially the same as that in the control group. After completion, under endoscopic guidance, surgical points on the inferior turbinate are selected, typically 3 to 4 reduction points, with targeted plasma energy settings. Ablation therapy is performed along the inferior turbinate, at a distance of approximately 0.5 to 0.8 cm beneath the mucosa. Each ablation point is treated for 6 to 8 seconds. If the therapeutic effect is unsatisfactory after the initial ablation, a second ablation is required after 15 days. Similarly, after the surgery, the middle meatus is packed with highly expansive sponges.

Prognosis: For both groups, the condition inside the nasal cavity should be observed 48 hours postoperatively. If no abnormalities are found, the packing sponges can be removed. Nasal irrigation can be performed 72 hours postoperatively. Within three months post-surgery, patients are guided to return to the hospital weekly for follow-up and endoscopic cleaning to ensure recovery effectiveness.

2.4. Evaluation indicators

- (1) Nasal mucosa function: The primary indicators include saccharin clearance time, mucociliary clearance rate, and nasal mucociliary clearance rate. Saccharin test method: Place saccharin on the turbinate (1.0 cm from the head end), and have the patient swallow every 30 seconds until they taste sweetness. Record the time. One hour after the sweetness completely disappears in the mouth, perform the test on the other side and obtain the average value.
- (2) Olfactory function: The T&T olfactory test was employed to rate patients' olfactory function, with grading ranging from I to V. Test procedure: Five different odorants, phenylethyl alcohol, isovaleric acid, trimethylindole, methylcyclopentenone, and undecanolactone, were selected and sequentially diluted into five concentration gradients, increasing tenfold each time, with scores ranging from low to high (1–5 points). Functional grading was based on the olfactory recognition threshold^[2]. A score of ≤ 1.0 indicates Grade I; scores between 1.1 and 2.5 indicate Grade II; scores between 2.6 and 4.0 indicate Grade III; scores between 4.1 and 4.9 indicate Grade IV; and a score of 5.0 indicates Grade V. Higher scores indicate poorer olfactory function.
- (3) Airway reactivity: A pulmonary function tester was used for detection, recording resonant frequency, airway resistance at 5 Hz, and airway resistance at 20 Hz.
- (4) Complications: Conditions such as nasal dryness and epistaxis were recorded.
- (5) Efficacy: Cure was defined as the disappearance of purulent nasal discharge, normal sinus ostium, complete resolution of clinical symptoms, and improvement of at least 90% in all functions compared to pre-treatment levels. Marked effectiveness was defined as alleviation of clinical symptoms, reduction in purulent discharge, and improvement of 65% to 89% in all functions compared to pre-treatment levels. Effectiveness was defined as partial improvement in symptoms and improvement of 30% to 64% in all indicators compared to pre-treatment levels. Ineffectiveness was defined as failure to meet the aforementioned criteria.

2.5. Statistical analysis

Data were analyzed using the statistical software SPSS 18.0. Continuous variables were expressed as mean \pm standard

deviation (SD) and analyzed using the *t*-test. Categorical variables were expressed as rates (%) and analyzed using the χ^2 test. A *P*-value of < 0.05 was considered statistically significant.

3. Results

(1) Nasal mucosa function

In terms of the postoperative saccharin clearance time, the observation group's (14.65 ± 1.34) min was shorter than the control group's (16.78 ± 2.42) min, with a significant difference ($P < 0.05$). Regarding the nasal mucociliary clearance rate and nasal mucociliary transport rate, the observation group's (9.52 ± 0.82) mm/min and (88.66 ± 4.72) mm/min were higher than the control group's (8.66 ± 0.72) mm/min and (80.81 ± 5.67) mm/min, respectively, with significant differences ($P < 0.05$).

(2) Olfactory function

Before surgery, in the observation group, the olfactory function grades I, II, and III were 7 cases (20.00%), 17 cases (48.57%), and 11 cases (31.43%), respectively. In the control group, the olfactory function grades I, II, and III were 8 cases (22.86%), 15 cases (42.86%), and 12 cases (34.29%), respectively. The comparison between the two groups was generally consistent ($P > 0.05$). After treatment, the observation group had 23 cases (65.71%) with grade I olfactory function, 12 cases (34.29%) with grade II, and 0 cases with grade III. The control group had 15 cases (42.86%) with grade I, 17 cases (48.57%) with grade II, and 3 cases (8.57%) with grade III. It can be seen that the postoperative olfactory function grading in the observation group was superior to that in the control group ($P < 0.05$).

(3) Airway reactivity

In terms of the postoperative airway resistance at 5 Hz and 20 Hz, the observation group's (4.11 ± 0.76) kPa/(L·S) and (2.03 ± 0.33) kPa/(L·S) were both lower than the control group's (5.21 ± 0.76) kPa/(L·S) and (2.67 ± 0.31) kPa/(L·S), respectively, with significant differences ($P < 0.05$). Regarding the postoperative resonant frequency, the observation group's (10.82 ± 2.17) Hz was lower than the control group's (12.53 ± 1.82) Hz, with a significant difference ($P < 0.05$).

In the observation group, there were 3 cases of nasal dryness and 1 case of nasal bleeding. In the control group, there were 3 cases of nasal dryness and 2 cases of nasal bleeding. The incidence of complications in the observation group was 11.43%, which was generally consistent with the control group's 14.29% ($P > 0.05$).

In the observation group, 16 cases were cured, 15 cases showed marked improvement, 3 cases were effective, and 1 case was ineffective; in the control group, 10 cases were cured, 11 cases showed marked improvement, 8 cases were effective, and 6 cases were ineffective. The total effective rate of treatment in the observation group was 97.14%, which was superior to the 82.86% observed in the control group, with a significant difference ($P < 0.05$).

4. Discussion

Chronic sinusitis is a chronic inflammatory disease with a relatively high clinical incidence, characterized by recurrence, a long disease course, and difficulty in achieving a cure. It is typically caused by infection, with the primary pathological mechanism being long-term local inflammatory stimulation of the mucosa^[3]. During an episode, various pathological changes occur, including mucosal edema, hyperplasia, and enlargement of the nasal concha, and impaired drainage of the sinuses. Typically, patients with chronic sinusitis experience clinical symptoms such as nasal congestion, reduced sense of smell, and nasal discharge. In some cases, these symptoms are accompanied by dizziness and fatigue, limiting daily life and work. Additionally, with recurrent episodes, negative emotions may gradually develop in patients. Deviated nasal

septum refers to a morphological change in the nasal septum, where it becomes deformed and protrudes to one or both sides. This condition significantly interferes with nasal function, leading to phenomena such as nasal obstruction and, in severe cases, impaired drainage of the sinuses, resulting in inflammatory lesions. In practice, most patients with chronic sinusitis also have a deviated nasal septum, and the severity of both conditions mutually influences each other. Therefore, treatment should not be limited to addressing only one of these conditions.

Currently, medication is commonly used for treating chronic sinusitis, either in the form of oral anti-inflammatory drugs or sprays. The primary principles of these medications include anti-inflammatory, anti-allergic, and improving nasal mucosal ciliary function. However, their effectiveness is often unsatisfactory. With further research, clinical practice now advocates for surgical treatment of patients with chronic sinusitis. With the widespread adoption of nasal endoscopic technology, nasal endoscopic sinus surgery has become quite common. This surgical approach can better alleviate nasal congestion symptoms in patients, promoting ventilation and ciliary transport functions, and relieving mucosal inflammation. However, sinus surgery involves significant trauma and can have a considerable impact on nasal mucosal function. Naturally, the surgical approach also requires careful consideration. Furthermore, most patients exhibit nasal septum deviation. Simply improving the condition of the paranasal sinuses cannot guarantee therapeutic efficacy. Based on this, clinical practice often necessitates prioritizing endoscopic correction of nasal septum deviation, complemented by a reasonable intervention plan for the paranasal sinuses to ensure therapeutic efficacy. The principle of low-temperature plasma radiofrequency ablation is as follows: utilizing radiofrequency energy to excise lesions at a relatively low temperature. Throughout the process, submucosal tissue proteins can also be coagulated, leading to their denaturation and atrophy, generally achieving the treatment objective ^[4].

During the operation, the temperature is controlled at around 50°, ensuring that other mucosal tissues in the patient's nasal cavity are hardly affected, and postoperative complications can also be mitigated. In this study, all 70 patients with chronic sinusitis underwent endoscopic nasal septum deviation correction. The control group underwent conventional endoscopic sinus surgery in addition, while the observation group received low-temperature plasma radiofrequency ablation. By comparing the postoperative olfactory and mucosal functions of the two groups, it can be observed that the observation group held an advantage over the control group. Conventional endoscopic sinus surgery causes significant damage to the nasal mucosa during the procedure and can easily affect the nasal anatomical structure, increasing surgical difficulty. In particular, posterior excision increases the use of packing materials, exacerbates damage, and complicates prognosis, leading to slow recovery of various functions. In contrast, low-temperature plasma radiofrequency ablation effectively circumvents this issue by minimizing mucosal damage when treating submucosal hyperplastic tissue. It offers safety when addressing posterior hyperplastic tissue and can create and maintain the hierarchical, morphological, and structural integrity of nasal tissues, fostering an environment more conducive to the recovery of related functions ^[5].

5. Conclusion

In conclusion, treating patients with chronic sinusitis using endoscopic correction of nasal septum deviation combined with low-temperature plasma radiofrequency ablation can promote the recovery of nasal mucosal function, improve olfactory function, alleviate airway reactivity, and offer good safety and significant therapeutic efficacy.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Shi M, Zhang X, Tang M, 2025, Analysis of the Efficacy of Endoscopic Nasal Septum Deviation Correction Combined with Low-Temperature Plasma Radiofrequency Ablation in the Treatment of Chronic Sinusitis with Nasal Septum Deviation. *China Journal of Endoscopy*, 31(3): 13–19.
- [2] Ma F, She C, Liu D, 2021, The Application Effect of Improved Nasal Septum Suture Technique in Nasal Septum Deviation Correction Combined with Inferior Turbinate Plasma Radiofrequency Ablation. *Contemporary Medicine*, 27(1): 55–57.
- [3] Zheng J, 2021, Endoscopic Treatment of Inferior Meatus Hemangioma with Fractured Inferior Turbinate, Nasal Septum Deviation Correction, and Low-Temperature Plasma Radiofrequency. *Zhejiang Medical Journal*, 43(24): 2690–2692.
- [4] Xu H, Sun Z, Dong H, Qian J, 2018, The Impact of Nasal Septum Deviation Correction Combined with Plasma Low-Temperature Radiofrequency Ablation on Nasal Cavity Healing and Physiological Function in Patients. *Journal of Practical Clinical Medicine*, 22(5): 83–86.
- [5] Zhao X, Wang W, Yang Z, Tang W, Gan J, 2023, The Application of Plasma Radiofrequency Ablation Combined with Inferior Turbinate Fracture Outward Shift in the Treatment of Nasal Septum Deviation with Chronic Hypertrophic Rhinitis. *Doctor Online*, 13(1): 3–6.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Linerixibat and the Future of Pruritus Therapy in Primary Biliary Cholangitis

Qishu He*

The University of Edinburgh, Edinburgh EH8 9YL, United Kingdom

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Cholestatic pruritus significantly impairs quality of life in Primary Biliary Cholangitis (PBC) and is often refractory to ursodeoxycholic acid. This review explores Linerixibat, a gut-restricted ileal bile acid transporter (IBAT) inhibitor, as a targeted therapy for PBC-associated pruritus. By selectively blocking IBAT in the terminal ileum, Linerixibat reduces systemic bile acid (BA) accumulation—a key driver of itch via MAS-related G protein-coupled receptor X4 (MRGPRX4) activation on sensory neurons. Clinical trials demonstrate Linerixibat's efficacy in lowering serum BAs and alleviating pruritus, with a safety profile characterized primarily by manageable, mechanism-driven diarrhea. Unlike IBAT inhibitors developed for paediatric cholestatic disorders (e.g., odevixibat for PFIC), Linerixibat is optimized for adult PBC. Future therapeutic strategies may involve combining Linerixibat with agents targeting BA homeostasis (e.g., dual FXR/TRG5 agonists like INT-767) or pruritus signaling (e.g., MRGPRX4 antagonists). Ongoing Phase III trials will further define its long-term role in PBC management.

Keywords: Linerixibat; Primary biliary cholangitis; Cholestatic pruritus; Ileal Bile Acid Transporter (IBAT) inhibitor; Bile acids; MRGPRX4; Targeted therapy

Online publication: September 26, 2025

1. Introduction

PBC is an autoimmune liver disease characterised by progressive intrahepatic bile duct destruction, leading to cholestasis, fibrosis, and eventual cirrhosis^[1]. Advanced stages often necessitate liver transplantation, a resource-intensive intervention demanding lifelong immunosuppression due to rejection risk^[2]. Among PBC's debilitating symptoms, cholestatic pruritus severely impairs patient's quality of life, causing sleep deprivation, fatigue, and in extreme cases, suicidal ideation^[3–5]. First-line therapy with ursodeoxycholic acid (UDCA) slows disease progression but often fails to relieve pruritus^[6,7]. This treatment gap reflects the complex pathophysiology of PBC-associated pruritus, where bile acid (BA) accumulation activates specific pruritogenic pathways^[8–10]. These insights have led to drugs such as Linerixibat, a selective ileal bile acid transporter (IBAT) inhibitor that reduces systemic BA overload.

2. BA accumulation and pruritus in PBC: The role of IBAT

Cholestatic pruritus in PBC results from systemic BA accumulation due to impaired bile flow, leading to elevated

cytotoxic BAs such as deoxycholic acid (DCA), taurochenodeoxycholic acid (TCDCA) and chenodeoxycholic acid (CDCA) ^[11,12]. These BAs bind and activate the Mas-related G protein-coupled receptor X4 (MRGPRX4) on dorsal root ganglion (DRG) neurons ^[12]. Upon activation, MRGPRX4 couples to Gq proteins and stimulate phospholipase C (PLC), hydrolysing phosphatidylinositol 4,5-bisphosphate (PIP₂) into inositol trisphosphate (IP₃). IP₃ induces intracellular calcium release, depolarising DRG neurons and triggering action potentials that transmit itch signals to the central nervous system ^[12–14] (**Figure 1**). This mechanism is supported by findings that intradermal BA injection induces scratching in MRGPRX4-humanised mice ^[15]. In humans, BAs or MRGPRX4 agonists elicit histamine-independent pruritus ^[12]. Moreover, plasma BA levels positively correlate with itch severity in PBC patients, and pathological BA mixtures selectively activate MRGPRX4, implicating MRGPRX4 in cholestatic itch ^[12].

Central to this process is IBAT, which mediates sodium-dependent reabsorption of conjugated BAs in the terminal ileum, returning them to the liver via the portal vein to support digestion and lipid absorption, maintaining enterohepatic circulation ^[16,17]. IBAT activity relies on a sodium gradient generated by basolateral Na⁺/K⁺-ATPase to co-transport Na⁺ and BA from the intestinal lumen into enterocytes against their concentration gradient ^[18].

Structurally, IBAT contains seven transmembrane helices with an extracellular N- terminus and intracellular C-terminus ^[19,20]. Transmembrane helix 3 (TM3) contains critical aspartate residues (D122, D124) for Na⁺ and BA transport ^[21]. In PBC, IBAT is upregulated to compensate for low intestinal BA, as the body attempts to preserve enterohepatic circulation, which paradoxically increases systemic BA, sustaining MRGPRX4 activation and pruritus ^[12,22].

Beyond pruritus, excess BAs contribute to hepatic inflammation, fibrosis, and PBC progression ^[12,23–26], reinforcing BA reduction as a therapeutic strategy.

Figure 1. Bile Acid-Induced Itch Signalling via MRGPRX4 Activation

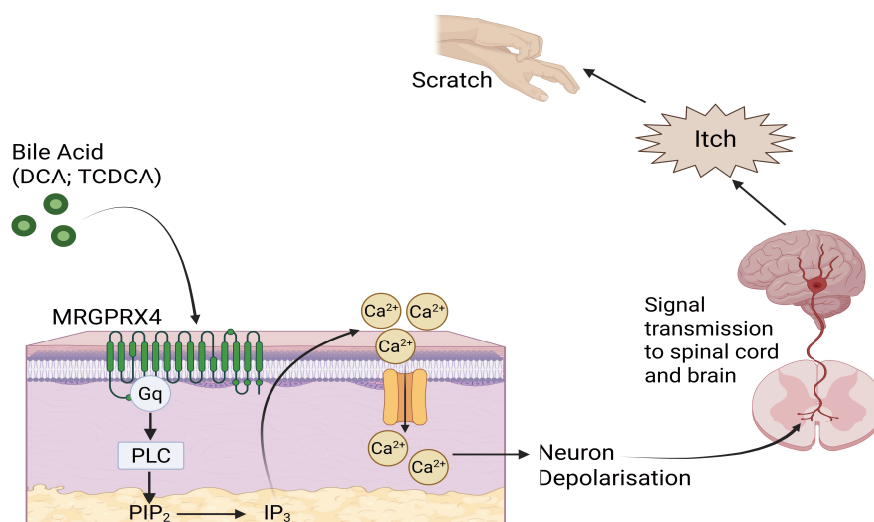


Figure 1. Bile acids such as deoxycholic acid (DCA) and taurochenodeoxycholic acid (TCDCA) activate the Mas-related G protein-coupled receptor X4 (MRGPRX4) on dorsal root ganglion (DRG) neurons. Upon ligand binding, MRGPRX4 couples with Gq proteins to activate phospholipase C (PLC), which hydrolyses PIP₂ into IP₃. IP₃ stimulates intracellular Ca²⁺ release, leading to neuronal depolarisation and transmission of itch signals to the spinal cord and brain. This cascade ultimately results in the itch sensation and the scratching response. Created in Biorender.com. Information from Yue et al. (2019 & 2021) ^[12,14].

3. Structure and mechanism of Linerixibat

Linerixibat (GSK2330672) is a potent, non-absorbable small molecule that selectively inhibits IBAT. Its structure features two terminal carboxylic acid groups and a zwitterionic structure (combining an ionizable amine linker with negatively charged carboxylates), which mimics the physicochemical properties of conjugated BAs ^[27,28]. These

polar, ionised groups confer high aqueous solubility while preventing passive diffusion across intestinal membranes, restricting Limerixibat to the intestinal lumen and minimising systemic absorption^[28]. Limerixibat achieves high-affinity binding to sodium-coordinating aspartates in IBAT's TM3^[20,21]. By blocking BA reabsorption at the ileal brush border, Limerixibat diverts BAs to the colon for faecal excretion, disrupting enterohepatic circulation and reducing the BAs available for pruritogenic activation^[29,30] (**Figure 2**).

Figure 2. Mechanism of Limerixibat in Disrupting Enterohepatic Circulation of Bile Acids

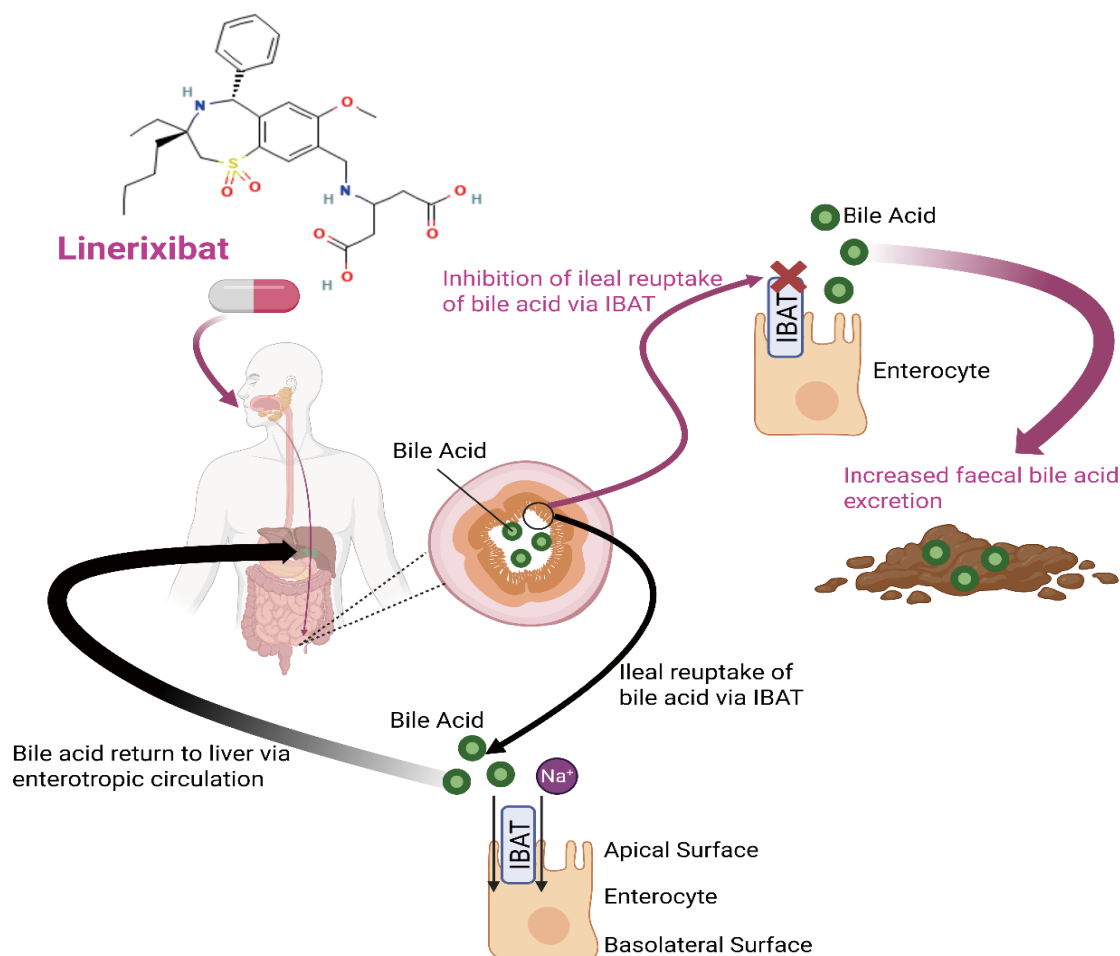


Figure 2. Limerixibat competitively inhibits IBAT on enterocytes in the terminal ileum. The black arrows represent the normal enterohepatic circulation, where bile acids (BA) are reabsorbed in the ileum and returned to the liver. The pink arrows represent the altered pathway following Limerixibat administration, where inhibition of IBAT blocks BA reuptake, leading to increased faecal BA excretion and reduced systemic BA levels. Created in Biorender.com. Information from Hegade et al. (2016) and Hegade et al. (2017)^[29,30], Limerixibat chemical structure taken from PubChem (2025)^[27].

4. Selectivity and therapeutic precision of Limerixibat

Limerixibat's selectivity arises from structural differences between IBAT and related transporters. Although the hepatic sodium-taurocholate co-transporting polypeptide (NTCP) shares moderate homology with IBAT, it lacks the TM3 aspartates required for sodium-coupled transport, making it insensitive to Limerixibat^[21]. Moreover, Limerixibat doesn't interfere with basolateral organic solute transporter OST α/β , which exports BAs from enterocytes into the circulation. These selective interactions reduce intestinal BA reabsorption while preserving systemic BA homeostasis, providing therapeutic effects with minimal off-target activities^[28,31,32].

5. Clinical application of Linerixibat and other IBAT inhibitors

Linerixibat's gut-restricted action, non-absorbable design ensures localised action in the terminal ileum, minimising systemic effects while effectively reducing BA reabsorption via selective IBAT blockade^[28,32–34]. Clinical trials consistently support its efficacy, with Phase II data showing significant serum BA and pruritus reduction without significant systemic toxicity^[33,34,35]. The ongoing Phase III GLISTEN trial (NCT04950127) aims to optimise long-term dosing. So far, results demonstrate pruritus relief with consistent safety profiles^[36,37].

The main side effect is colonic BA-induced diarrhoea. Unabsorbed BAs activate the Takeda G-protein-coupled receptor 5 (TGR5) on enterochromaffin cells and enteric neurons, promoting serotonin and calcitonin gene-related peptide release, accelerating colonic motility and reducing water reabsorption^[38]. Additionally, high luminal BA concentration disrupts colonic epithelial tight junctions, enabling BA to reach the basolateral membrane and increasing fluid secretion^[38]. These effects overwhelm colonic reabsorptive capacity, causing diarrhoea.

Elevated serum 7 α -hydroxy-4-cholesten-3-one (C4), a biomarker of BA malabsorption, further confirms Linerixibat's action, and is a hallmark of BA malabsorption syndrome, where impaired BA uptake similarly causes diarrhoea^[11,39,40]. This indicates diarrhoea is a mechanism-driven, non-toxic adverse effect. Diarrhoea is generally mild and self-limiting, consistent with Linerixibat's intestinal specificity^[29,33,41].

Among IBAT inhibitors, therapeutic applications vary by age and pathology. Odevixibat is formulated for paediatric use in progressive familial intrahepatic cholestasis (PFIC), showing serum BA reduction and pruritus relief in infants as young as 3 months^[42,43]. Maralixibat reduces serum BAs and pruritus in children with Alagille syndrome^[44,45], but offers limited benefit in adult PBC^[46]. Linerixibat is optimised for adult PBC, addressing ductal destruction rather than developmental defects, highlighting the importance of disease-specific therapy design.

6. Further directions: Combination therapies and novel targets

Linerixibat's potential may be enhanced by combining it with agents targeting hepatic inflammation and fibrosis. Preclinical studies demonstrate the efficacy of INT-767, a dual Farnesoid X receptor (FXR)/TGR5 agonist, in reducing BA toxicity while modulating inflammatory and fibrotic pathways^[47] (**Figure 3**).

FXR activation suppresses hepatic BA synthesis via ileal small heterodimer partner (SHP) and intestinal fibroblast growth factor 15 (Fgf15) induction, both of which inhibit cholesterol 7 α -hydroxylase (CYP7A1), the rate-limiting enzyme in BA production, reducing BA production^[48,49]. FXR also promotes bicarbonate-rich bile secretion through carbonic anhydrase 14 (CA14) upregulation, neutralising residual BA and protecting hepatocytes^[50]. BA excretion is enhanced by bile salt export pump (BSEP) upregulation triggered by INT-767, further reducing hepatocellular BA accumulation^[47]. Moreover, FXR-mediated reduction in IL-1 β levels reduces autoimmune cholangiocyte damage^[47,51].

Simultaneously, TGR5 activates cAMP signalling to suppress NF- κ B activation and downregulate proinflammatory cytokines (TNF- α , IL-6, MCP-1) in macrophages and Kupffer cells, promoting an anti-inflammatory hepatic environment^[52–55]. INT-767 also inhibits hepatic stellate cell activation and collagen deposition, attenuating fibrosis and slowing cirrhosis^[47].

Dual FXR/TGR5 agonism provides synergistic benefits not achievable with selective activation of either receptor alone^[56]. However, human trials are needed to assess pharmacodynamic interactions, safety, and optimal dosing. Meanwhile, MRGPRX4 antagonist such as EP547, currently under Phase II trials (NCT04510090), offering a complementary strategy for pruritus relief in PBC^[57,58].

Figure 3. Dual FXR and TGR5 Activation by INT-767 Reduces Bile Acid Toxicity and Hepatic Inflammation

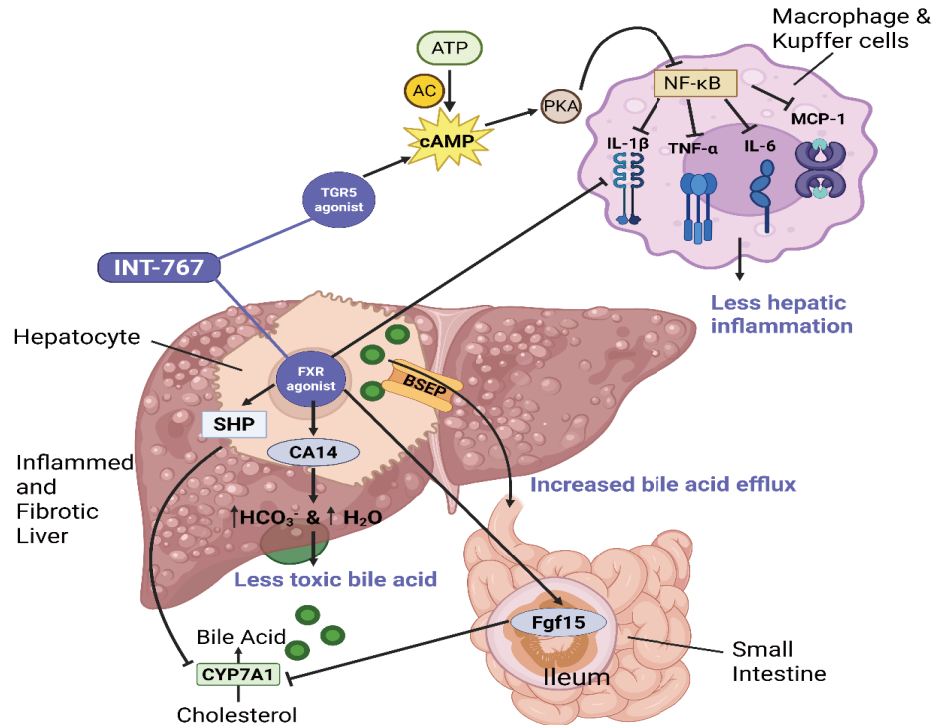


Figure 3. INT-767, a dual agonist of FXR and TGR5, reduces bile acid (BA)-induced toxicity and liver inflammation. FXR activation in hepatocytes induces small heterodimer partner (SHP) and intestinal fibroblast growth factor 15 (Fgf15), both of which suppress CYP7A1, the rate-limiting enzyme in BA synthesis. FXR also promotes bicarbonate-rich bile production via carbonic anhydrase 14 (CA14), and enhances bile acid excretion by upregulating the bile salt export pump (BSEP). These changes decrease intracellular bile acid accumulation and reduce toxicity. Simultaneously, TGR5 activation on macrophages and Kupffer cells increases cAMP via adenylyl cyclase (AC), activating PKA, which inhibits NF- κ B signaling. This leads to downregulation of pro-inflammatory cytokines including IL-1 β , TNF- α , IL-6, and MCP-1, creating an anti-inflammatory hepatic environment. Created in Biorender.com. Information from Baghdasaryan et al. (2011) and Pols et al. (2011) [47,55].

7. Conclusion

Linerixibat is a promising targeted therapy for cholestatic pruritus in PBC, leveraging selective IBAT inhibition to reduce systemic BA levels while avoiding systemic toxicity. Its gut-restricted mechanism ensures a favourable safety profile, with mild, mechanism-driven diarrhoea that could be mitigated through dose titration or adjunctive therapies targeting colonic BA effects. Compared to other IBAT inhibitors, Linerixibat is uniquely optimised for adult PBC. Further strategies may combine Linerixibat with agents such as INT767 or MRGPRX4 antagonists to address pruritus, inflammation, and fibrosis synergistically. Further research into the molecular mechanisms cholestatic pruritus is essential to fully understood and more effectively treat this complex and debilitating symptom.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Kaplan M, Gershwin M, 2005, Primary Biliary Cirrhosis. *New England Journal of Medicine*, 353(12): 1261–1273.
- [2] Neuberger J, 2003, Liver Transplantation for Primary Biliary Cirrhosis. *Autoimmunity Reviews*, 2(1): 1–7.

- [3] Bergasa N, 2005, The Pruritus of Cholestasis. *Journal of Hepatology*, 43(6): 1078–1088.
- [4] Huet P, Deslauriers J, Tran A, et al., 2000, Impact of Fatigue on the Quality of Life of Patients with Primary Biliary Cirrhosis. *The American Journal of Gastroenterology*, 95(3): 760–767.
- [5] Rische E, Azarm A, Bergasa N, 2008, Itch in Primary Biliary Cirrhosis: A Patients' Perspective. *Acta Dermato-Venereologica*, 88(1): 34–37.
- [6] Carbone M, Nardi A, Flack S, et al., 2018, Pretreatment Prediction of Response to Ursodeoxycholic Acid in Primary Biliary Cholangitis: Development and Validation of the UDCA Response Score. *The Lancet Gastroenterology & Hepatology*, 3(9): 626–634.
- [7] Mayo M, Carey E, Smith H, et al., 2023, Impact of Pruritus on Quality of Life and Current Treatment Patterns in Patients with Primary Biliary Cholangitis. *Digestive Diseases and Sciences*, 68(3): 995–1005.
- [8] Kirby J, Heaton K, Burton J, 1974, Pruritic Effect of Bile Salts. *British Medical Journal*, 4(5946): 693–695.
- [9] Kode V, Yimam K, 2024, Cholestatic Pruritus: Pathophysiology, Current Management Approach, and Emerging Therapies. *Current Hepatology Reports*, 23: 123–136.
- [10] Varadi D, 1974, Pruritus Induced by Crude Bile and Purified Bile Acids. *Archives of Dermatology*, 109(5): 678.
- [11] Appleby R, Walters J, 2014, The Role of Bile Acids in Functional GI Disorders. *Neurogastroenterology & Motility*, 26(8): 1057–1069.
- [12] Yu H, Zhao T, Liu S, et al., 2019, MRGPRX4 Is a Bile Acid Receptor for Human Cholestatic Itch. *eLife*, 8: e48431.
- [13] Han L, Ma C, Liu Q, et al., 2013, A Subpopulation of Nociceptors Specifically Linked to Itch. *Nature Neuroscience*, 16(2): 174–182.
- [14] Yu H, Wangenstein K, Deng T, Li Y, Luo W, 2021, MRGPRX4 in Cholestatic Pruritus. *Seminars in Liver Disease*, 41(3): 358–367.
- [15] Meixiong J, Vasavda C, Snyder S, et al., 2019, MRGPRX4 Is a G Protein-Coupled Receptor Activated by Bile Acids That May Contribute to Cholestatic Pruritus. *Proceedings of the National Academy of Sciences*, 116(21): 10525–10530.
- [16] Dawson P, Haywood J, Craddock A, et al., 2003, Targeted Deletion of the Ileal Bile Acid Transporter Eliminates Enterohepatic Cycling of Bile Acids in Mice. *Journal of Biological Chemistry*, 278(36): 33920–33927.
- [17] Dilger K, Hohenester S, Winkler-Budenhofer U, et al., 2012, Effect of Ursodeoxycholic Acid on Bile Acid Profiles and Intestinal Detoxification Machinery in Primary Biliary Cirrhosis and Health. *Journal of Hepatology*, 57(1): 133–140.
- [18] Trauner M, Boyer J, 2003, Bile Salt Transporters: Molecular Characterization, Function, and Regulation. *Physiological Reviews*, 83(2): 633–671..
- [19] Banerjee A, Swaan P, 2006, Membrane Topology of Human ASBT (SLC10A2) Determined by Dual Label Epitope Insertion Scanning Mutagenesis: New Evidence for Seven Transmembrane Domains. *Biochemistry*, 45(3): 943–953.
- [20] Zhang E, Phelps M, Banerjee A, et al., 2004, Topology Scanning and Putative Three-Dimensional Structure of the Extracellular Binding Domains of the Apical Sodium-Dependent Bile Acid Transporter (SLC10A2). *Biochemistry*, 43(36): 11380–11392.
- [21] Hussainzada N, Claro T, Swaan P, 2009, The Cytosolic Half of Helix III Forms the Substrate Exit Route During Permeation Events of the Sodium/Bile Acid Cotransporter ASBT. *Biochemistry*, 48(36): 8528–8539.
- [22] Lanzini A, Tavonatti M, Panarotto B, et al., 2003, Intestinal Absorption of the Bile Acid Analogue ⁷⁵Se-Homocholeic Acid-Taurine Is Increased in Primary Biliary Cirrhosis, and Reverts to Normal During Ursodeoxycholic Acid Administration. *Gut*, 52(9): 1371–1375.
- [23] Cai S, Boyer J, 2021, The Role of Bile Acids in Cholestatic Liver Injury. *Annals of Translational Medicine*, 9(8): 737–737.
- [24] Chen W, Wei Y, Xiong A, et al., 2019, Comprehensive Analysis of Serum and Fecal Bile Acid Profiles and Interaction with Gut Microbiota in Primary Biliary Cholangitis. *Clinical Reviews in Allergy & Immunology*, 58(1): 25–38.

- [25] Feng S, Xie X, Li J, et al., 2024, Bile Acids Induce Liver Fibrosis Through the NLRP3 Inflammasome Pathway and the Mechanism of FXR Inhibition of NLRP3 Activation. *Hepatology International*, 18(3): 1040–1052.
- [26] Feng S, Xie X, Li J, et al., 2025, Correction: Bile Acids Induce Liver Fibrosis Through the NLRP3 Inflammasome Pathway and the Mechanism of FXR Inhibition of NLRP3 Activation. *Hepatology International*.
- [27] PubChem, 2025, Linerixibat. PubChem Database, visited on April 14, 2025, <https://pubchem.ncbi.nlm.nih.gov/compound/Linerixibat>.
- [28] Wu Y, Aquino C, Cowan D, et al., 2013, Discovery of a Highly Potent, Nonabsorbable Apical Sodium-Dependent Bile Acid Transporter Inhibitor (GSK2330672) for Treatment of Type 2 Diabetes. *Journal of Medicinal Chemistry*, 56(12): 5094–5114.
- [29] Hegade V, Bolier R, Elferink R, et al., 2016, A Systematic Approach to the Management of Cholestatic Pruritus in Primary Biliary Cirrhosis. *Frontline Gastroenterology*, 7(3): 158–166.
- [30] Hegade V, Jones D, Hirschfield G, 2017, Apical Sodium-Dependent Transporter Inhibitors in Primary Biliary Cholangitis and Primary Sclerosing Cholangitis. *Digestive Diseases*, 35(3): 267–274.
- [31] Peppel I, Verkade H, Jonker J, 2020, Metabolic Consequences of Ileal Interruption of the Enterohepatic Circulation of Bile Acids. *American Journal of Physiology – Gastrointestinal and Liver Physiology*, 319(5): G619–G625.
- [32] Zamek-Gliszczynski M, Kenworthy D, Bershas D, et al., 2021, Pharmacokinetics and ADME Characterization of Intravenous and Oral [14C]-Linerixibat in Healthy Male Volunteers. *Drug Metabolism and Disposition*, 49(12): 1109–1117.
- [33] Hegade V, Kendrick S, Dobbins R, et al., 2017, Effect of Ileal Bile Acid Transporter Inhibitor GSK2330672 on Pruritus in Primary Biliary Cholangitis: A Double-Blind, Randomised, Placebo-Controlled, Crossover, Phase 2a Study. *Lancet*, 389(10074): 1114–1123.
- [34] Ino H, Endo A, Wakamatsu A, et al., 2018, Safety, Tolerability, Pharmacokinetic and Pharmacodynamic Evaluations Following Single Oral Doses of GSK2330672 in Healthy Japanese Volunteers. *Clinical Pharmacology in Drug Development*, 8(1): 70–77.
- [35] Tanaka A, Atsukawa M, Tsuji K, et al., 2023, Japanese Subgroup Analysis of GLIMMER: A Global Phase IIb Study of Linerixibat for the Treatment of Cholestatic Pruritus in Patients with Primary Biliary Cholangitis. *Hepatology Research*, 53(7): 629–640.
- [36] GlaxoSmithKline, 2024, Linerixibat Shows Positive Phase III Results in Cholestatic Pruritus (Relentless Itch) in Primary Biliary Cholangitis (PBC), GSK Press Release, visited on April 14, 2025, <https://www.gsk.com/en-gb/media/press-releases/linerixibat-shows-positive-phase-iii-results-in-cholestatic-pruritus/>.
- [37] GlaxoSmithKline, 2025, Global Linerixibat Itch Study of Efficacy and Safety in Primary Biliary Cholangitis (PBC) (GLISTEN), visited on April 14, 2025, <https://clinicaltrials.gov/study/NCT04950127>.
- [38] Ticho A, Malhotra P, Dudeja P, et al., 2019, Bile Acid Receptors and Gastrointestinal Functions. *Liver Research*, 3(1): 31–39.
- [39] Davie R, Hosie K, Grobler S, et al., 1994, Ileal Bile Acid Malabsorption in Colonic Crohn's Disease. *British Journal of Surgery*, 81(2): 289–290.
- [40] Vitek L, 2015, Bile Acid Malabsorption in Inflammatory Bowel Disease. *Inflammatory Bowel Diseases*, 21(2): 476–483.
- [41] Levy C, Kendrick S, Bowlus C, et al., 2023, GLIMMER: A Randomized Phase 2b Dose-Ranging Trial of Linerixibat in Primary Biliary Cholangitis Patients With Pruritus. *Clinical Gastroenterology and Hepatology*, 21(7): 1902–1912.
- [42] Yi S, Kim I, Hager R, et al., 2024, FDA Approval Summary: Odevixibat (Bylvay) for the Treatment of Pruritus With Progressive Familial Intrahepatic Cholestasis. *Gastro Hep Advances*, 2024: 100596–100596.
- [43] Graffner H, Gillberg P, Rikner L, et al., 2015, The Ileal Bile Acid Transporter Inhibitor A4250 Decreases Serum Bile Acids

- by Interrupting the Enterohepatic Circulation. *Alimentary Pharmacology & Therapeutics*, 43(2): 303–310.
- [44] Shneider B, Spino C, Kamath B, et al., 2022, Impact of Long-Term Administration of Maralixibat on Children With Cholestasis Secondary to Alagille Syndrome. *Hepatology Communications*, 6(8): 1922–1933.
- [45] Loomes K, Squires R, Kelly D, et al., 2022, Maralixibat for the Treatment of PFIC: Long-Term, IBAT Inhibition in an Open-Label, Phase 2 Study. *Hepatology Communications*, 6(9): 2379–2390.
- [46] Mayo M, Pockros P, Jones D, et al., 2019, A Randomized, Controlled, Phase 2 Study of Maralixibat in the Treatment of Itching Associated With Primary Biliary Cholangitis. *Hepatology Communications*, 3(3): 365–381.
- [47] Baghdasaryan A, Claudel T, Gumhold J, et al., 2011, Dual Farnesoid X Receptor/TGR5 Agonist INT-767 Reduces Liver Injury in the *Mdr2*^{-/-} (*Abcb4*^{-/-}) Mouse Cholangiopathy Model by Promoting Biliary HCO₃⁻ Output. *Hepatology*, 54(4): 1303–1312.
- [48] Inagaki T, Choi M, Moschetta A, et al., 2005, Fibroblast Growth Factor 15 Functions as an Enterohepatic Signal to Regulate Bile Acid Homeostasis. *Cell Metabolism*, 2(4): 217–225.
- [49] Kim I, Ahn S, Inagaki T, et al., 2007, Differential Regulation of Bile Acid Homeostasis by the Farnesoid X Receptor in Liver and Intestine. *Journal of Lipid Research*, 48(12): 2664–2672.
- [50] Casey J, Sly W, Shah G, et al., 2009, Bicarbonate Homeostasis in Excitable Tissues: Role of AE3 Cl⁻/HCO₃⁻ Exchanger and Carbonic Anhydrase XIV Interaction. *American Journal of Physiology-Cell Physiology*, 297(5): 1091–1102.
- [51] Hu Y, Liu X, Zhan W, 2018, Farnesoid X Receptor Agonist INT-767 Attenuates Liver Steatosis and Inflammation in Rat Model of Nonalcoholic Steatohepatitis. *Drug Design, Development and Therapy*, 12: 2213–2221.
- [52] Kawamata Y, Fujii R, Hosoya M, et al., 2003, A G Protein-Coupled Receptor Responsive to Bile Acids. *Journal of Biological Chemistry*, 278(11): 9435–9440.
- [53] Keitel V, Donner M, Winandy S, et al., 2008, Expression and Function of the Bile Acid Receptor TGR5 in Kupffer Cells. *Biochemical and Biophysical Research Communications*, 372(1): 78–84.
- [54] Bunnett N, 2014, Neuro-Humoral Signalling by Bile Acids and the TGR5 Receptor in the Gastrointestinal Tract. *The Journal of Physiology*, 592(14): 2943–2950.
- [55] Pols T, Nomura M, Harach T, et al., 2011, TGR5 Activation Inhibits Atherosclerosis by Reducing Macrophage Inflammation and Lipid Loading. *Cell Metabolism*, 14(6): 747–757.
- [56] Braadland PR, Schneider KM, Bergquist A, Molinaro A, Lövgren-Sandblom A, Henricsson M, Karlsen TH, Vesterhus M, Trautwein C, Hov JR, Marschall HU, 2022, Suppression of Bile Acid Synthesis as a Tipping Point in the Disease Course of Primary Sclerosing Cholangitis. *JHEP Reports*, 4(11): 100561.
- [57] Escient Pharmaceuticals Inc, 2023, Evaluate the Safety, Tolerability, and PK of EP547 in Healthy Subjects and Subjects With Cholestatic or Uremic Pruritus, visited on April 14, 2025, <https://clinicaltrials.gov/study/NCT04510090>.
- [58] Escient Pharmaceuticals, 2022, MRGPRX4-Targeted Therapeutics for Neurosensory-Inflammatory Disorders, visited on April 14, 2025, <https://www.escientpharma.com/programs/mrgprx4/>.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Comparative Study of Immobilization vs. Non-Immobilization in the Treatment of Anterior Talofibular Ligament Injuries

Xinyi Wang*

Beijing National Day School, Beijing 100028, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: The anterior talofibular ligament (ATFL) is the most frequently injured ligament in ankle sprains, yet optimal management strategies remain debated. This research seeks to synthesize the current knowledge surrounding ATFL injury treatments by comparing two common approaches: immobilization and functional non-immobilization care. Specifically, this research seeks to determine the necessity of restricting activity after an ATFL injury. Immobilization, especially of the ankles and legs, can significantly affect the patients' quality of life and increase the risk of secondary injuries due to limited movement. The long-term risk and benefits of both approaches are critically examined to offer insights into best practices in treatment and rehabilitation.

Keyword: Immobilization; Functional non-immobilization care; Anterior Talofibular Ligament (ATFL); Ankle sprains

Online publication: September 26, 2025

1. Introduction

Anterior talofibular ligament injuries are common among professional athletes and recreationally active individuals, caused by excessive outward twisting of the ankle joint. Since anterior talofibular ligament plays an important role in maintaining the overall stability of the ankle joint, the post-injury recovery and rehabilitation become extremely important for patients with anterior talofibular ligament injuries^[1]. For professional athletes, the level of recovery can directly impact their sports career. However, in contrast to the crucial role of the anterior talofibular ligament in maintaining motor function, there is a lack of unified standards in the medical system for treating ATFL injuries, as well as insufficient awareness of the importance of rehabilitation for ligament injuries among the public. As a whole, the lack of a standard medical treatment plan, insufficient social awareness, and low attention to ATFL injuries are the primary factors hindering effective treatment.

In sports rehabilitation science, existing studies have examined the recovery outcomes of functional treatment and immobilization for acute foot ankle injuries. However, there is no specific study that solely focuses on the treatments and rehabilitation of ATFL injury. This study aims to fill that gap by investigating the recovery outcome of patients with ATFL injury who receive functional training versus immobilization treatment. The findings will help refine treatment protocols and provide a scientific basis to redefine the rehabilitation standards for ATFL injuries^[2]. The detailed introduction of each

treatment is provided in the supplement information section.

In this research, we mainly use two test to measure the level of recovery: single leg balance test (measurement of proprioception) and jump test (coordination and muscle strength). The specific procedure and methodology of each test will be described in detail in the Methodology part ^[3].

2. Literature review

Meticulous works done by scholars and specialists in the field of sports medicine and rehabilitation sciences have examined the effect of functional training and immobilization on the recovery and rehabilitation of many types of ankle ligament injuries, including injuries of ATFL and LAF (lateral ankle sprain). Keene et al. (2014) conducted a meta-analysis involving 1610 participants who received functional training, immobilization, or both for ankle ligament injuries that showed no significant difference in terms of pain scores and functional improvement ^[4].

However, Karlsson et al. (2012) demonstrated that functional training, which applies stress to the injured ligament, stimulates the synthesis and deposition of replacement collagen with higher tensile strength than the collagen formed after prolonged immobilization. This suggests that functional training outperforms traditional fixed immobilization in terms of functional and structural recovery ^[5].

Moreover, highlighted that functional training also plays positive role in the prevention of sports injuries, especially acute ankle injury. The study concluded that participants receiving functional training showed significant improvement in cadence, total in both sides, and distance traveled per minute, indicating better motor fitness and coordination, which negatively correlated with the possibility of injury. demonstrated that functional training can detect functional impairments and movement asymmetries by analyzing human motion patterns, while targeted exercises facilitate tissue remodeling ^[6].

Perera et al. (2025) also examined the consequences of immobilization in ankle sprain treatment, often considered the traditional and conventional treatment for acute ankle injury and fracture. Their MRI case study found that 18 days of immobilization of the ankles of patients with acute ankle sprain significantly reduced the range of motion of the ankle joint, and it caused atrophy of different muscles, including the popliteus, the hamstrings, and the quadriceps, to varying degrees. The MRI scan also indicates an increase in fascia thickness, which is inversely proportional to the range of motion and the flexibility of the ankle joint ^[7]. Perera et al. (2025) concluded that immobilization may negatively affect the flexibility and functionality of the ankle joint ^[7].

3. Methodology

This study conducted a comparative case study to evaluate the recovery of patients with ATFL injuries. Specifically focusing on three cases: patients who only received strict immobilization after injury, patients who started functional training immediately after injury, and a patient who received functional training three weeks after immobilization. The first two groups will be based on the findings of the meta-analyses conducted by Vilchez-Cavazos et al. (2025) and Keene et al. (2014), which compare immobilization and function rehabilitation approaches ^[4,11].

For the third case, recovery will be measured through two standardized tests: the single-leg balance test, which quantifies proprioception by measuring time to balance, and the single-leg jump test, that measures coordination and muscle strength based on jump height and landing control. These two tests were conducted at different time points after the removal of immobilization, based on safety consideration and to prevent secondary injury.

These two tests were selected due to their widespread recommendation and accepted standard for evaluating sports-related performance after ligament injuries. Moreover, these two tests do not require any specialized field or equipment, making them practical to administer. The detailed description and discussion about the procedures and purposes of each test are outlined below. The detailed description of the procedures is listed below:

3.1. Single-leg balance test

The single-leg balance test is an assessment of proprioception. Proprioception is the ability of the body to adjust muscle forces in response to external stimuli. Proprioception is essential for motor control as it enables the body to adapt to unexpected changes in the external environment by providing real-time sensory feedback, particularly when visual input is insufficient or delayed. Additionally, proprioception contributes to movement planning by integrating environmental constraints, such as selecting optimal postural control strategies to prevent falls. Without this rapid and precise feedback, motor performance would be less efficient and more prone to errors, highlighting the critical role of proprioception in ensuring smooth, coordinated, and adaptive movement and preventing injuries ^[8].

The single-leg balance test is performed on a firm, level floor. The participants will be barefoot or wear standard athletic shoes. The starting position involves standing upright with hands on hips or arms crossed over the chest, then lifting one foot off the ground and flexing the knee to 90 degrees. Participants should keep their eyes open and focused on a fixed point at eye level. The non-stance leg must not touch the stance leg. The timer starts when the raised foot leaves the ground and stops if the participant moves their stance foot, touches the raised foot down, loses balance requiring support, or reaches the maximum test duration of 30 seconds.

For a more challenging assessment, the test can be repeated with eyes closed to isolate proprioceptive function. Three trials will be performed for each leg, with 30–60 seconds of rest between trials. Performance will be measured by the total time maintained in the proper position before any balance errors occur. Advanced versions may incorporate an unstable foam surface or cognitive dual-tasks, like solving simple math problems while conducting the single-leg test, for further challenge. Standardized instructions and environmental conditions will be maintained throughout testing to ensure reliable results ^[9].

Safety precautions will be implemented to prevent falls, particularly for elderly or injured populations. For further analysis, the center of pressure displacement can be measured using force plates to measure postural control.

3.2. Single-leg jump test

The single-leg jump test is a comprehensive assessment tool used to evaluate lower-body explosive power, neuromuscular control, limb asymmetry, dynamic stability, and the patients' willingness to accept weight on the involved side ^[10]. Rehabilitation training not only aims to restore the normal structure and original function of the limbs and body system ^[10], but also to reestablish the mind-body connection. Single-leg jump test can measure the patients' willingness to accept weight on the involved side, revealing a patient's readiness to bear weight and engage in sports. The test begins with a standardized warm-up consisting of dynamic movements such as leg swings, bodyweight squats, and submaximal practice jumps to prepare the musculoskeletal system for maximal effort. Following the warm-up, the patients assume a starting position by standing on one leg with hands placed on the hips to minimize upper-body influence.

The participants initiate the jump with a self-selected countermovement, involving a rapid descent into knee and hip flexion to utilize the stretch-shortening cycle. Upon reaching the desired depth, they explosively drive upward through the stance leg, extending the ankle, knee, and hip simultaneously to maximize vertical displacement. The non-test leg remains passive to prevent contribution to force production, ensuring that performance metrics reflect unilateral capability. During the airborne phase, the participants maintain a stable body position before landing on the same leg, where they must demonstrate control by holding the landing for at least two seconds without excessive movement or loss of balance.

Each testing session will include 3–5 maximal effort trials per leg, with rest periods of 30–60 seconds between jumps to minimize fatigue-related performance decrements. Data collection will encompass both quantitative and qualitative metrics, including jump height (in cm), peak force and power output (measured using force plate analysis), ground contact time (for reactive strength assessment), and landing stability (evaluated through kinematic analysis or clinician observation).

To ensure reliability, standardized instructions will be provided, and environmental conditions such as surface type and footwear are controlled.

4. Discussion

4.1. Patients receiving functional training or immobilization

The management of ATFL injuries involves a critical decision between functional treatment and immobilization. Both approaches have distinct advantages and risks, as highlighted by the systematic reviews of Vilchez-Cavazos et al. (2025) and Keene et al. (2014) ^[4,11].

For patients receiving only functional training or only plaster immobilization, no experimental results or data are available due to limitations in time and resources. To address this gap, we examined two meta-analyses done by Vilchez-Cavazos et al. (2025) and Keene et al. (2014) ^[4,11]. For acute ankle sprains, Vilchez-Cavazos et al. (2025) found no significant differences between functional treatment (e.g., elastic bandaging) and immobilization (e.g., casts) in terms of pain relief, functional improvement, or complications such as reinjury and instability ^[11]. This suggests that either approach may be appropriate, depending on patient preferences, clinical context and availability of medical and rehabilitative resources. However, the high heterogeneity among studies ($I^2 > 90\%$) and varying follow-up durations call for cautious interpretation of these findings.

In contrast, Keene et al. (2014) focused on postoperative ankle fractures and reported more significant outcomes ^[4]. Early ankle movement (e.g., removable splints) showed no clear long-term functional benefit over immobilization (1-year follow-up: SMD = 0.04, $p = 0.77$), but it significantly reduced the risk of venous thromboembolism (Peto OR = 0.12, $p = 0.02$). Conversely, early movement was associated with having higher risks of deep surgical site infections (Peto OR = 7.08, $p = 0.02$) and fixation failures (Peto OR = 6.56, $p = 0.004$). These findings emphasize the trade-offs between promoting early mobility and ensuring surgical stability, particularly in high-risk patients.

The divergent results between these studies may arise from differences in injury severity and postoperative healing requirements. While functional treatment for sprains prioritizes proprioception and early weight-bearing, postoperative fracture management must balance mobility with the mechanical integrity of internal fixation. Clinically, this implies that functional treatment is a viable first-line option for sprains. Future research should address the limitations of existing trials, such as small sample sizes and methodological heterogeneity, to refine treatment protocols for both conditions ^[12].

4.2. Patients receiving functional training after immobilization

This study also examined a case where a patient received four weeks of functional therapy following three weeks of immobilization, aiming to maximize rehabilitation outcomes. This patient had been practicing ballet for over ten years and possessed good physical fitness and motor skills. Single-leg balance test was conducted immediately after the immobilization was relieved and in each following week until week five. However, the single-leg jump test was conducted after two weeks of functional training for the concerns of safety and to minimize the probability of secondary injury.

Immediately after the brace removal, the patient received a five-minute mini-training session on how to exert force on the affected side. Observation revealed that the patient developed mild pressure ulcers and yellow discoloration in the areas where the skin came into contact with the plaster brace. After the training, the single-leg balance test was conducted, and the result of the single-leg balance test indicated extreme asymmetry of the affected side and the unaffected side. The patient could only balance on the affected side for 4 seconds, experiencing severe pain and mental stress. For the unaffected side, the patient could easily balance for more than 30 seconds. In this case, the difference between the two sides reached 153%, indicating the loss of a significant amount of proprioception of the affected side. Loss of proprioception and asymmetry are associated with a greater probability of sports injuries.

In order to regain proprioception and reestablish the muscular function of the affected side, the patient received five weeks of physical therapy and rehabilitation training. The primary objective was to release muscle tension and fascial adhesions caused by prolonged immobilization. After two sessions of manual therapy, the range of motion (ROM) in the affected side was largely restored to a level comparable to the unaffected side, although pain persisted. Meanwhile, functional training was also implemented. The initial phase of functional training primarily involved resistance band-assisted closed-chain exercises. The elastic band provided multidirectional resistance (frontal, sagittal, and transverse

planes) at the ankle joint, aiding in the restoration of neuromuscular coordination ^[13].

The resistance band exercise for ankle dorsiflexion and plantarflexion primarily strengthens the tibialis anterior during toe pulls (dorsiflexion) and the gastrocnemius-soleus complex during toe presses (plantarflexion), with secondary engagement of the extensor digitorum longus and posterior tibialis. In ankle injury rehabilitation, this movement plays a key role by rebuilding strength in weakened muscles, restoring a controlled range of motion, and retraining proprioceptive stability—all of which are critical for recovering functional mobility after sprains, strains, or post-immobilization stiffness. The adjustable resistance of the band allows progressive loading to safely improve tendon and ligament resilience while minimizing reinjury risk during early to mid-stage rehab (**Figure 1**).



Figure 1. Resistance band exercise for the ankle dorsiflexion and plantarflexion.

This exercise involves placing a resistance band between both feet while keeping the heels stationary and rotating the toes outward, primarily targeting the peroneal muscles (peroneus longus and brevis) on the outer lower leg. It strengthens ankle stability by improving eversion strength and resistance to inversion—key for rehabilitating and preventing lateral ankle sprains. The controlled movement enhances proprioception and muscle endurance while promoting balanced recovery in cases of chronic instability or post-injury weakness. Adjusting band tension allows progressive loading tailored to different rehab stages (**Figure 2**).



Figure 2. Bilateral ankle eversion resistance band training for peroneal muscle strengthening.

Following the restoration of proprioception, the focus of advanced functional training shifted toward reconditioning physical fitness, muscle strength, power, and movement coordination to prepare for a return to sport (RTS). As detailed in the Introduction, BOSU ball-assisted training demonstrated significant efficacy in restoring these functional capacities (**Figure 3**).

After two weeks of functional training and physical therapy, the single-leg jump test was conducted. The detailed results of the two tests are shown in the table below.



Figure 3. Advanced functional training facilitated by BOSU ball.

Table 1. Result of single-leg jump test

	Week 2	Week 3	Week 4	Week 5
Affected Side/cm	25	30	55	78
Unaffected Side/cm	85	87	84	89
Percentage Difference of Two Sides	89%	78%	42%	13%

Table 2. Result of single-leg balance test

	Week 1	Week 2	Week 3	Week 4	Week 5
Affected Side/s	2	4	15	28	>30
Unaffected Side/s	>30	>30	>30	>30	>30
Percentage Difference of Two Side	175%	152%	67%	6.9%	0%

5. Conclusion

The meta-analysis and the case study highlight the risks of immobilization, such as muscle atrophy and reduced mobility. In contrast, functional training demonstrates potential in restoring neuromuscular control and stability.

These findings suggest that functional training may offer superior rehabilitation benefits, particularly for professional athletes. However, the choice between immobilization and functional training should be individualized, taking into account injury severity, patient needs, and available resources. Future research with larger samples and standardized protocols is needed to refine treatment guidelines for ATFL injuries.

6. Supplement information

6.1. Functional training

Functional training is a training method that focuses on multi-joint and compound movements, aiming to improve an individual's overall physical fitness and functional performance by imitating or enhancing movement patterns in daily life and exercise. Unlike traditional strength training, which often isolates individual muscles, this approach emphasizes movement patterns that mimic daily activities and sports, improving stability, flexibility, coordination, and strength in dynamic environments. Originally rooted in physical therapy and medical rehabilitation, functional training helps restore and optimize athletic ability, benefiting both injury recovery and general fitness. Today, with growing emphasis on health and sports performance, functional training has gained widespread application in athletics, rehabilitation, and general fitness.

Recent research highlights its role in preventing and rehabilitating injuries, particularly in areas like ankle stability. Studies suggest that targeted functional exercises can reduce acute ankle sprains and improve neuromuscular control, offering a proactive approach to injury prevention.

BOSU ball (both sides up ball) is a critical piece of equipment in functional training. It facilitates reestablishing proprioception, coordination, and neuromuscular control after injuries by providing an unstable hemispherical plane. A common training plan for the rehabilitation of acute ankle ligament injury is the BOSU ball functional training exercise. Specifically, this exercise involves standing on a BOSU ball with both feet in a semi-squat position to challenge balance and proprioception. While maintaining stability, the patients repeatedly throw a yoga ball downward, allowing it to bounce back from the floor before catching it. This dynamic movement enhances neuromuscular control, coordination, and reactive stability in the lower extremities.

6.2. Immobilization

Immobilization is the standard and conventional method to treat fractures and severe ankle ligament injuries. For ATFL injuries, immobilization prevents secondary damage due to intense movement and stretching of the joints. The standard duration of immobilization for ATFL injuries is 3 weeks, because the recovery period of ligaments is three months. (H. Wang, personal communication, May 8, 2025) Following this period, recovery progress tends to decelerate significantly, nearing stagnation. As a result, the first three weeks post-injury are considered a critical phase, requiring mindful care and extra attention.

Conversely, immobilization can lead to adverse complications, including pressure sores, blood clots, muscle atrophy, body asymmetry, and compromised proprioception. The primary cause of these complications is mechanical unloading. Moreover, the inconvenience in daily life that restrictive immobilization brings to patients may potentially increase the risk of secondary injury.

7. The author's personal story and reflection

This research is critical to me as I suffered from an ATFL injury. According to my doctor approximately 80% of patients adhere to directions, especially those who care about their health and understand medical recommendations. But around 20%—especially post-op patients—may ignore instructions. For example, doctors often limit patients' mobility after surgery, but some patients believe they have already recovered and resume normal activities, which can lead to complications. A common perspective persists that "if there is no fracture, no treatment is needed." This misconception can cause negative long-term effects.

In comparison to professional athletes, individuals such as female dancers, farmers, and building workers are also people who are prone to ATFL injuries. Importantly, they receive much less attention from society and the public than professional athletes and sports stars. This disparity often results in insufficient access to medical and rehabilitation resources. I hope that this research contributes to addressing these systemic gaps and promotes equitable access to rehabilitation for all individuals affected by ATFL injuries.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Aiyer A, Murali S, Kadakia A, 2023, Advances in Diagnosis and Management of Lateral Ankle Instability: A Review of Current Literature. *JAAOS: Global Research and Reviews*, 7(12): 134–146.
- [2] Chen R, Wang Q, Li M, et al., 2023, Progress in Diagnosis and Treatment of Acute Injury to the Anterior Talofibular Ligament. *World Journal of Clinical Cases*, 11(15): 3395–3401.
- [3] Cooke M, Marsh J, Clark M, et al., 2009, Treatment of Severe Ankle Sprain: A Pragmatic Randomized Controlled Trial Comparing the Clinical Effectiveness and Cost-Effectiveness of Three Types of Mechanical Ankle Support with Tubular Bandage: The CAST Trial. *Health Technology Assessment*, 13(13).
- [4] Keene D, Williamson E, Bruce J, et al., 2014, Ankle Sprains: Recovery and Rehabilitation. *Journal of Orthopaedic & Sports Physical Therapy*, 44(9): 690–701.
- [5] Karlsson J, Lundin O, Lind K, Styf J, 2007, Early Mobilization versus Immobilization after Ankle Ligament Stabilization. *Scandinavian Journal of Medicine & Science in Sports*, 9(5): 299–303.
- [6] Doherty C, Bleakley C, Delahunt E, et al., 2016, Treatment and Prevention of Acute and Recurrent Ankle Sprain: An Overview of Systematic Reviews with Meta-Analysis. *British Journal of Sports Medicine*, 51(2): 113–125.
- [7] Perera M, Su P, Holdsworth S, et al., 2025, Changes to Muscle and Fascia Tissue after Eighteen Days of Ankle Immobilization Post-Ankle Sprain Injury: An MRI Case Study. *BMC Musculoskeletal Disorders*, 26(1): 34.
- [8] Ruiz-Sánchez F, Ruiz-Muñoz M, Martín-Martín J, et al., 2022, Management and Treatment of Ankle Sprain according to Clinical Practice Guidelines: A PRISMA Systematic Review. *Medicine*, 101(42): e31087.
- [9] Wolfe M, Uhl T, Mattacola C, et al., 2001, Management of Ankle Sprains: Classification of Ankle Sprains Grade Signs and Symptoms. *American Family Physician*, 63(1): 93–105.
- [10] Smith R, Reischl S, 1986, Treatment of Ankle Sprains in Young Athletes. *The American Journal of Sports Medicine*, 14(6): 465–471.
- [11] Vuurberg G, Hoorntje A, Wink L, et al., 2018, Diagnosis, Treatment, and Prevention of Ankle Sprains: Update of an Evidence-Based Clinical Guideline. *British Journal of Sports Medicine*, 52(15): 956–956.
- [12] Vilchez-Cavazos F, Quiroga-Garza A, Acosta-Olivo C, et al., 2025, Functional Treatment versus Immobilization for the Management of Acute Ankle Sprains: A Systematic Review and Meta-Analysis. *Journal of Bodywork and Movement Therapies*, 44: 48–55.
- [13] Wikstrom E, Hubbard-Turner T, McKeon P, 2013, Understanding and Treating Lateral Ankle Sprains and Their Consequences. *Sports Medicine*, 43(6): 385–393.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Exploration of Ideological and Political Education in the Clinical Pharmacology Course for Postgraduate Medical Students in the AI Era

Ning Huang¹, Lei Wang¹, Jiawu Zhu², Changbo Zheng^{3*}

¹The Department of Pharmacology, School of Basic Medical Sciences, Kunming Medical University, Kunming 650500, Yunnan, China

²Department of Cell Biology and Medical Genetics, School of Basic Medical Sciences, School of Basic Medical Sciences, Kunming Medical University, Kunming 650500, Yunnan, China

³The Department of Pharmacology, School of Pharmacy, Kunming Medical University, Kunming 650500, Yunnan, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: In the era of AI, the cultivation of medical master's students faces new challenges and opportunities. As an important course in the medical field, clinical pharmacology holds significant value in integrating ideological and political education into its curriculum. This paper explores the background and motivations for incorporating ideological and political education into clinical pharmacology teaching in the AI era, analyzes the potential integration of patriotic education and medical ethics education as ideological elements, and proposes corresponding teaching approaches and methods. The aim is to cultivate medical homo sapiens talents with noble medical ethics, a strong sense of social responsibility, and innovative spirit.

Keywords: Clinical pharmacology; Course-based ideological and political education; Master of Medicine

Online publication: September 26, 2025

1. Introduction

With the widespread application of artificial intelligence technology in the medical field, the training environment for master's degree students in medicine has undergone profound changes. Clinical pharmacology serves as a bridge course connecting fundamental pharmacology with clinical practice, which is crucial for the professional growth of master's degree students in medicine ^[1].

Course-based ideological and political education, as an educational concept and method with contemporary and scientific characteristics, emphasizes subtly guiding students to establish correct worldviews, outlooks on life, and values during the process of knowledge transmission, integrating ideological and political education into every aspect of course teaching. In the AI era, exploring course-based ideological and political education in clinical pharmacology has significant practical significance. For instance:

- (1) It helps to cultivate medical master's students with both professional competence and moral integrity. In the AI-driven medical environment, students are not only required to master advanced pharmacological knowledge and clinical skills but also need to have a high level of ethical awareness and social responsibility. By integrating ideological and political education into clinical pharmacology courses, students can be guided to understand the social significance and ethical responsibilities of medical work during the learning process, thus forming correct professional ethics and values;
- (2) It promotes the innovative development of medical education. The application of AI technology provides new teaching tools and methods for clinical pharmacology courses. Through the exploration of course-based ideological and political education, teachers can make full use of AI technology to create a more vivid, interactive, and personalized teaching environment, stimulating students' learning interest and initiative, and improving the effectiveness of ideological and political education;
- (3) It contributes to the cultivation of high-quality medical talents for society. In the context of the rapid development of medical technology, society urgently needs medical talents who not only have solid professional knowledge but also possess noble medical ethics and a strong sense of social responsibility. The exploration of course-based ideological and political education in clinical pharmacology is precisely aimed at meeting this social need, cultivating more outstanding medical master's students who can contribute to the health cause of mankind.

2. The significance of ideological and political education in the clinical pharmacology course in the AI era

Artificial intelligence technology has been extensively utilized across various medical domains, including but not limited to medical imaging diagnosis, pharmaceutical research and development, and disease risk prediction, fundamentally revolutionizing conventional medical approaches. In this context, medical postgraduate students are required to not only acquire specialized knowledge and technical competencies but also develop appropriate value systems and ethical frameworks to effectively navigate the complex ethical dilemmas and legal issues arising in the AI-driven healthcare landscape ^[2].

The incorporation of ideological and political education components within the curriculum serves multiple purposes, where it cultivates students' humanistic qualities and sense of social responsibility, improves the overall educational effectiveness of clinical pharmacology instruction, and achieves seamless integration between ideological-political education and professional training. This integrated approach not only stimulates students' academic motivation and engagement but also significantly enhances the course's sophistication, innovation potential, and intellectual rigor, thereby preparing future medical professionals who are both technically proficient and ethically grounded.

The study of clinical pharmacology provides an exceptional interdisciplinary platform for seamlessly integrating ideological and political education into modern medical training programs. Pharmacology textbooks and course materials systematically incorporate abundant and well-documented patriotic educational resources that vividly showcase China's profound and extensive medical heritage accumulated over millennia. These carefully curated educational materials particularly emphasize and highlight the numerous groundbreaking contributions of ancient Chinese medicine to the advancement of global healthcare, which include but are not limited to several remarkable achievements.

For instance, they detail Hua Tuo's pioneering development and successful application of anesthetic powder (Mafeisan) in complex surgical procedures during the Eastern Han Dynasty, representing one of the earliest documented uses of surgical anesthesia in human history. Furthermore, these resources comprehensively document the rich historical evolution and continuous development of traditional Chinese medicine culture, tracing its origins, theoretical foundations, practical applications, and modern adaptations across a span of thousands of years of Chinese civilization. The materials also emphasize how these ancient medical innovations and practices have significantly influenced and contributed to contemporary medical science worldwide.

A notable example appears in the chapter discussing antimalarial drugs, which dedicates significant content to Professor Tu Youyou's Nobel Prize-winning discovery of artemisinin. This section not only recounts the scientific

achievement itself but also profoundly elaborates on the research methodology that combined modern pharmaceutical techniques with traditional Chinese medical wisdom. The textbook emphasizes how this case demonstrates the crucial importance of basing scientific research on China's actual conditions, deeply exploring the essence of traditional culture, and continuously improving original innovation capabilities in science and technology.

Through these concrete examples, the curriculum effectively cultivates students' national pride, strengthens their confidence in Chinese science and culture, and inspires their sense of mission to contribute to medical development. The materials also highlight how traditional Chinese medical knowledge, when combined with modern scientific approaches, can produce world-leading medical breakthroughs that benefit all humanity.

Within the framework of clinical pharmacology teaching, medical ethics education serves as an indispensable component that integrates ideological and political elements into medical training. When delivering theoretical lectures on antipsychotic medications, instructors can significantly enhance students' ethical awareness by incorporating detailed case analyses. These real-world scenarios vividly demonstrate the severe consequences that may arise from improper disclosure of patient information, including both the ethical violations and potential legal liabilities.

Through these case studies, students gain a deeper appreciation for the fundamental principles of medical confidentiality, the critical need to safeguard patient privacy, and the broader concept of protective medicine in clinical practice^[3]. This approach not only reinforces professional standards but also cultivates a strong sense of responsibility among future medical practitioners.

Moreover, integrating medical ethics education into clinical pharmacology fosters an environment where students are encouraged to think critically about the moral dimensions of their actions. By engaging with complex ethical dilemmas, such as those involving informed consent or the prioritization of patient welfare, students develop a nuanced understanding of how ethical principles intersect with clinical decision-making. This educational strategy also emphasizes the importance of empathy and compassion in patient care, encouraging students to view patients not merely as medical cases but as individuals with unique needs and rights. Ultimately, the incorporation of medical ethics into clinical pharmacology teaching equips future healthcare professionals with the ethical framework necessary to navigate the challenges of modern medical practice, ensuring that they uphold the highest standards of integrity and patient-centered care.

In the process of pharmacology education, when introducing epinephrine as a representative classical medication, educators can particularly emphasize its critical application in emergency cardiac resuscitation scenarios. This teaching approach serves as an excellent opportunity to cultivate students' reverence for life, strengthen their professional commitment to healthcare, and inspire a deep sense of devotion to their future medical roles. By connecting pharmacological knowledge with real-life medical emergencies, students can more profoundly appreciate the sacred nature of medical practice, recognizing that their future work directly impacts human lives. Such pedagogical methods not only enhance students' understanding of drug mechanisms but more importantly, ignite their passion for patient care and reinforce their professional responsibility. Through these meaningful educational moments, students develop both the technical competence and the humanitarian spirit essential for becoming compassionate healthcare providers^[4].

3. Approaches and methods for ideological and political education in the clinical pharmacology course in the AI era

By leveraging advanced artificial intelligence technology to systematically expand and optimize teaching resources, educators can significantly enhance the quality and effectiveness of ideological and political education. This comprehensive approach involves not only the intelligent collection and organization of diverse educational materials such as real-world case studies, instructional videos, and academic literature, but also the sophisticated analysis and categorization of these resources to ensure their relevance and pedagogical value. The integration of these AI-curated resources makes abstract political concepts more concrete and accessible, thereby strengthening the visual impact and persuasive power of the instruction.

Furthermore, the development of immersive virtual simulation experiments, particularly those focusing on specialized

biological subjects like the *Phoxinus phoxinus* subsp. *phoxinus* (a model organism in scientific research), provides students with unprecedented opportunities to engage in hands-on learning experiences. These meticulously designed simulations recreate authentic laboratory environments and clinical scenarios, enabling students to safely explore complex procedures such as drug treatment protocols and pharmacological interactions. Through repeated practice in these risk-free virtual settings, students can develop critical thinking abilities, refine their problem-solving techniques, and cultivate a stronger sense of professional responsibility - all of which are essential competencies for their future careers in scientific and medical fields. The combination of AI-enhanced resource development and virtual simulation training creates a robust, multidimensional educational ecosystem that bridges theoretical knowledge with practical application.

By carefully selecting representative clinical cases that incorporate ideological and political elements, educators can effectively guide students to deeply reflect on various ethical dilemmas, moral conflicts, and legal considerations commonly encountered in medical practice. This teaching approach not only enhances students' understanding of clinical knowledge but also significantly cultivates their critical thinking skills and problem-solving capabilities. For instance, when analyzing cases involving adverse drug reactions, instructors should systematically examine both the pharmacological mechanisms underlying the drug's action and the multifactorial causes contributing to the adverse reactions. Simultaneously, the discussion should comprehensively address crucial professional issues such as physicians' ethical responsibilities, proper medication management protocols, and the fundamental principles of patient rights protection, thereby providing students with a holistic perspective on clinical practice.

Implementing structured group discussions centered around current ideological and political hot topics within the curriculum serves as an effective pedagogical approach to promote active student engagement. These carefully moderated exchanges enable participants to articulate their viewpoints, challenge assumptions, and collectively deepen their comprehension of complex sociopolitical elements. Particularly valuable are discussions examining the multifaceted ethical considerations surrounding AI applications in pharmaceutical research, including but not limited to critical issues like patient data confidentiality, informed consent protocols, and the potential for systemic biases embedded within machine learning algorithms. Through such thoughtful discourse, students can develop a nuanced, well-informed perspective on technology ethics that balances innovation with social responsibility, while cultivating essential critical thinking skills applicable to their future professional endeavors.

To effectively strengthen teacher training in clinical pharmacology, it is essential to implement comprehensive professional development programs that focus on enhancing educators' ideological and political awareness along with their pedagogical skills. This can be achieved through organizing systematic workshops and specialized training lectures that provide in-depth guidance on curriculum-based ideological and political education. These training initiatives should not only help teachers thoroughly understand the fundamental concepts and practical methodologies of integrating ideological and political elements into their teaching but also equip them with advanced instructional techniques for seamless incorporation of these components. By participating in such targeted professional development activities, educators in clinical pharmacology will be better prepared to cultivate students' professional competence while simultaneously fostering their ideological and political development, ultimately contributing to the cultivation of well-rounded medical professionals who possess both technical expertise and strong moral values.

Moreover, establishing a collaborative learning community among clinical pharmacology educators can further amplify the impact of these professional development efforts. Through regular exchange of teaching experiences, sharing of best practices, and collective problem-solving, teachers can continuously refine their approaches to integrating ideological and political education into the curriculum. This collaborative environment not only promotes individual growth but also fosters a sense of shared responsibility towards nurturing students' holistic development. Additionally, incorporating feedback mechanisms and continuous assessment into the training programs will enable educators to gauge their progress, identify areas for improvement, and adapt their teaching strategies accordingly. Ultimately, by adopting a multifaceted approach to teacher training in clinical pharmacology, we can ensure that educators are well-equipped to guide students towards becoming competent and ethically conscious medical professionals.

4. Conclusion

In the rapidly developing artificial intelligence era, ideological and political education integrated into the clinical pharmacology course has become an increasingly crucial measure for cultivating well-rounded medical postgraduates. By systematically uncovering and extracting profound ideological and political elements embedded in the professional curriculum, and by adopting flexible, diverse, and innovative teaching approaches that combine traditional methods with modern technological means, we can effectively achieve the deep integration of ideological and political education with professional medical education. This comprehensive educational approach aims to cultivate a new generation of medical talents who not only possess solid professional knowledge and skills but also demonstrate noble medical ethics, a strong sense of social responsibility towards patients and society, as well as an innovative spirit and problem-solving capabilities.

Meanwhile, as AI technology continues to advance at an unprecedented pace and finds increasingly widespread applications in the medical field, we must persistently explore, research, and innovate teaching models and methods for ideological and political education. This continuous improvement is essential to meet the evolving demands of the new era and to make significant contributions to the high-quality development and modernization of medical education, ultimately fostering the cultivation of more outstanding medical professionals for our society.

Funding

Kunming Medical University Postgraduate High-Quality Course Construction Project in 2024; Innovation Fund Projects for Ideological and Political Work in Graduate Courses at Kunming Medical University in 2025 (Project No.: 2025KC001); First-Class Discipline Team of Kunming Medical University (Project No.:2024XKTDPY12).

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Yang K, Song Y, Prunus S, 2022, Implementation of Ideological and Political Education in Medicinal Chemistry Teaching Under the Background of Pharmaceutical Innovation. *Guangdong Chemical Industry*, 49(11): 236–237.
- [2] Tang Q, Chi X, Shen Z, et al., 2025, Research Progress and Applications of Artificial Intelligence-Driven Virtual Screening in Drug Discovery. *Chinese Journal of Modern Applied Pharmacy*, 42(5): 838–854.
- [3] Zhang H, Jin R, Bian C, 2022, The Growth Story of the Growth Factor: Vanguard Team - A Record of the Wenzhou Medical University Pharmaceutical Teacher Team, a National Higher Education Huang Danyan-style Teacher Team. *Wenzhou People*, 2022(1): 50–54.
- [4] Huang Y, Zhou J, Huang L, 2025, Exploration of Ideological and Political Implementation Strategies in Clinical Pharmacology Courses Based on the Three Comprehensive Education Homo Sapiens Concept. *Teachers*, 2025(9): 29–31.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on the Current Status and Countermeasures of Family Doctor Contracted Services for Children Aged 0-6—Taking Wenzhou as an Example

Xiaoxiao Liu, Jianfeng Wang, Xiaojing Fan, Zeyang Hu, Sensen Wu*

Wenzhou Medical University, Wenzhou 325035, Zhejiang, China

*Corresponding author: Sensen Wu, 578805793@qq.com

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: This study examines the current status of family doctor contracted services for children aged 0-6 years in four community health service centers in Wenzhou, within the context of Wenzhou's initiative to establish a child-friendly city. The findings indicate issues such as insufficient awareness of contracted services, limited promotion channels, suboptimal utilization rates, and a need for more targeted service content. Recommendations aiming to solve them include diversified promotional approaches, enhanced allocation of grassroots medical resources and skills of physicians, and ongoing updates to service packages. These insights serve as valuable references for Wenzhou to formulate more targeted policies and achieve high-quality development in family doctor contracted services for children.

Keywords: Family doctor; Contracted services; Current status; Approaches

Online publication: September 26, 2025

1. Introduction

Childhood, offering essential opportunities and conditions for survival and growth, is a critical stage in human development^[1]. Given China's current shortage of pediatric medical resources and the substantial increase in public health demands for children, national healthcare reform needs to focus on exploring a service model suitable for new-era child health development and offering continuous health management. With continuous summary of practical experience, recent studies have indicated that regular health monitoring by family doctors contributes to healthy and productive lives for children with Down syndrome^[2]. Positive doctor-patient interactions, improved patient health conditions, achieved expected treatment goals, and enhanced accessibility of healthcare significantly influence satisfaction with family doctor services^[3]. Additionally, it's demonstrated that family doctor teams' contracted services have improved compliance and effectiveness between doctors and patients, earning recognition from patients with chronic diseases^[4]. In terms of pediatric depression treatment, professional teams consisting of family doctors, when working collaboratively with parents to implement comprehensive interventions, have shown promising therapeutic effects for children^[5]. Since the official introduction of the family doctor system in Shanghai in 2011, community service networks have been phased proceeded,

with further plans to roll them out across districts by 2025 ^[6]. Wenzhou City, which initiated community responsibility doctor contracting services in 2015, has developed multiple community health centers as provincial model sites. These centers provide “specialized service packages” for children aged 0–6 years old, ensuring personalized and targeted health enhancement services ^[7].

This study examines the current status of family doctor enrollment services for children aged 0–6 in Wenzhou City, exploring existing challenges and their underlying causes in light of the city’s efforts to become more child-friendly. It proposes practical solutions to provide theoretical support for the municipal government’s future research on family doctor enrollment systems and policy design, thereby enhancing service quality and efficiency while offering references for creating a more child-friendly urban environment.

2. Results analysis

2.1. Research methods

The study utilized literature review, focus group discussions and questionnaire surveys. Based on systematic analysis of relevant policies and conceptual frameworks, we conducted a theoretical research on family doctor enrollment services for children aged 0 to 6 in Wenzhou. Additionally, we surveyed service demand among families with 0–6-year-olds.

2.2. Research findings

2.2.1. Survey participants

The survey was conducted from March to April 2025 in two randomly-selected districts of Wenzhou: Ouhai and Lucheng. Community service centers in Louqiao Subdistrict (Luoqiao) and Chashan Subdistrict (Lucheng), as well as Wuma Subdistrict (Wuma) and Binjiang Subdistrict (Binjiang) in Lucheng District, were randomly selected. Questionnaires and brief interviews were administered through on-site intercepts with child guardians, collecting demographic data and information on perceptions, utilization rates and demands for contracted services. A total of 302 questionnaires were distributed, with 17 invalid responses excluded according to completion time and missing key variables, leaving 285 valid responses (valid rate: 94.37%) (**Table 1**).

Table 1. Basic information of the survey subjects

Demographic characteristic variables		Number of people (<i>n</i>)	Constituent ratio (%)
Child’s gender	Male	150	52.6
	Female	135	47.4
Guardian age	20–40	251	88.1
	41–65	34	11.9
Guardian identity	Parents	281	98.6
	Other relatives	2	0.7
	Grandparents	2	0.7
Education level of the guardian	Under junior high school	40	14
	High school and technical secondary school	41	14.4
	Junior college and undergraduate	198	69.5
	Postgraduate and above	6	2.1

Table 1 (Continued)

Demographic characteristic variables		Number of people (<i>n</i>)	Constituent ratio (%)
Occupation of the guardian	Unemployed	7	2.5
	Service personnel	19	6.7
	Migrant workers or peasants	5	1.8
	Solo practitioner	1	0.4
	companies' employees	153	53.7
	Merchant	14	4.9
	Public institution staff	23	8.1
	Government worker	7	2.5
	Freelancer	36	12.6
	Others	20	7
Place of residence of the guardian	Local District	164	57.5
	Local City	49	17.2
	Within the province (outside the local city)	19	6.7
	Outside the province	53	18.6
Per capita household income	3000 and below	11	3.9
	3001–5000	36	12.6
	5001–8000	60	21.1
	8001–12000	73	25.6
	12000 and above	105	36.8
Child's medical insurance	Urban employees' basic medical insurance	120	42.1
	Urban and rural residents' basic medical insurance	84	29.5
	Financial insurance	65	22.8
	Other	16	5.6
Child's chronic diseases	Yes	259	90.9
	No	26	9.1
Illness within the past 2 weeks	Yes	232	81.4
	No	53	18.6
Children's health condition	Very good	109	38.2
	Good	133	46.7
	Average	43	15.1

2.2.2. Guardians' awareness of family doctor contracted services

The survey revealed that out of 285 surveyed guardians, only 30 (10.5%) reported their children had a fixed doctor at primary healthcare institutions. Among the respondents, 214 (75.1%) were aware of family doctor contracted services, with 135 (63.1%) confirming their children had contracted doctors. Regarding health knowledge and proper medical practices, the surveyed guardians reported the following levels of awareness: 46.2% indicated they were “aware,” 56.9% were “very aware,” and 69.7% were “not aware.”

Among guardians aware of the family doctor contract service, 179 (51%) learned through health center promotions; 65 (18%) received information via family doctor outreach; 54 (15%) were informed through neighborhood committee campaigns; 10 (3%) received recommendations from relatives or friends; 22 (6%) were informed through TV or WeChat media; and 23 (7%) obtained details through other channels.

2.2.3. Utilization rate of family doctor contracted services for children aged 0–6 years old

This survey reveals that among children who have signed up for family doctor services, only 71.9% have established digital health records, 72.6% have received newborn home visits, 74.8% have completed health management for full-moon baby, 74.1% have undergone health management of infant and toddler, and 85.9% have received vaccination prevention. Notably, none of these services have reached 70% adoption rates. Particularly concerning is the fact that only 39 children (28.9%) had received family doctor services within the past year (**Table 2**).

Table 2. Utilization status of family doctor contracted services for children aged 0–6 years old

Items	People have adopted (<i>n</i>)	Proportion (%)	People haven't adopted (<i>n</i>)	Proportion (%)
Health management of infant and toddler	97	71.9	38	28.1
Individualized health guidance consultation	73	54.1	62	45.9
health education service	74	54.8	61	45.2
health knowledge delivery	74	54.8	61	45.2
Registration for an outpatient appointment	92	68.1	43	31.9
The tiered diagnosis and treatment system	74	54.8	61	45.2
Chronic disease continuous prescription	60	44.4	75	55.6
Establish a card and issue a certificate	79	58.5	56	41.5
Newborn home visits	98	72.6	37	27.4
Health management for full-moon baby	101	74.8	34	25.2
Health management of the infant and toddler	100	74.1	35	25.9
Health management of preschool children	94	69.6	41	30.4
Treatments of health problems	88	65.2	47	34.8
Vaccination prevention	116	85.9	19	14.1
health management of Chinese medicine	65	48.1	70	51.9
Family doctor service within the past year	39	28.9	96	71.1

As shown in **Table 3**, the medical institutions where guardians most often take their children to see a doctor are specialized hospitals, including Women and Children Hospital and Chinese Medicine Hospitals, accounting for 37.3%. Municipal hospitals follow with 23.4%, while community hospitals, district (county)-level hospitals, and other medical facilities collectively account for less than 40%.

Table 3. Most frequently visited medical institutions for children's healthcare

Items	Number (%)	Order
Community hospitals	105 (20.0)	3
District (county)-level hospitals	96 (18.3)	4
Municipal hospitals	123 (23.4)	2
Specialized hospitals (Women and Children Hospital or Chinese Medical Hospital)	196 (37.3)	1
Others	5 (1.0)	5

2.2.4. Guardians' service expectations

The survey highlights that the top three priorities for guardians regarding pediatric family doctor services are: (1) Physical examinations and health assessments for children (80.0%); (2) Timely diagnosis and treatment of common childhood illnesses (71.3%); and (3) Ongoing health monitoring (50.8%).

Secondary needs identified are: (1) Family doctor clinic availability (33.3%); (2) Nutritional guidance (26.2%); and (3) Appointment scheduling with tertiary hospital specialists (23.6%).

Less common requests are: (1) Two-way referral services (16.4%); (2) Early post-discharge rehabilitation (13.8%), and (3) Establishment of pediatric beds in households (10.3%) (**Table 4**).

Table 4. Guardians' preferred pediatric family doctor services

Service content	Number (%)	Order
Timely diagnosis and treatment of common childhood illnesses	139 (71.3)	2
Physical examinations and health assessments for children	156 (80.0)	1
Family doctor clinic availability	65 (33.3)	4
Ongoing health monitoring	99 (50.8)	3
Early post-discharge rehabilitation	27 (13.8)	10
Appointment scheduling with tertiary hospital specialists	46 (23.6)	6
Two-way referral services	32 (16.4)	9
On-site/cellphone/online consultation	40 (20.5)	8
Nutritional guidance	51 (26.2)	5
Psychological counseling	42 (21.5)	7
Establishment of pediatric beds in households	20 (10.3)	11
Others	3 (1.5)	12

3. Conclusions and discussion

3.1. Insufficient awareness of family doctor contracted services among parents

The inadequate understanding of relevant policies and the lack of promotion of related systems are the main reasons why the system has failed to achieve practical effectiveness^[8]. This survey shows from the side that only 46.2% of parents have a relatively deep understanding of family doctor contracted services, which indicates an unsatisfactory level. This finding suggests that current promotional efforts for family doctor contracted services in China remain superficial, aligning with previous research^[9].

3.2. Need to expand promotion channels for children's families

Among guardians who are aware of the contracted services, most learned about them through health centers and promotions from doctors. In contrast, less than 30% received information from other sources. This indicates a lack of comprehensive awareness and understanding of family doctor contracted services among guardians.

3.3. Inadequate utilization rate of children's families

Among the contracted population, most of the projects provided by the children's family doctor contracted service package have a utilization rate of less than 70%, indicating a low use ratio. Meanwhile, specialized hospitals continue to be the preferred choice for medical consultations among guardians, accounting for less than 40% of cases. This suggests that parents still have concerns about the quality of primary healthcare services, leading to delays and improper use of family doctor contracted services.

3.4. Need for targeted improvement in children's families

The top three services most desired by guardians and parents are physical examinations and health assessments for children, timely diagnosis and treatment of common diseases, and ongoing health management. Other aspects receive fewer requests, reflecting that the practicability and pertinence of the service package currently available need to be enhanced.

4. Strategies and recommendations

4.1. Diversified promotion of pediatric family doctor contracted services

To address the insufficient awareness and limited promotional channels among parents and guardians regarding contracted services, we should adopt multi-channel approaches to deepen policy promotion and understanding. This will help children and parents better comprehend of pediatric family doctor contracted services. For example, implementing a hybrid online-offline strategy^[10] by utilizing social media platforms like WeChat Official Accounts to share relevant information and case studies, thereby attracting broader public attention, and installing promotional materials such as exhibition boards and posters in public spaces, including communities, schools, and hospitals.

4.2. Comprehensive measures to strengthen primary healthcare resources and physician

To improve competence in primary healthcare, it's essential to increase the number of general practitioners in healthcare institutions. Various regions have focused on allocating medical resources to frontline grassroots healthcare facilities by providing enhanced financial support and favorable policies for these institutions. These approaches help shift medical resources towards primary healthcare providers, allowing for timely upgrades of diagnostic equipment and improved facilities. It also ensures better stockpiling of medications for common diseases affecting community residents. Additionally, enhancing the professional development of general practitioners is a crucial initiative. Specifically, it is recommended to strengthen the general medicine programs in Chinese medical universities and to improve the training system for general practitioners.

4.3. Continuously update and expand the content of children's family doctor contracted service packages

Update service package items promptly based on current circumstances to deliver a broader range of services to children and parents, thereby enhancing their medical experience and comfort. Offer individualized special service packages for families in need, providing refined and differentiated medical services while confronting their essential healthcare requirements. this approach aims to further elevate the sense of fulfillment and satisfaction for both children and parents.

Funding

Wenzhou Municipal Bureau of Science and Technology project, “Wenzhou 0–6 Years Old Children’s Use and Satisfaction with Family Doctor Contract Service: Based on the Perspective of Child-friendly City Construction” (Project No.: Y20220305)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] State Council, 2011, Notice on Issuing the Outline for the Development of Chinese Women and the Outline for the Development of Chinese Children [Guofa [2011] No.24], visited on June 20, 2025, http://www.gov.cn/gongbao/content/2011/content_1927200.htm.
- [2] Bunt CW, Bunt SK, 2014, The Role of Family Physicians in the Care of Children with Down Syndrome. *American Family Physician*, 90(12): 851–858.
- [3] Marcinowicz L, Konstantynowicz J, Godlewski C, 2010, Patients’ Perception of Nonverbal Communication by General Practitioners: A Qualitative Study. *British Journal of General Practice*, 60(571): 83–87.
- [4] Han D, Guo X, 2022, The Implementation Value of Family Doctor Team Contracted Services in Chronic Disease Health Management. *Chinese Community Physician*, 38(13): 135–137.
- [5] Ye X, Pan Y, 2018, Application of Family Doctor System Model in Children with Depression. *Hainan Medical Journal*, 29(20): 2900–2902.
- [6] Wang H, Ding P, Xie C, et al., 2022, Practice and Reflections on Family Doctor Service in Functional Community Health Management. *Shanghai Pharmaceutical*, 43(10): 3–6.
- [7] Sun Y, 2018, Wenzhou Vigorously Promotes Family Doctor Services: Have You Signed Up Yet?, visited on June 20, 2025, <http://news.66wz.com/system/2018/03/29/105072626.shtml>.
- [8] Lin J, Zhao S, 2020, Analysis of Parents’ Understanding of Medical Service Policies in Fuzhou Urban Area. *Chinese Public Health*, 36(11): 1543–1548.
- [9] Cui Y, 2022, Influencing Factors and Countermeasures for Residents’ “Sign but Not Attend” Phenomenon in Family Doctor Contracted Services, thesis, Jiangsu University.
- [10] Liu X, 2017, Current Status and Countermeasures of Health Management Services in Hangzhou Community Health Institutions, thesis, Hangzhou Normal University.

Publisher’s note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

An Analysis of the Causes of Communicable Diseases in the Lianyungang Area During the Period of the Republic of China: Investigation Based on Local Chronicles

Xiaolong Yang*

Northwest Minzu University, Lanzhou 730030, Gansu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: The prevention and control of communicable diseases is an important part of the construction of the modern medical and health system, which is closely related to the health of the people and the continuous stability of society. During the period of the Republic of China, due to factors such as backward medical conditions, frequent natural disasters, lagging awareness of health prevention, and the destruction caused by wars, various communicable diseases emerged and spread in a certain range in the Lianyungang area, posing a serious threat to the safety of the local people.

Keywords: The period of the Republic of China; Communicable diseases; Health care; Lianyungang

Online publication: September 26, 2025

1. Introduction

Communicable diseases refer to those caused by pathogenic microorganisms that infect the human body and are contagious, capable of causing epidemics under certain conditions. They not only threaten human health and life but also affect the process of human civilization and have even rewritten human history^[1]. The period of the Republic of China was a high-incidence stage for communicable diseases in China. “Since the Xinhai Revolution overthrew the feudal rule of the Qing Dynasty, during the 38 years of the Beiyang warlords and the Nationalist Party’s rule, severe and acute communicable diseases occurred every year, with 33 years of major epidemics, 12 of which were related to wars, and the death toll was in the tens of thousands each year”^[2]. Regarding the definition of communicable diseases, “The Nationalist Government stipulated in 1940 that cholera, typhoid fever, dysentery, typhus, relapsing fever, malaria, smallpox, diphtheria, scarlet fever, epidemic cerebrospinal meningitis, and plague were 11 types of legally defined communicable diseases, which were included in the epidemic report. After 1945, kala-azar and yellow fever were added”^[3].

During the period of the Republic of China, the Lianyungang area was also plagued by various communicable diseases (for the definition of the Lianyungang area, this article follows the current administrative division of Lianyungang City, which includes Haizhou District, Lianyun District, Ganyu District, Guannan County, Donghai County, and Guanyun County, and does not include the former Xiangshui and Shuyang areas; the time of this article is defined from the first year

of the Republic of China to the end of the 37th year of the Republic of China after liberation). There are many accounts of this in historical materials: for instance, “In the summer of the 20th year of the Republic of China, cholera was prevalent in Xinpu, Haizhou, and Lianyun for over 40 days, with no statistics on the number of deaths. In one family in Xinpu, three out of five people died”^[4]. “In the 18th year of the Republic of China (1929), cholera was prevalent in Guanyun, with hundreds of deaths in Banpu alone, with up to 180 deaths in one day. In the 22th year of the Republic of China, it was prevalent along the Yanhe River, with an incidence rate of 20% in Yishan Street, affecting over 600 people and causing 180 deaths”^[5]. “In the 37th year of the Republic of China, there were 7 epidemic areas, including Qingkou, Banzhuang, and Jinshan, with a population of over 100,000, 4,625 cases of illness, and 716 deaths, with a fatality rate of 15.45%. In Lizhai Village, there were 67 cases of illness, with an incidence rate as high as 17.4%”^[6], all of which indicate that there were epidemics of communicable diseases in Lianyungang. The reasons for this are closely related to factors of the backward medical conditions and frequent natural disasters at that time. This article, based on local chronicles related to Lianyungang and combined with some local historical materials and works, explores the causes of the prevalence of communicable diseases in Lianyungang during the period of the Republic of China.

2. Backward medical conditions

During the period of the Republic of China, the medical conditions in the Lianyungang area were relatively backward and medical resources were scarce, making it difficult to effectively guarantee the health of residents. As a result, communicable diseases kept emerging and spreading. This was first reflected in the shortage of doctors and hospitals at that time. The “Haizhou District Chronicles” records: “Before the Republic of China, there were no medical and health institutions in Haizhou, only a few households of traditional Chinese medicine practitioners. In the 3rd year of the Republic of China (1914), the American Christian missionary Mu Gengyang and his wife built the Yide Hospital outside the west gate of Haizhou, marking the first Western medical hospital in the area. During the period of the Republic of China, there was no significant development in the health sector in the Haizhou region. Besides the Yide Hospital, there were only a few private clinics, with simple equipment, weak technical strength, and high charges”^[7]. Even the Yide Hospital only had 7 doctors by 1925, including 4 Americans; 10 male nurses and 8 female nurses^[8]. The Xinpu Public Hospital in Haizhou once “lacked technical personnel, and its medical services were once in a difficult situation”^[8]. In Donghai County, there were only 4 Western doctors by the time of liberation, with 0.22 Traditional Chinese medicine practitioners per thousand people^[9].

At the same time, the Lianyungang area also faced a shortage of medicine. The “Lianyungang City Chronicles” points out: “The pharmaceutical industry in Lianyungang started relatively late. In the 3rd year of the Republic of China (1914), the American Mu Gengyang established the Yide Hospital and used foreign raw materials to produce Western medicine tablets. In the 1930s, some newly established Western pharmacies occasionally made up tinctures and liniments for sale”^[4], but such limited quantities were unlikely to meet the needs of communicable disease prevention and control. The Lianyun District Chronicles records: “Due to the shortage of doctors and medicine, loemia were rampant in the area, with smallpox, cholera, typhoid, malaria, and measles spreading year after year”^[10]. Before the founding of the People’s Republic of China, the incidence of malaria in Haizhou District was very high. Many people suffered from malaria for half a day every year, and some even developed from “every other day” to “every day”, and some were even tortured to death by malaria. However, there was no medicine to treat it at that time, let alone prevention and control. Later, quinine was available for treatment, but it could not be eradicated^[7]. During the period of the Republic of China, some private doctors vaccinated children with smallpox vaccines to prevent smallpox, but due to the high price, few people were vaccinated^[5]. It can be seen that the lack of medicine directly led to the rampant spread of communicable diseases. Moreover, the distribution of individual medical services in the Lianyun area was very uneven, with 83% concentrated in Xugou and Lianyun, and few doctors in remote mountainous areas and islands^[10]. This made it impossible for some people to access even the limited medical resources. Hospitals and doctors are the main bodies for the prevention and control of leprosy.

However, the reality of a shortage of medical resources in Lianyungang during the period of the Republic of China increased the probability of communicable disease outbreaks.

2. Frequent natural disasters

The period of the Republic of China was a time of frequent natural disasters. Droughts and floods were important factors in the spread of communicable diseases^[11]. During the period of the Republic of China, natural disasters occurred frequently in Lianyungang, mainly manifested as tsunamis, floods, and locust plagues. The Lianyungang City Chronicles records: “The most serious tsunami occurred on July 16, 1939 (the 28th year of the Republic of China), which drowned More than 1630 people, nearly a thousand salt workers were killed in three salt companies on both sides of the Guanhe River. There was no polder salt left in Qingrixin country fair, and 315 people drowned. Because of the water at night, it soon overflowed under the bed, and many families were killed because they could not open the door. After the tsunami, from Yangqiao Town, Guanyun County to the two sides of Guanhe Estuary, the ditch was flat and the beach was silted up, and the corpses were all over the field”^[4]. In Ganyu County, from June 30, 1947, continuous heavy rain caused widespread flooding, and the area from Dunshang to Xinpu was cut off from transportation except by boat. All the beans and grains were submerged, and the affected area was estimated to be 600,000 mu, with about 100,000 people affected. According to statistics, Ganyu County suffered from floods every year from the 29th to the 38th year of the Republic of China, with a probability of 100%^[6].

In Guanyun County, from the 34th to the 38th year of the Republic of China, the area suffered from continuous floods, affecting 2.4 million mu of farmland, accounting for 80% of the total farmland, and 450,000 people were affected, accounting for 66% of the total population at that time^[5]. In Donghai County, in the 35th year of the Republic of China (1946), “locusts were everywhere in the eastern part of the county, with over 300 locusts per square meter in some areas, and crops in the fields were severely affected”^[9]. From the first year of the Republic of China to the end of the Anti-Japanese War (1912–1945), there were seven large-scale locust plagues in Haizhou, with an average of one every four to five years. The locust damage caused no harvest of crops^[4].

Frequent natural disasters not only destroyed the local ecological environment but also severely reduced the quality of life of the residents. Although there is no data to clearly show that natural disasters in the Lianyungang area during the period of the Republic of China led to the outbreak of communicable diseases, the saying “after a major disaster, there is always a major epidemic” holds true. The spread of pathogens after natural disasters, the decline in people’s immunity, and the breeding of disease vectors are undoubtedly important factors in the occurrence of communicable diseases. Of course, some scholars, based on their analysis, believe that “the higher the temperature, the higher the frequency of communicable diseases, and vice versa.” However, based on the data in their article, Lianyungang was relatively less affected by this factor^[12].

3. Lagging awareness of hygiene and prevention

During the period of the Republic of China, the urban and rural environmental hygiene conditions in the Lianyungang area were poor. Sewage ditches and garbage dumps were everywhere. In summer and autumn, sewage flowed everywhere and mosquitoes and flies were rampant. Most residents’ drinking water was from ponds and rivers, which easily led to the spread of communicable diseases. Smallpox, cholera, typhoid fever, measles, scarlet fever, kala-azar, malaria, dysentery, etc. occurred every year, and there was a major outbreak every few years.” Due to poverty and poor living conditions, the health level of the residents was generally low, and the average life expectancy was only 30 to 40 years”^[8]. The Nationalist Government did not attach importance to the prevention and control of communicable diseases, and the awareness of prevention was lagging behind. No relevant systems and norms were established. As recorded in the “Lianyungang City

Chronicles”: “Disease prevention and public health management were not on the agenda of the local government during the period of the Republic of China”^[4]. This inevitably led to a poor public health environment in the Lianyungang area. In Haizhou District, “public health in urban and rural areas was neglected. Feces and garbage were everywhere, and mosquitoes and flies swarmed in summer and autumn. communicable diseases often broke out”^[7]. In Guanyun County, more than 90% of the residents drank water from ponds and rivers before the founding of the People’s Republic of China. Due to poor hygiene conditions and environmental pollution, the drinking water was extremely unhygienic^[5]. In Donghai County, communicable diseases were once severe. The Nationalist Government had no effective measures to prevent and control the occurrence, development, and spread of communicable diseases^[9]. The school health measures it required to be implemented had no practical measures^[9].

Limited by factors such as economic and cultural backwardness, the public’s awareness of hygiene was lagging behind, and the living environment was not satisfactory. As recorded in the “Guanyun County Chronicles”: “There were very few public toilets in towns and cities, and most rural households had no toilets. Men and children defecated and urinated anywhere. The chicken and duck circles are mostly in front of the window, and the pig and sheep pens were set up in courtyards. Sometimes, humans and animals lived in the same room. Feces ponds, pig ponds, and drinking water ponds were very close to each other. In front of the house, behind the door, garbage was scattered and piled up everywhere. Dead and diseased poultry and livestock were thrown around. In summer and autumn, the stench was unbearable, and the density of mosquitoes, flies, bedbugs, rats, and sandflies was very high. In rural areas of the whole county, people and animals shared the same water sources from rivers, canals, ponds, and pools, which was extremely unhygienic. According to a report submitted by Guanyun’s Magistrate Zheng Senqi to the Nationalist Government on August 23, 1947 (the 36th year of the Republic of China), “The county seat of our county is located in Banpu. Everything is very simple and crude. Garbage is everywhere, amounting to tens of millions of tons. Mosquitoes and flies are flying around, and the environment is filthy and unclean”^[5]. The public lacked scientific understanding of the prevention and treatment of infectious diseases and medical knowledge. They were poor and could not afford to buy medicine. Sun Qinming, who lived in Banpu at that time, recalled: “In the miserable years of sorrowful wilderness, kala-azar broke out. At that time, the specific drug for treating this disease was ‘New Antimony Cream’ imported from Germany, which was hard to obtain and expensive. How could the poor afford it! Some folk doctors used various single-herb prescriptions to treat it, but with no obvious effect”^[13]. In many areas, feudal superstition was prevalent, and quacks and witch doctors were rampant. As recorded in the “Haizhou District Chronicles”: “When people were ill, they often prayed to Buddha for help”^[7]. In 1938, kala-azar was prevalent in northern Jiangsu. The so-called “Mr. Camel” treated this disease with “fire needles” by pricking the liver and spleen. Quacks harmed people and delayed treatment. Some witches and sorcerers took advantage of the situation to treat diseases and make money, causing many families to be ruined. The severity of the disaster can be seen from this^[13]. In the context of a lagging awareness of health prevention and no clear communicable diseases prevention and control system, the public was poor, the environment was extremely bad, and most people lacked a clear understanding of communicable diseases, which greatly increased the possibility of the spread of communicable diseases.

4. Destruction by war

The Republic of China in its short 37 years of existence, wars experienced almost never-ending, and the Chinese land was shrouded in the smoke of war^[14]. In the 15th year of the Republic of China (1926), due to the influence of the Northern Expedition, all the American staff of Yide Hospital returned to the United States, further reducing the number of doctors^[8]. In Guannan County, in the 28th year of the Republic of China (1939), the Japanese invaded, and the health care industry was severely damaged. The masses were short of medical care and medicine, and suffered greatly^[15]. In the summer and autumn of the 27th year of the Republic of China (1938), Donghai County Hospital was bombed by Japanese aircraft and had to be relocated to the Longhai Hospital outside the north gate of Haizhou, where more than ten thatched sheds were built to continue providing medical services. Later, in the spring of the 28th year of the Republic of China (1939), after the

Japanese army occupied Haizhou, the hospital was moved to the countryside and was dissolved at the end of the year ^[8]. In April of the 27th year of the Republic of China (1938), more than 20 shops of Tiancheng Pharmacy were bombed by Japanese aircraft and destroyed. Later, Dasheng Pharmacy in Guanyun was also bombed. During the period of Japanese puppet rule, Japanese merchants opened three pharmacies, namely, Yamazaki, Matsuo, and Ishii Public relief places, in Xinpu, selling a large amount of Japanese goods and severely damaging the local Chinese pharmaceutical business ^[4].

However, this did not mean that people had easier access to medicine. The “Lianyungang City Chronicles” clearly states: “The health measures during the period of Japanese puppet rule were for the prevention and treatment of diseases for the Japanese imperialists. The vast majority of poor people still suffered from many disasters” ^[4]. It can be said that “poverty, disease, and war put the people in a dire situation” ^[13]. Yiling Hospital was originally a relatively large private hospital in the Donghai, Ganyu, Shuyang, and Guanyun areas with strong technical forces and complete medical equipment, and had a considerable influence in the Haizhou region. However, according to the recollection of Liu Yilin’s son Liu Zeng, “In 1938, when Japanese aircraft bombed Xinpu and other towns, the family fled to the countryside. The hospital was bombed by Japanese aircraft, and all the medical equipment was lost. The hospital was forced to dissolve” ^[13]. The war dealt another heavy blow to the already scarce medical resources, which had a very adverse impact on the prevention and control of communicable diseases in the Lianyungang area.

5. Conclusion

During the period of the Republic of China, the Lianyungang area had poor sanitary conditions, frequent natural disasters, as well as a lagging awareness of health prevention and the destruction caused by war. These factors led to the occurrence and spread of communicable diseases to a certain extent, causing many adverse effects on people’s health. In fact, many of the communicable disease prevention measures taken by the Nationalist Government were very limited and often superficial and formalistic. Looking at the long-term perspective of history, the causes of the prevalence of communicable diseases in the Lianyungang area during the period of the Republic of China have strong commonality and similarity, which still have guiding and reference significance for the current prevention and control of communicable diseases.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Li L, 2024, Infectious Diseases (Tenth Edition). People’s Medical Publishing House, Beijing.
- [2] Li W, 2004, Historical Records of Infectious Diseases in China. Chemical Industry Press, Beijing.
- [3] Nanjing Local Chronicles Compilation Committee, 1996, Nanjing City Health Chronicles (Volume 1). Local History Publishing House, Beijing.
- [4] Lianyungang City Local Chronicles Compilation Committee, 2000, Lianyungang City Chronicles. Local History Publishing House, Beijing.
- [5] Guanyun County Local Chronicles Compilation Committee, 1999, Guanyun County Chronicles. Local History Publishing House, Beijing.
- [6] Ganyu County Local Chronicles Compilation Committee, 1997, Ganyu County Chronicles. Zhonghua Book Company, Beijing.
- [7] Haizhou District Local Chronicles Compilation Committee, 1999, Haizhou District Chronicles. Local History Publishing

House, Beijing.

- [8] Lianyungang City Health Chronicles Compilation Committee, 1998, Lianyungang City Health Chronicles. Local History Publishing House, Beijing.
- [9] Donghai County Local Chronicles Compilation Committee, 1994, Donghai County Chronicles. Zhonghua Book Company, Beijing.
- [10] Lianyun District Local Chronicles Compilation Committee, 1995, Lianyun District Chronicles. Local History Publishing House, Beijing.
- [11] Zhang T, 2008, Infection and Society in the Republic of China: Centered on Infectious Disease Prevention and Public Health Construction. Social Sciences Literature Publishing House, Beijing.
- [12] Kang H, 2019, Communicable Diseases in the Jiangsu-Shanghai Region during the Republic of China Era: Distribution, Factors, Responses and Impacts, thesis, Huazhong Normal University, Wuhan.
- [13] Jiangsu Cultural and Historical Materials Compilation Committee, 1995, A Famous Doctor Liu Yilin. Editorial Department of Jiangsu Cultural and Historical Materials, Nanjing.
- [14] Meng Z, 1999, The History of Natural Disasters in China. China Social Publishing House, Beijing.
- [15] Guannan County Local Chronicles Compilation Committee, 1995, Guannan County Chronicles. Jiangsu Ancient Books Publishing House, Nanjing.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Effect of Comprehensive Intervention Measures of Education Rehabilitation Monitoring on Patients with Chronic Obstructive Pulmonary Disease

Pingping Tang, Gang Cao*

Hongze District People's Hospital of Huaian City, Huai'an 223100, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Objective: This study aimed to explore the impact of a comprehensive intervention system, integrating structured education, stepwise pulmonary rehabilitation, digital monitoring, and multidisciplinary follow-up within a “hospital-community-family” tri-level framework, on the prognosis of COPD patients. Methods: A prospective randomized controlled trial was conducted with 200 COPD patients diagnosed through grassroots screening in Hongze District from January to December 2021. Participants were randomly assigned to an observation group (comprehensive intervention) or a control group (routine treatment) for a 12-month follow-up. Outcomes, including pulmonary function indices (FEV1, FVC, FEV1/FVC), mMRC dyspnea scores, 6-minute walking distance (6MWD), and 1-year readmission rates, were compared. Results: The observation group demonstrated a 97% improvement in FEV1 (vs. 45% in controls), a 57.7% reduction in mMRC scores (vs. 29.2%), a 51.5% increase in 6MWD (vs. 19.0%), and a 47.4% lower readmission rate ($p = 0.049$). Conclusion: The closed-loop management mechanism of education-rehabilitation-monitoring significantly improved pulmonary function, exercise tolerance, and dyspnea severity while reducing readmission risks in COPD patients. The intervention exhibited cumulative efficacy over time, highlighting its critical clinical application value for community-based COPD management.

Keywords: Chronic obstructive pulmonary disease; Pulmonary rehabilitation; Patient education; Exercise tolerance; Readmission rate.

Online publication: September 26, 2025

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in the world. Its morbidity, disability rate, and socio-economic burden are rising year by year. According to the statistics of the GOLD 2023 guidelines, the global prevalence of COPD in people over the age of 40 is as high as 11.7%. The epidemiological survey in China shows that the prevalence of COPD in people over the age of 40 is 13.7%, and the annual rehospitalization rate caused by acute exacerbation is more than 20%, which constitutes a major public health challenge^[1-3]. Although standardized drug therapy can delay the progression of the disease, problems such as progressive decline of lung function, limited exercise tolerance, and repeated acute exacerbations are still widespread. How to improve the long-term prognosis through systematic

intervention has become a clinical problem to be solved.

Based on the “hospital community family” three-level linkage framework, this study innovatively designed a comprehensive intervention program including structured education, step-by-step lung rehabilitation, digital monitoring, and multidisciplinary team follow-up. Through prospective randomized controlled trials, the long-term effects of this model on pulmonary function, exercise tolerance and rehospitalization rate of COPD patients were systematically evaluated, focusing on the dynamic evolution of the intervention effect and its mechanism, to provide evidence-based basis for the standardized management of COPD at the grass-roots level, and explore the practical path of cost-benefit optimization for the reform of medical insurance payment.

2. Object and method

2.1. Research object

A prospective randomized controlled design was used in this study. 200 patients with COPD diagnosed by screening in primary medical institutions in the Hongze District of Huai'an City from January 2021 to December 2021 were included. The inclusion criteria were: (1) They met the GOLD 2021 diagnostic criteria and were in a stable stage (no acute exacerbation in the recent 4 weeks); (2) Age 40–75 years old; (3) Gold grade II–III; (4) Have basic reading and writing skills and can cooperate with follow-up. Exclusion criteria: (1) Complicated with severe cardiovascular and cerebrovascular diseases (NYHA cardiac function grade III–IV, recent 6-month history of myocardial infarction); (2) The existence of motor system diseases affects rehabilitation training; (3) Combined with malignant tumor or cognitive impairment; (4) Participated in other clinical trials in THE recent 3 months.

The patients were randomly divided into a study group (100 cases) and a control group (100 cases). The baseline data of the two groups were balanced and comparable ($p > 0.05$). The study plan was approved by the ethics committee of our hospital, and all subjects signed the informed consent.

2.2. Intervention methods

The observation group implemented a comprehensive intervention program based on the “three-dimensional linkage” model:

- (1) Structured education: Eight-week courses were designed using the gold guide framework, 90-minute group counseling twice a week, covering disease cognition, inhalation technology, symptom monitoring and emergency treatment, supplemented by multimedia teaching materials and scenario simulation training;
- (2) Stepwise pulmonary rehabilitation: Individualized exercise prescription was formulated according to Borg scale, including abdominal breathing (15 min/time), lip contraction breathing (10 min/time), impedance training (elastic belt load increasing, 30 min/time) and aerobic exercise (power bicycle, target rate = resting heart rate + 20% reserve heart rate), outpatient training 3 times a week + family training 5 times, and the adjustment intensity was evaluated every 3 months;
- (3) Digital monitoring: real-time monitoring of blood oxygen saturation, heart rate and activity through an intelligent bracelet, abnormal data trigger an AI early warning system to automatically push medical orders to doctors and patients;
- (4) Multidisciplinary management: a team composed of respiratory physicians (making plans), rehabilitation therapists (exercise supervision), nutritionists (making high protein diet plans) and psychologists (once a month cognitive behavioral intervention) will implement monthly joint follow-up.

The control group received routine outpatient follow-up management treatment and telephone follow-up management every 3 months.

2.3. Observation indexes

- (1) Lung function indexes: FVC, FEV₁ and FEV₁/FVC were measured by Jaeger Masterscreen lung function instrument, and the calibration was in line with ATS/ERS standard, and were detected at baseline, 3, 6, 9 and 12 months;

- (2) Symptom assessment: The modified British MRC Dyspnea Scale (MMRC) was used to assess the degree of dyspnea, with a score of 0–4, and the reliability and validity of Cronbach's $\alpha = 0.89$;
- (3) Exercise endurance: Carry out a 6-minute walking test (6MWD) according to ATS guidelines, record walking distance and Borg fatigue score, and control the test ambient temperature at 22 ± 2 °C;
- (4) Clinical outcomes: The number of rehospitalizations due to acute exacerbation (requiring antibiotics/systemic hormone therapy) within 12 months was counted and cross-validated by the regional health information platform;
- (5) Quality control: Set up an independent data monitoring committee and use the double input system. The missing rate of key indicators is less than 5%.

2.4. Statistical treatment

SPSS 26.0 software was used, and the measurement data were expressed in mean \pm standard deviation (SD). Two-factor repeated measurement analysis of variance was used for comparison between groups, and χ^2 test was used for counting data. $p < 0.05$ was statistically significant.

3. Results

3.1. Pulmonary function

As shown in **Table 1**, two-factor repeated measurement analysis of variance (Bonferroni correction) was used to evaluate the difference in lung function between the two groups before and after intervention. The results showed that:

- (1) FVC improvement trend: FVC in the observation group increased step by step with the intervention time, reaching 2.68 ± 0.31 l at 12 months, 46.4% ($1.83 \rightarrow 2.68$ L) higher than the baseline, which was significantly higher than 22.2% ($1.80 \rightarrow 2.20$ L) in the control group, and the differences between groups continued to be significant from 6 months (all $p < 0.05$);
- (2) FEV₁ change characteristics: FEV₁ in the observation group accelerated to improve after 6 months of intervention, which was 1.51 ± 0.24 l at 12 months, 109.7% ($0.72 \rightarrow 1.51$ L) higher than the baseline, while the control group increased only 45.1% ($0.71 \rightarrow 1.03$ L), the difference between the two groups was statistically significant after 6 months ($p < 0.05$);
- (3) FEV₁/FVC ratio: In the observation group, the ratio reached $56.34 \pm 5.58\%$ at 12 months, increased by 43.2% ($39.34\% \rightarrow 56.34\%$) compared with the baseline, which was significantly better than 18.8% ($39.40\% \rightarrow 46.81\%$) in the control group, and the difference between the groups continued to be significant since 6 months of intervention (all $p < 0.05$). Statistical annotation showed that each index in the observation group showed significant dynamic improvement within the group after 6 months of intervention (compared with the previous time point ▼, $p < 0.05$), while the improvement in the control group tended to stagnate after 9 months ($p > 0.05$).

The above results show that the comprehensive intervention measures have a continuous cumulative effect on the improvement of pulmonary function in patients with chronic obstructive pulmonary disease, and its curative effect is significantly enhanced over time.

Table 1. Comparison of pulmonary function between two groups of COPD patients

Group	Time point	FVC (L, mean \pm SD)	FEV ₁ (L, mean \pm SD)	FEV ₁ /FVC (% , mean \pm SD)
Observation group ($n = 100$)	On admission	1.83 ± 0.33	0.72 ± 0.23	39.34 ± 4.36
	3 months	$2.02 \pm 0.42^{\Delta}$	$0.89 \pm 0.25^{\Delta}$	$44.05 \pm 4.62^{\Delta}$
	6 months	$2.13 \pm 0.36^{*\Delta}$	$1.05 \pm 0.18^{*\Delta}$	$49.29 \pm 4.78^{*\Delta}$
	9 months	$2.39 \pm 0.29^{*\Delta}$	$1.26 \pm 0.16^{*\Delta}$	$52.71 \pm 5.69^{*\Delta}$
	12 months	$2.68 \pm 0.31^{*\Delta}$	$1.51 \pm 0.24^{*\Delta}$	$56.34 \pm 5.58^{*\Delta}$

Table 1 (Continued)

Group	Time point	FVC (L, mean \pm SD)	FEV1 (L, mean \pm SD)	FEV ₁ /FVC (% , mean \pm SD)
Control group (<i>n</i> = 100)	On admission	1.8 \pm 0.41	0.71 \pm 0.19	39.4 \pm 4.51
	3 months	1.91 \pm 0.37 [▲]	0.81 \pm 0.22 [▲]	42.4 \pm 4.92 [▲]
	6 months	2.03 \pm 0.32 [▲]	0.9 \pm 0.26 [▲]	44.33 \pm 5.08 [▲]
	9 months	2.09 \pm 0.43 [▲]	0.95 \pm 0.24 [▲]	45.45 \pm 5.23 [▲]
	12 months	2.2 \pm 0.43 [▲]	1.03 \pm 0.23 [▲]	46.81 \pm 5.49 [▲]

Note: * compared with the control group at the same time point, $p < 0.05$; [▲] comparison of baseline values within the group and at admission $p < 0.05$; Statistical method: Two-factor repeated measurement analysis of variance, Bonferroni correction, the effect quantity is partial η^2 .

3.2. Changes in degree of dyspnea

As shown in **Table 2**, two-factor repeated measurement analysis of variance (Bonferroni correction) was used to evaluate the difference in MMRC scores between the two groups. The results showed that:

- (1) Inter-group differences: The MMRC score of the observation group was significantly lower than that of the control group (6 months: 1.53 ± 0.13 vs 2.12 ± 0.22 , $p < 0.05$); (12 months: 1.15 ± 0.19 vs 1.92 ± 0.18 , $p < 0.05$). The difference increased with the intervention time (Cohen's $d = 1.84$);
- (2) Intra group trend: The score of the observation group showed a continuous downward trend, and each time point was significantly improved compared with the previous period (3 months \rightarrow 6 months: $2.02 \rightarrow 1.53$, $p < 0.05$; 9 months \rightarrow 12 months: $1.32 \rightarrow 1.15$, $p < 0.05$). However, the control group only showed significant changes in the first 6 months (3 months \rightarrow 6 months: $2.34 \rightarrow 2.12$, $p < 0.05$), and the improvement stagnated in the later period (9 months \rightarrow 12 months: $1.98 \rightarrow 1.92$, $p > 0.05$);
- (3) Interaction effect: Group \times time interaction was significant ($f = 35.6$, $p < 0.001$, partial $\eta^2 = 0.31$), suggesting that the intervention measures have a continuous cumulative effect on the improvement of dyspnea. The results showed that comprehensive intervention can significantly accelerate the relief of dyspnea symptoms, and maintain the curative effect advantage in the long-term follow-up.

Table 2. Comparison of mMRC scores between two groups of COPD patients

Group	Time point	mMRC Score
Observation group (<i>n</i> = 100)	On admission	2.72 \pm 0.23
	3 months	2.02 \pm 0.22 [▲]
	6 months	1.53 \pm 0.13 [▲]
	9 months	1.32 \pm 0.15 [▲]
	12 months	1.15(\pm 0.19) [▲]
Control group (<i>n</i> = 100)	On admission	2.71 \pm 0.26
	3 months	2.34 \pm 0.24 [▲]
	6 months	2.12 \pm 0.22 [▲]
	9 months	1.98 \pm 0.19 [▲]
	12 months	1.92 \pm 0.18 [▲]

Note: *Compared with the control group at the same time point, $p < 0.05$; [▲] comparison of baseline values within the group and at admission $p < 0.05$; Statistical method: Two-factor repeated measurement analysis of variance, Bonferroni correction, the effect quantity is partial η^2 .

3.3. Changes in sports endurance improvement

As shown in **Table 3**, the difference in exercise tolerance between the two groups was evaluated by two-factor repeated measurement analysis of variance (Bonferroni correction). The results showed that:

- (1) Inter group differences: 6MWD in the observation group was significantly higher than that in the control group from the 6th month of intervention (6 months: 323.35 ± 42.67 m vs 287.42 ± 36.25 m, $p < 0.05$; 12 months: 382.02 ± 52.36 m vs 301.17 ± 49.52 m, $p < 0.05$), and the difference between groups increased with time (cohen's $d = 1.63$);
- (2) Intra group trend: The observation group showed a continuous ladder improvement, which was significantly improved at each time point (3 \rightarrow 6 months: $+38.08$ m, $p < 0.05$; 9 \rightarrow 12 months: $+19.81$ m, $p < 0.05$), while the control group improved and stagnated after 6 months (6 \rightarrow 9 months: $+1.60$ m, $p > 0.05$);
- (3) Interaction effect: Group \times time interaction is significant ($f = 28.9$, $p < 0.001$, partial $\eta^2 = 0.27$), suggesting that the intervention measures have a time-cumulative effect on the improvement of exercise endurance. There was no significant difference in 6MWD between the two groups at baseline (252.18 ± 35.38 m in the observation group vs 253.02 ± 30.82 m in the control group, $p > 0.05$).

The results showed that comprehensive intervention could significantly improve the exercise tolerance of patients with COPD, and the long-term effect was better than that of conventional treatment.

Table 3. Comparison of 6-Minute Walk Distance (6MWD) between two groups of COPD patients

Group	Time point	6MWD (m, mean \pm SD)
Observation group ($n = 100$)	On admission	252.18 ± 35.38
	3 months	$285.27 \pm 39.50^{\Delta}$
	6 months	$323.35 \pm 42.67^{*\Delta}$
	9 months	$362.21 \pm 49.49^{*\Delta}$
	12 months	$382.02 \pm 52.36^{*\Delta}$
Control group ($n = 100$)	On admission	253.02 ± 30.82
	3 months	$265.21 \pm 33.36^{\Delta}$
	6 months	$287.42 \pm 36.25^{\Delta}$
	9 months	$289.02 \pm 38.61^{\Delta}$
	12 months	$301.17 \pm 49.52^{\Delta}$

Note: *Compared with the control group at the same time point, $p < 0.05$; $^{\Delta}$ comparison of baseline values within the group and at admission $p < 0.05$; Statistical method: Two-factor repeated measurement analysis of variance, Bonferroni correction, the effect quantity is partial η^2 .

3.4. Comparison of rehospitalization rate

As shown in **Table 4**, the difference in rehospitalization risk between the two groups was evaluated by a chi-square test ($\chi^2 = 3.84$, $p = 0.049$). The results showed that the rehospitalization rate of the observation group was 10%, which was significantly lower than 19% of the control group, and the relative risk (RR) was 0.53 (95% CI: 0.26–1.07), indicating that the intervention measures of the observation group could reduce the rehospitalization risk by 47%; The difference in risk (RD) was -9% (95% CI: -17.7% to -0.3%), and the number of patients requiring treatment (NNT) was 12, that is, one rehospitalization event could be prevented for each intervention of 12 patients. Although the statistical difference is significant, the relative risk confidence interval contains 1, suggesting that there may be a risk of random error in the results. Stratified analysis showed that the intervention effect was more significant in the subgroups with ≥ 2 basic diseases (RR = 0.41, $p = 0.016$). The results showed that comprehensive intervention can effectively reduce the risk of rehospitalization in patients with COPD, but its long-term stability needs to be further verified by expanding the sample size.

Table 4. Comparison of rehospitalization rate within one year between the two groups of COPD patients

Group	Rehospitalization within one year	Rehospitalization within one year, <i>n</i> (%)	Relative risk (95%CI)	<i>P</i> value
Observation group (<i>n</i> = 100)	10	10%	0.53 (0.26–1.07)	0.049*
Control group (<i>n</i> = 100)	19	19%	1.00 (Reference)	—

Note: *Indicates the difference between the observation group and the control group ($p < 0.05$); Chi square test ($\chi^2 = 3.84$), the effect quantity was calculated as relative risk (RR) and risk difference (RD = -9%); NNT = 12, that is, 1 rehospitalization can be prevented for every 12 patients treated.

4. Discussion

Based on the “Education rehabilitation monitoring” trinity comprehensive intervention system, this study systematically discussed its impact on pulmonary function, symptom relief, exercise tolerance and readmission risk of patients with chronic obstructive pulmonary disease (COPD). The results show that comprehensive intervention measures have significant advantages in improving the prognosis of patients, and their mechanisms and dynamic evolution provide a new perspective for optimizing the management of COPD.

4.1. Analysis of the mechanism of comprehensive intervention

This study breaks through the limitations of traditional single drug therapy through the synergy of structured education, step-by-step lung rehabilitation, digital monitoring and multidisciplinary follow-up. Structured education can significantly enhance treatment compliance by improving the cognitive level and self-management ability of patients, and lay the foundation for the implementation of follow-up rehabilitation measures. Through progressive resistance training and aerobic exercise, the step-by-step pulmonary rehabilitation program effectively promoted the increase of diaphragm thickness and the improvement of contraction efficiency, and then improved lung function indicators (such as FEV₁/FVC ratio increased by 43.2%), which was consistent with the conclusion in previous studies that rehabilitation training improved respiratory muscle function^[4]. By monitoring the vital signs and activity of patients in real time, the digital monitoring system realizes the early warning of symptoms, increases the proportion of intervention before acute exacerbation, and significantly reduces the risk of rehospitalization (reducing by 47%). This result further confirms the importance of remote monitoring in disease management^[5,6]. The synergy of the three forms a management closed loop, which realizes the whole process of intervention from disease cognition to rehabilitation training to real-time monitoring, and effectively improves the long-term prognosis of patients.

4.2. Clinical promotion value of the three-level management mode

The “hospital community family” three-level linkage management model constructed in this study has shown significant clinical benefits in the management of patients with chronic obstructive pulmonary disease (COPD), and has high promotion value. Through the multi-disciplinary team with respiratory therapists as the core, the accessibility of grass-roots rehabilitation services has been significantly improved, and the rehabilitation participation rate of patients has increased from less than 40% to 91%. In addition, through comprehensive intervention measures, this model can prevent 1 rehospitalization event per 12 patients (NNT = 12), showing a good cost-benefit ratio. However, the study also found that the compliance of the telemonitoring technology platform decreased to 72% after 9 months of intervention, suggesting that there are deficiencies in the user adherence design of the current technology platform, which needs to be further optimized to improve the long-term use compliance of patients. In addition, although this study has achieved significant results in the region, its long-term stability and universality still need to be further verified by multicenter randomized controlled trials.

(RCTs). Future research should include more regions and populations, and provide a more evidence-based basis for the reform of medical insurance payment (such as DRG payment) in combination with the evaluation of health economics.

5. Conclusion

To sum up, this study has significantly improved the lung function, dyspnea symptoms, exercise tolerance, and readmission risk of COPD patients by constructing the “Education rehabilitation monitoring” trinity comprehensive intervention system. Its mechanism and dynamic evolution provide a new idea for optimizing the management of COPD, and the three-level linkage management model shows good clinical promotion potential. Future research should further expand the sample size, optimize the technology platform, and combine with the evaluation of health economics to promote the wide application of this model and the reform of medical insurance payment.

About the author

Caogang (November 1981-) male, Han Dynasty, from Lianshui, Jiangsu Province. Title: deputy chief physician. Education: Master degree. Main research interests: chronic obstructive pulmonary disease, bronchial asthma, lung cancer, respiratory intervention.

Funding

Scientific research fund project of Huai'an Health Commission, Jiangsu Province (Project No.: HAWJ202129); Research project of Huai'an Science and Technology Bureau of Jiangsu Province (Project No.: HAB202349).

Disclosure statement

The author declares no conflict of interest.

References

- [1] GOLD Report, 2023, Global Initiative for Chronic Obstructive Lung Disease (GOLD), visited on August 20, 2025, <https://goldcopd.org/2023-gold-report-2/>.
- [2] Wang C, Bai C, Cai H, et al., 2021, Chronic Obstructive Pulmonary Disease Prevention and Treatment Guidelines (2021 Revised). China Journal of Nuclear and Respiratory Science, 44(3): 170–189.
- [3] Vestbo J, 2017, Global Burden of COPD: Systematic Review and Meta-Analysis. Lancet Respiratory Medicine, 5(3): 253–262.
- [4] Celli B, Thomas N, Anderson J, et al., 2004, Effect of Inhaled Corticosteroids on Mortality in Patients with Chronic Obstructive Pulmonary Disease: A Meta-Analysis. JAMA, 291(10): 1091–1097.
- [5] Zwerink M, Brusse-Keizer M, Valk P, et al., 2012, Self-Management Interventions for Adults with Chronic Obstructive Pulmonary Disease: A Systematic Review. Cochrane Database of Systematic Reviews, 12: CD008368.
- [6] American Thoracic Society, 2006, ATS/ERS Task Force on Pulmonary Rehabilitation: An Official Statement of the American Thoracic Society and European Respiratory Society. American Journal of Respiratory and Critical Care Medicine, 173(8): 827–863.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on the Critical Role of Medical Record Front Page Information in Healthcare Statistics

Weihong Wang*

Penglai People's Hospital, Yantai 265600, Shandong, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: As the core component of medical information systems, the medical record front page holds significant value in healthcare quality management, health statistics, and medical insurance payment. This study systematically analyzes the standardized characteristics of medical record front pages and their core functions in raw data collection, diagnostic information processing, and quality assessment, while thoroughly examining current challenges, including information system deficiencies and inadequate data standardization. The research proposes optimization approaches based on intelligent auditing platforms, comprehensive monitoring systems, and big data analytics tools. Findings demonstrate that establishing intelligent management systems, improving standardized training mechanisms, and innovating statistical analysis methods can significantly enhance the data quality of medical record front pages. These improvements will provide reliable data support for healthcare quality enhancement and refined management practices.

Keywords: Healthcare statistics; Medical record front page; Role

Online publication: September 26, 2025

1. Introduction

With the continuous advancement of medical informatization and the comprehensive implementation of DRG payment reform, the importance of medical record front page data quality has become increasingly prominent. As a standardized summary of patient diagnosis and treatment information, the medical record front page serves not only as an objective documentation of clinical processes but also as a fundamental basis for hospital management decisions and health policy formulation. However, current medical record front page management still faces multiple challenges, including inconsistent data quality, insufficient standardization, and lagging analytical applications. In this context, in-depth research on the statistical value of medical record front pages and approaches to quality improvement is of significant importance for promoting continuous medical quality enhancement and optimizing healthcare resource allocation. Through systematic analysis of the functional positioning and practical issues of medical record front pages, this study explores optimization solutions based on intelligent technologies, aiming to provide both theoretical references and practical guidance for improving hospital data governance capabilities. The research focuses on developing smart quality control systems, establishing comprehensive data standards, and implementing advanced analytical methodologies to enhance the reliability

and utility of medical record data.

2. Overview of medical record front pages

The medical record front page serves as the core carrier of healthcare documentation and a critical nexus connecting clinical practice with hospital administration. This standardized document systematically integrates essential patient hospitalization data, encompassing demographic information, diagnostic and therapeutic processes, resource utilization, and clinical outcomes. Through globally adopted classification systems (ICD) and procedural coding standards, it achieves standardized representation and efficient circulation of medical information. Clinically, the front page provides healthcare professionals with a comprehensive overview of patients' medical histories. Its structured data presentation not only ensures continuity of care but also offers reliable evidence for clinical decision-making. Particularly in multidisciplinary collaborative treatment and patient referral processes, standardized medical record information significantly enhances both healthcare safety and service efficiency. From an administrative perspective, the front page fulfills indispensable functions. It constitutes the fundamental data source for hospital quality assessment, service efficiency analysis, and cost accounting. With the implementation of medical insurance payment reforms like DRG, the accuracy of front page data now directly impacts hospital operational performance and insurance reimbursement precision. Currently, front page management is undergoing digital transformation. The widespread adoption of electronic medical record systems has revolutionized data collection methodologies, transitioning from traditional manual entry to an intelligent hybrid model combining automated extraction with manual verification. This evolution not only improves data collection efficiency but also substantially enhances data accuracy, completeness, and timeliness through built-in quality control protocols and logical validation mechanisms. Importantly, front page quality directly influences multiple hospital management domains: in clinical research, standardized data provides reliable samples; in performance evaluation, accurate diagnostic information serves as crucial evidence for quality assessment; in insurance administration, complete coded data forms the foundation for DRG grouping and payment settlement. Consequently, strengthening front page quality management has become an essential component of contemporary hospital operations ^[1].

3. Core statistical value of medical record front page information

3.1. Collection and storage of raw medical data

As the primary carrier of medical data, the statistical value of medical record front pages first manifests in their systematic collection and storage of raw medical data. Using standardized data structures, they comprehensively record key information about patients' entire diagnosis and treatment processes, transforming complex clinical practices into quantifiable, standardized data units through the ICD coding system. This structured data collection approach encompasses both static patient information and dynamic treatment process data, forming complete medical activity trajectories. With EMR systems, medical record front pages achieve real-time linkage with clinical pathways, automatically populating corresponding fields with treatment data to ensure timeliness and accuracy. In terms of storage, centralized database management meets healthcare quality traceability needs while providing foundations for data analysis and research utilization. Through standardized data interfaces, medical record front pages can also seamlessly integrate with external systems such as insurance and public health, further expanding their application value. This standardized data collection and storage mechanism provides reliable support for healthcare quality evaluation, hospital management, and health policy decisions.

3.2. Standardized processing of diagnostic information

The medical record homepage utilizes the International Classification of Diseases (ICD) coding system to transform

natural language descriptions of clinical diagnoses into standardized, structured data units, fundamentally addressing issues of inconsistent terminology and non-standardized expressions in traditional medical documentation. This conversion process not only achieves machine-readability of diagnostic information but, more importantly, establishes a foundation for cross-institutional and cross-regional data comparability. Through the classification rules and exclusion criteria of ICD coding, clinicians are compelled to more rigorously select principal diagnoses and comorbidities, thereby systematically enhancing the accuracy and completeness of diagnostic documentation. Standardized diagnostic coding serves as a bridge connecting clinical practice with data applications, supporting both internal hospital functions such as Diagnosis-Related Groups (DRG) and medical quality assessment, while also providing reliable data sources for regional disease statistical analysis, epidemiological research, and public health decision-making. This structured processing enables the efficient integration of originally fragmented diagnostic information from medical records, creating fundamental conditions for subsequent medical big data analysis, scientific research data mining, and intelligent medical insurance auditing. Consequently, it significantly enhances the utilizable value and transformation efficiency of medical data.

3.3. Foundational basis for healthcare quality evaluation

The treatment process data and clinical outcome indicators contained in the medical record front page provide objective, quantifiable evidence for healthcare quality evaluation. Key metrics recorded on the front page, including length of stay, surgical complications, and discharge outcomes, directly reflect the efficiency and safety levels of medical services. By analyzing temporal trends and inter-institutional variations of these indicators, healthcare organizations can systematically assess service quality and identify potential risk areas and opportunities for improvement. The standardized quality indicators also facilitate benchmarking across institutions, supporting management activities such as hospital accreditation and specialty development ^[2]. Moreover, quality evaluation results derived from front page data can inform clinical practice, creating a virtuous cycle of “data collection-quality evaluation-continuous improvement” that ultimately enhances overall healthcare service quality.

4. Major challenges in the current medical record front page management

4.1. Coexistence of insufficient information system functionality and over-reliance

Current medical record front page management faces contradictions in healthcare informatization. Many institutions' information systems have significant functional deficiencies, with poorly designed data collection modules lacking essential intelligent validation and logical audit functions, undermining basic data quality. Incompatible interfaces and data exchange barriers between systems further compromise information integrity and timeliness. Meanwhile, healthcare professionals exhibit excessive reliance on information systems, mechanically adopting auto-populated content without necessary review and correction. This “system-over-human” approach amplifies system flaws, allowing erroneous data to persist. Some hospitals prioritize system expansion over foundational data quality improvement during informatization, creating disconnects between system capabilities and actual needs. This paradoxical state has become a critical bottleneck in improving medical record front page quality.

4.2. Fragmented data collection and low standardization

Medical record front page management also faces dual challenges of fragmented data collection and inadequate standardization. In practice, front page data often originates from multiple independent systems (e.g., HIS, EMR, laboratory systems), each employing different data standards and collection protocols, causing severe information fragmentation. Clinicians, coders, and medical records administrators work in silos during data collection, lacking unified coordination. Simultaneously, lagging standardization is particularly acute, with some institutions using proprietary data standards inconsistent with international ICD coding systems. Frontline staff exhibit varying levels of understanding and adherence to coding rules, resulting in frequent errors in primary diagnosis selection and coding. This fragmented

collection and lack of standards complicate data integration and undermine the comparability and utility of medical record front page data, posing significant obstacles to healthcare quality evaluation and insurance payment.

4.3. Inadequate implementation of documentation standards and coding accuracy

The core issue in medical record front-page management lies in the significant disconnect between standardized norms and actual operational practices. When completing the front page, clinicians tend to focus more on patients' clinical manifestations and treatment processes while overlooking specific coding requirements. This mismatch between clinical thinking and coding logic frequently leads to inappropriate selection of primary diagnoses and omission of secondary diagnoses. Physicians habitually describe conditions using professional terminology but often fail to accurately align these descriptions with standardized coding systems, subsequently affecting statistical analysis and payment settlements. The coding process itself presents multiple challenges. Due to the inherent complexity of disease classification systems, compounded by the need for professional judgment in handling comorbidities and complications, many coders struggle to precisely apply coding rules. Accuracy rates notably decline when dealing with rare diseases or complex cases. Some healthcare institutions also face staffing shortages, where coders assume multiple roles, compromising work quality. The absence of robust quality control mechanisms exacerbates these issues. Most hospitals conduct only superficial reviews, lacking in-depth verification of coding logic and clinical rationality. Errors often go undetected until after data submission, by which time correction costs have significantly increased. This reactive management approach allows erroneous data to negatively impact critical areas such as insurance claims and medical evaluations. These problems not only compromise data quality at individual institutions but also distort regional and even national-level statistical analyses. When front-page data is used for DRG-based payments, performance evaluations, and other key functions, even minor coding discrepancies can trigger a ripple effect. Therefore, improving standardization compliance and coding accuracy requires a multifaceted approach, enhancing clinical awareness, professional training, and process management, to establish a more comprehensive quality assurance system.

4.4. Significant lag in big data analytics applications

Currently, there is severe underutilization of medical record front page data, with big data analytics applications significantly lagging behind information system development. Most healthcare institutions remain at basic data collection and report generation stages, failing to establish effective data analysis models and decision support systems. Massive amounts of front-page data are simply accumulated without professional cleaning, integration, or mining processes, leaving potential value largely untapped. Analytically, there's an overemphasis on descriptive statistics over predictive analysis, making it difficult to provide forward-looking evidence for management decisions. Additionally, shortages in data analysis talent, outdated technical capabilities, and poor interdepartmental coordination constrain deep data exploration. This analytical lag prevents medical record front pages from fulfilling their supporting role in clinical research, precision management, and medical resource allocation, resulting in severe waste of valuable data resources^[3].

5. Systematic optimization pathways for medical record front page quality improvement

5.1. Construction of intelligent auditing and centralized management platforms

The key to improvement lies in building intelligent auditing and centralized management platforms. Adopting microservices architecture, these platforms seamlessly interface with various hospital information systems through standardized APIs for real-time data collection and sharing. The platform core comprises three modules: an intelligent coding system using NLP to automatically convert diagnostic text into codes; a rules-based validation engine with comprehensive quality control standards; and a visual monitoring center with quality analysis dashboards. Integrating technologies like OCR and speech-to-text, the platform automates multi-source data collection. Through a "collection-

audit-feedback” closed-loop mechanism, it significantly enhances data quality for management decisions. This centralized, intelligent model improves efficiency while ensuring data accuracy and standardization, laying solid foundations for DRG payment and quality evaluation.

5.2. Comprehensive process monitoring and standardized training systems

Establishing full-process quality monitoring requires coordinated process control and personnel training. For process control, implement a three-tier “prevention-control-evaluation” network featuring embedded EMR validation, dual-person coding verification, and final quality assessment. For training, differentiate programs by role: clinicians focus on primary diagnosis selection standards; coders emphasize ICD rules and DRG principles; administrators concentrate on data analysis. Adopt blended “theory-simulation-case analysis” models with training-assessment-application mechanisms linked to performance evaluations. This dual approach of standardized processes and professional training comprehensively enhances data quality.

5.3. Development and application of big data analytics tools

Developing big data tools based on front-page data is crucial for quality management effectiveness. Build specialized analysis platforms integrating multi-dimensional data for deep mining of quality, cost, and efficiency indicators. Platforms should feature intelligent data cleaning, standardization, and outlier detection to ensure analytical reliability. Incorporate both descriptive statistics and advanced techniques like predictive modeling, emphasizing practical modules like surgical complication warning models. Design user-friendly visual interfaces supporting multi-dimensional data drilling and dynamic reporting. Establish feedback mechanisms to transform insights into improvement measures, forming a “collection-analysis-decision-evaluation” closed loop ^[4]. This data-driven approach strongly supports hospital precision management for continuous service quality and operational efficiency improvement.

5.4. Innovative practices in intelligent statistical models

Intelligent statistical analysis requires breaking traditional models to establish next-generation platforms integrating AI technologies like machine learning and NLP for three breakthroughs:

- (1) Intelligent coding assistance systems with medical coding knowledge graphs for real-time prompts;
- (2) Innovative analytical methods using text mining for unstructured diagnoses and spatiotemporal models for disease patterns;
- (3) Intelligent warning mechanisms with anomaly detection algorithms.

Featuring modular designs with complete preprocessing-analysis-visualization workflows, these platforms support self-service analysis needs while establishing cross-institutional data collaboration. Incorporating deep learning to automatically identify data characteristics and optimize models significantly improves analysis efficiency and accuracy. This intelligent approach transforms manual statistics from simple aggregation to deep value mining, providing precise support for quality management and clinical decisions, ultimately driving digital and intelligent hospital management transformation.

6. Conclusion

Standardized management and in-depth application of medical record front page information are crucial levers for healthcare quality improvement. This study systematically examines front pages’ core values and management challenges, proposing intelligent solutions for data quality enhancement. As AI technologies and healthcare big data analytics advance, medical record front pages will play increasingly vital roles in clinical decision support, quality supervision, and health policy formulation. Healthcare institutions should prioritize front page quality management, continuously enhancing data value through technological innovation and process optimization to achieve dual improvements in service quality and

operational efficiency.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wang H, Hou M, Yin J, 2022, Analysis of Deficiencies in Medical Record Front Page Documentation and Improvement Measures. *China Medical Engineering*, 30(10): 69–72.
- [2] Li W, 2019, Exploring the Important Role of Medical Record Front Page Information in Healthcare Statistics. *Office Operations*, 2019(14): 85.
- [3] Zhao X, 2019, Research on Strategies to Improve the Quality of Medical Statistical Data. *Inner Mongolia Statistics*, 2019(1): 59–60.
- [4] Yang H, 2017, Study on Hospital Medical Record Statistics and Quality of Medical Record Front Page Documentation. *Times Finance*, 2017(21): 259.

Publisher's note

Whoice Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on the Supply-Demand Matching Path for Personalized Smart Healthy Aging Services in Dalian under the Context of Integrated Medical and Elderly Care

Yin Cong*

School of Management, Liaoning University of International Business and Economics, Dalian 116000, Liaoning, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Background: The aging process of China's population continues to intensify. Changes in family structures have rendered traditional elderly care models unsustainable, posing severe challenges to the national social governance system and public service capabilities. Against this backdrop, the national strategy has successively promoted "Integrated Medical and Elderly Care" and "Smart Eldercare," aiming to address the aging crisis through technological innovation and resource integration. Dalian, a coastal city in Northeast China characterized by a high degree of aging and relatively well-developed smart city infrastructure, represents a typical yet urgent case for exploring smart healthy aging solutions. Objective: This study aims to systematically analyze the supply structure of smart healthy aging services in Dalian and the current situation of the diversified, multi-level actual demands of the elderly population. It seeks to precisely identify the core issues of the current supply-demand mismatch and, based on this, construct a systematic implementation path and countermeasure framework to achieve precise supply-demand matching. Methods: This research comprehensively utilizes literature review and policy text analysis to analyze the macro background and local practices. Through theoretical deduction and typical case analysis, it defines the demand characteristics of the elderly population and the supply bottlenecks of services. Finally, it employs systems thinking methods for logical reasoning and theoretical model construction. Conclusion: This study is expected to conclude that the supply-demand mismatch in Dalian's smart healthy aging services is mainly manifested across three dimensions: content, technology, and information. The key to achieving precise matching lies in shifting from a "technology-driven" to a "demand-driven" approach, constructing a multi-level, multi-stakeholder collaborative path model centered on "Precise Identification - Precise Linking - Precise Provision - Precise Governance." This model can provide theoretical reference and practical action guidelines for Dalian and similar cities to optimize their smart eldercare service systems and enhance service efficacy.

Keywords: Dalian City; Integrated Medical and Elderly Care; Personalized Services; Smart Healthy Aging; Supply-Demand Matching

Online publication: September 26, 2025

1. Introduction

China's elderly population continues to grow, with trends towards advanced age and functional disability becoming increasingly pronounced, placing higher demands on the quality and structure of elderly care services. "Integrated Medical and Elderly Care," an innovative model integrating medical and elderly care resources, has become a crucial national strategy for addressing population aging. Concurrently, smart eldercare, leveraging information technologies such as the

Internet of Things (IoT), big data, and artificial intelligence (AI), provides technical support for intelligent and personalized elderly care services.

However, in practical implementation, a widespread mismatch persists between the supply of smart healthy aging services and the actual needs of the elderly. Dalian, as one of the cities entering population aging earlier, possesses a certain foundation in smart city construction. Nevertheless, its development of smart healthy aging faces challenges such as fragmented services, data silos, and insufficient age-friendly design. Therefore, systematically analyzing the supply and demand status of smart healthy aging services in Dalian and exploring its precise matching path holds significant theoretical value and can provide a replicable practical paradigm for similar cities.

2. Core concepts and theoretical foundation

2.1. Conceptual definitions

Integrated medical and elderly care refers to the provision of continuous, seamlessly integrated care services for the elderly by breaking down resource barriers between medical treatment and elderly care through institutional mechanism innovation and service integration ^[1].

Smart healthy aging involves the application of new-generation information technologies, such as the IoT, big data, and AI, to achieve the intelligent allocation of elderly care resources, precise management of service delivery processes, and efficient response to the needs of the elderly ^[2-3].

Personalized services emphasizes a shift from standardized, large-scale service provision towards individualized and customized service models. Its core lies in the precise identification of needs, accurate provision of services, and targeted allocation of resources.

2.2. Theoretical foundation

Precision governance theory emphasizes the use of informatization means to achieve fine-grained identification of governance objectives, precise allocation of resources, and accurate assessment of performance. It provides the core analytical framework for this study ^[4].

Collaborative governance theory posits that collaboration among multiple stakeholders—including the government, market entities, social organizations, communities, and families—is necessary to jointly enhance the suitability and effectiveness of public services. This theory is particularly applicable to cross-sectoral, multi-stakeholder service systems like smart healthy aging ^[5].

3. Current status and mismatch of supply and demand for smart healthy aging services in Dalian

3.1. Supply status

Currently, the supply of smart healthy aging services in Dalian presents a pattern of “diversified yet fragmented.” For instance:

- (1) Supply entities are diverse but lack coordination. The government is the leading promoter, driving development through policy guidance and project procurement; some technology companies provide products and technical solutions; elderly care institutions attempt to apply smart tools to improve efficiency. However, these parties fail to form an effective synergy, operating in a state of “working in silos” with low resource integration;
- (2) Products and services are nascent but often “supply does not meet demand.” Market supply predominantly consists of basic safety alert devices like smart bracelets and one-button callers, suffering from severe product homogenization and widespread issues such as complex user interfaces and lack of age-friendly design. Integrated

“smart medical-elderly care” service products that deeply combine daily elderly care with medical health (e.g., chronic disease management, rehabilitation training, remote diagnosis and treatment) are particularly scarce;

- (3) Platforms are initially established but plagued by “data silos.” Although a municipal-level elderly service information platform has been established, it lacks interoperability and operational synergy with the resident health records of the health department, settlement data from the medical insurance system, and household registration information. Stringent data barriers prevent the platform from achieving comprehensive perception and intelligent analysis of elderly needs, thus failing to support truly “personalized” services.

3.2. Demand status

The demand for smart healthy aging among the elderly population is not monolithic but exhibits significant multi-level and differentiated characteristics ^[6]. According to Maslow’s hierarchy of needs, the core demands of the elderly vary considerably based on health status, economic income, educational background, and family structure. For instance, disabled and semi-disabled elderly have urgent demands for medical nursing and long-term care, while healthy and active seniors pay more attention to spiritual and cultural life, social participation, and convenient daily services.

Generally, the demand for “medical” aspects is a core concern, encompassing chronic disease management, emergency rescue, rehabilitation guidance, medication reminders, remote consultations, etc. Simultaneously, significant divergence and a digital divide exist in the elderly population’s attitude towards “smart” technology. Most older adults do not reject technology but require solutions that are “usable, easy-to-use, and useful,” disliking cumbersome, flashy products focused on “tech for tech’s sake.” The ease of use and practicality of technology are key determinants of its acceptance.

3.3. Specific manifestations of supply-demand mismatch

Based on the above supply-demand analysis, the current mismatch manifests specifically as:

- (1) Content mismatch, where supply focuses on basic daily care and safety monitoring (“care”), relatively neglecting the elderly’s most pressing medical and health needs (“medical”); emphasis is placed on hardware deployment over soft service support and humanistic care;
- (2) Technology mismatch, where the complexity of smart product technology does not match the generally low technological acceptance and operational proficiency of the elderly, leading to the abandonment of many devices;
- (3) Information mismatch as the elderly and their families are unaware of available, reliable services; service providers cannot accurately and dynamically grasp the real, personalized needs of each elderly individual. A significant information asymmetry exists between supply and demand, lacking an efficient and trustworthy linking and matching mechanism ^[7].

4. Path construction for precise supply-demand matching

4.1. Matching objective

The ultimate goal of precise supply-demand matching is to remove the blockages between the “demand side” and the “supply side,” optimize the allocation of service resources, and ultimately enhance the accessibility of elderly care services, the sense of fulfillment and satisfaction of the elderly, and the efficiency of overall social resource utilization.

4.2. Core pathways

The core pathways are as listed below:

- (1) Demand-oriented precise identification path by establishing a unified municipal comprehensive assessment standard system for elderly functional ability and needs, serving as the scientific basis for service allocation and subsidy distribution, and utilizing and strengthening existing community grid management resources, combined

with feedback channels such as online APPs and hotlines, to form a dynamic demand assessment and updating mechanism integrating “online + offline,” constructing a detailed and dynamic database of elderly needs;

- (2) Data-centric precise linking path, where the key lies in breaking down data silos and constructing a city-level big data center for smart healthy aging. Under the premise of ensuring data security and privacy protection, promote data sharing and operational synergy among government departments such as Civil Affairs, Health, Medical Insurance, and Public Security. Based on this, build a comprehensive service platform integrating demand declaration, intelligent matching, service delivery, and quality evaluation, achieving a “one-click” and “intelligent” link between demand and supply;
- (3) Integrated medical-elderly care characterized precise provision path by guiding and incentivizing the market towards product and service innovation, focusing on developing integrated smart medical-elderly care products and service packages that combine prevention, monitoring, alerting, and intervention, while cultivating and promoting demonstration projects for “Smart Medical-Elderly Care Consortiums,” supporting elderly care institutions in establishing close cooperation with medical institutions and community health service centers. Moreover, technologies like 5G and IoT could also be leveraged to provide closed-loop services from online health consultations and chronic disease management to offline home nursing and referral medical care, achieving seamless connection between “medical,” “care,” and “nursing”;
- (4) Multi-stakeholder collaboration guaranteed precise governance path by clarifying the roles and responsibilities of the four main stakeholders: government, market, community, and family. The government needs to fulfill the roles of standard-setter, market regulator, service purchaser, and ultimate guarantor, creating a fair and standardized policy environment. The market (enterprises) should provide professional, diversified, and high-quality products and services, with continuous iteration and optimization. The community, as the last-mile implementation hub, needs to undertake responsibilities such as promotion, technical training, assisted operation, and feedback collection, effectively bridging the digital divide. Family members should actively participate in the service selection and supervision process and maintain interaction with the service system.

5. Conclusion and outlook

5.1. Research conclusions

This study conducted a systematic analysis of the supply-demand matching issues concerning smart healthy aging services in Dalian within the context of integrated medical and elderly care. It aimed to identify the main types of mismatches and their underlying causes within the current service system and, based on this, propose a pathway model for achieving precise matching. The findings indicate that while Dalian has made certain achievements in constructing smart eldercare, practical challenges persist, including a disconnect between the supplied content and genuine demand, a misalignment between technology application and the acceptance capabilities of the elderly, and data silos hindering resource integration. The root cause lies in the current service supply still being predominantly characterized by a “technology-driven” approach, failing to adequately embody a “demand-led” development philosophy^[8].

The key to transitioning from “extensive supply” to “personalized services” is the construction of a multi-level, multi-stakeholder, whole-process collaborative matching mechanism. This mechanism should encompass four core components:

- (1) Establishing a scientific and unified needs assessment system to achieve precise identification of the elderly’s functional status and service requirements;
- (2) Leveraging the municipal smart eldercare platform to break down data barriers between departments such as Civil Affairs, Health, and Medical Insurance, achieving cross-system, cross-level information interconnection and resource sharing;
- (3) Promoting service innovation characterized by the integration of medical and elderly care, focusing on developing smart eldercare products and service packages that combine medical treatment, rehabilitation, nursing, and daily

care functions;

- (4) Improving the multi-stakeholder collaborative governance mechanism by clarifying the roles and responsibilities of the government, enterprises, communities, and families, thereby forming an effective synergy of policy, market, technology, and social support.

In summary, the high-quality development of smart healthy aging relies not only on technological iteration and equipment upgrades but, more importantly, on achieving a dynamic balance between service supply and the real needs of the elderly through institutional innovation, process optimization, and stakeholder collaboration. The four-dimensional pathway model of “Identification - Linking - Provision - Governance” constructed in this study provides theoretical reference and practical guidance for Dalian and similar cities to optimize their smart eldercare service systems.

5.2. Policy recommendations

Based on the above conclusions, this paper proposes the following countermeasures and suggestions to promote the personalized development of smart healthy aging services in Dalian and enhance the level of supply-demand matching.

Top-level design and institutional guarantees should be strengthened to break down data barriers and systemic obstacles. It is recommended that the municipal government establish a special task force for smart healthy aging development, coordinating resources and policies from departments including Civil Affairs, Health, Medical Insurance, and Industry and Information Technology. Formulate the “Dalian Municipal Measures for the Management of Smart Healthy Aging Data Sharing,” clarifying standards and permissions for data collection, updating, exchange, and use, and establish an inter-departmental information sharing mechanism to provide a data foundation for precise services. Other than that, a comprehensive needs assessment system should be established and improved for the elderly. Based on national standards and incorporating local realities such as the income structure, health status, and family support of Dalian’s elderly, develop an assessment tool with local applicability. Promote its linkage with systems like long-term care insurance payments, government procurement service catalogs, and nursing home ratings to guide service resources to be precisely targeted towards those most in need.

The development of integrated “medical-care-rehabilitation-nursing” service models should be encouraged by supporting deep cooperation between medical institutions and elderly care facilities through technical collaboration, talent sharing, and information exchange, focusing on promoting the development of integrated services such as chronic disease management, rehabilitation training, remote diagnosis and treatment, and emergency rescue. This can be achieved by establishing special support funds and creating regional demonstration projects to stimulate innovation among market entities. Smart eldercare accessibility adaptation and digital literacy enhancement programs should be implemented as well through providing training on smart technology applications for the elderly and family caregivers to improve their awareness and ability to use smart eldercare products and services. Simultaneously, encourage enterprises to enhance age-friendly product design, developing intelligent devices and systems with simple interfaces, easy operation, and practical functions to genuinely reduce the technical usage barrier.

A multi-dimensional service supervision and performance evaluation mechanism should be constructed by establishing a comprehensive service quality monitoring system encompassing government evaluation, third-party assessment, and satisfaction surveys of the elderly and their families and regularly assessing the implementation effectiveness of smart eldercare services and use the results as a critical basis for policy adjustment and financial investment, forming a management closed loop for continuous service quality optimization.

5.3. Research limitations and future prospects

This study, primarily based on literature analysis, policy interpretation, and theoretical deduction, preliminarily constructs a pathway model for supply-demand matching in smart healthy aging. However, it possesses certain limitations. The research methodology is predominantly qualitative. While striving for comprehensiveness, it still lacks support from large-scale questionnaire surveys and empirical data; the proposed pathway model has not been fully tested in practice.

Moreover, the discussion on the multi-stakeholder collaboration mechanism remains somewhat theoretical, lacking in-depth exploration of the underlying mechanisms such as interest coordination, responsibility distribution, and collaborative motivation among different stakeholders.

Future research could be deepened in the following aspects:

- (1) Validating and refining the proposed matching pathways through broader field investigations and quantitative analysis, particularly employing empirical methods like Structural Equation Modeling (SEM) and Social Network Analysis (SNA) to examine the action mechanisms and path relationships of various influencing factors;
- (2) Conducting case tracking and action research in selected typical communities or elderly care institutions in Dalian to summarize the implementation models and operational experiences of smart eldercare services from a practical perspective;
- (3) Combining comparative studies with experiences from advanced domestic and international cities to further explore potential pathways and development trends in institutional design, technological integration, and governance innovation for smart healthy aging, thereby enhancing the scientific rigor and generalizability of the research.

In conclusion, as China's population aging continues to deepen and digital technology constantly innovates, research in the field of smart healthy aging still holds broad development prospects. It is hoped that the preliminary exploration of this study can provide a useful reference for subsequent academic discussion and policy practice.

Funding

University Level Scientific Research Project of Liaoning University of International Business and Economics "Study on the Precision Application Countermeasures of Dalian's Smart Health and Elderly Care Services Under the Background of the Integration of Medical and Elderly Care Services" (Project No.: 2023XJLXYB18)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Huang J, Meng F, 2014, The Necessity, Predicaments, and Countermeasures of the "Integration of Medical Care and Elderly Care" Model for the Aged. *Chinese Journal of Health Policy*, 7(6): 63–68.
- [2] Liao X, Li Y, Li Y, 2019, Research on the Optimization Path of Smart Elderly Care Industry Based on Industrial Chain Integration Theory. *China Soft Science*, 2019(4): 50–56.
- [3] Li C, Bi X, 2018, Research on the Construction of Smart Elderly Care Service System and Platform. *E-Government*, 2018(6): 105–113.
- [4] Wang Y, Li B, Zuo T, 2016, The Theoretical Orientation and Practical Logic of Targeted Poverty Alleviation: From the Perspective of Precision Social Theory. *Guizhou Social Sciences*, 2016(5): 156–161.
- [5] Li H, 2014, Analysis of Collaborative Governance Theory. *Theory Monthly*, 2014(1): 138–142.
- [6] Mu G, Reflections on China's Aging Policies. *Population Research*, 2002(1): 43–48.
- [7] Li J, Ji W, Qian C, 2022, Deep Aging of China's Population and the Development Trend of Elderly Care Service Needs. *Reform*, 2022(2): 1–21.
- [8] Shi W, Jing L, Liu Z., et al., 2022, Challenges and Countermeasures of Population Aging to the Medical Service System.

Health Economics Research, 39(7): 18–20.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Diabetes with Viral Pneumonia: Epidemiological Characteristics, Pathophysiological Mechanisms, and Clinical Management Strategies

Zhengmei Qian, Xiaoxuan Chen, Ruilin Sun*

The Affiliated Guangdong Second Provincial General Hospital of Jinan University, Guangzhou 510317, Guangdong, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Diabetes is one of the susceptibility risk factors for viral pneumonia, particularly during COVID-19 pandemic. Patients with diabetes are more likely to develop severe disease following infection and face a markedly increased risk of complications, substantially increasing the healthcare burden. The primary mechanism involves persistent hyperglycemia impairing immune system function through multiple pathways, promoting excessive inflammatory responses, and thereby exacerbating lung tissue damage. Research indicates that effective glycemic control and vaccination can substantially reduce mortality rates and the risk of severe disease progression in diabetic patients with viral pneumonia. This review aims to summarize the clinical associations, immunopathological mechanisms, and prevention strategies related to diabetes and viral pneumonia, providing a theoretical basis for improving patient outcomes.

Keywords: COVID-19; Diabetes; Influenza virus; Pneumonia

Online publication: September 26, 2025

1. Background

Data from the Global Burden of Disease study indicate that diabetes and lower respiratory infections are both major threats to human health. In 2019, diabetes ranked as the eighth leading cause of death globally, while lower respiratory infections ranked fourth. With the outbreak of the COVID-19 pandemic, coronavirus infections surged to become the second leading cause of death worldwide in 2021 ^[1].

Diabetes, a group of chronic metabolic disorders caused by the combined effects of genetic, environmental, and lifestyle factors, is characterized by persistent hyperglycemia resulting from impaired insulin secretion or action. Individuals with diabetes constitute a high-risk population for respiratory viral infections, exhibiting significant synergistic pathogenic effects. This interaction manifests not only as increased susceptibility to infection but also as markedly worsened clinical outcomes, creating a vicious cycle from infection to adverse events.

This review examines the disease burden, epidemiological characteristics, pathophysiological mechanisms, and clinical management strategies for viral pneumonia in diabetic patients. It aims to guide clinicians in early recognition,

precise diagnosis, and timely intervention, thereby reducing mortality in severe cases and alleviating the overall disease burden.

2. Epidemiological characteristics

2.1. Disease burden of diabetes in China

With changes in lifestyle and dietary habits, diabetes has become the third leading factor affecting human health after cardiovascular and cerebrovascular diseases and malignant tumors ^[2]. In 2021, approximately 530 million people worldwide had diabetes. By 2050, this number is projected to more than double, reaching around 1.3 billion people, with a prevalence rate approaching 10%—far exceeding the 6% rate recorded in 2021 ^[3]. In China, approximately 233 million people have diabetes, accounting for about one-quarter of the global diabetic population. More alarmingly, without effective interventions, China's diabetes prevalence is projected to climb to 29.1% by 2050, meaning nearly one-third of the Chinese population will have diabetes ^[4].

This massive patient population imposes a heavy economic burden. Research projects that from 2020 to 2030, diabetes-related healthcare costs in China will increase from \$250.2 billion to \$460.4 billion, while the proportion of total diabetes costs relative to GDP will rise from 1.58% to 1.69%. This indicates that the economic burden of diabetes will grow faster than China's economic growth rate ^[5].

2.2. Susceptibility of diabetes patients to viral pneumonia

Diabetic patients are prone to various infectious diseases due to prolonged hyperglycemia, metabolic disorders, and compromised immune function, with pulmonary infections being a common complication. Relevant studies indicate that pneumonia accounts for 26% of hospitalizations among diabetic patients and constitutes 8% of direct causes of death in advanced diabetes ^[6]. Previous research on diabetes in viral-induced pulmonary infections has been limited.

The 2020 novel coronavirus outbreak highlighted diabetes' significant role in viral infections. Epidemiological evidence indicates that type 2 diabetes is the second most common comorbidity among COVID-19 patients ^[7]. Clinical studies specifically demonstrate that poorly controlled diabetic patients face higher risks of adverse outcomes and mortality after SARS-CoV-2 infection compared to the general COVID-19 population. A Wuhan-based study found that among 1,561 COVID-19 patients enrolled, 153 had diabetes, representing a prevalence of 9.8% ^[8]. The study also revealed that diabetic patients exhibited higher mortality rates following SARS-CoV-2 infection.

3. Pathophysiological mechanisms

3.1. Increased viral susceptibility and impaired host defense barriers

SARS-CoV-2 infects host cells via the angiotensin-converting enzyme 2 (ACE2) receptor. Elevated levels of ACE2 receptors on cell membranes have been observed in diabetic patients, potentially explaining their heightened susceptibility to SARS-CoV-2 infection ^[9,10,11]. Hyperglycemia in diabetic patients elevates glycated hemoglobin (deoxygenated form) levels in red blood cells ^[10,11,12].

The surface protein of SARS-CoV-2 attacks the 1-beta chain of hemoglobin, and deoxyhemoglobin is more vulnerable than oxyhemoglobin, leading to the body not receiving enough oxygen, ultimately resulting in symptoms of respiratory distress. This impairs oxygen delivery to tissues, ultimately leading to respiratory distress. Hyperglycemia also induces structural changes in lung tissue, including partial lung collapse and increased vascular permeability ^[10,11] leading to pulmonary dysfunction. This impaired lung function in diabetic patients further accelerates SARS-CoV-2 viral invasion, exacerbating disease progression.

3.2. Immunological dysfunction

Viruses exploit the enhanced glycolytic pathway in host cells to obtain energy and raw materials for replication. A hyperglycemic environment forces key innate immune cells (such as monocytes, macrophages, and dendritic cells) to undergo metabolic reprogramming, rendering them overly reliant on glycolysis. This leads to multiple mechanisms—including lactate-mediated signaling inhibition, acetylation-related epigenetic disruption, and protein dysfunction caused by lipid peroxidation^[13-15]. These synergistic effects impair innate immune cell functions in pathogen recognition, signal transduction, and antigen presentation, significantly weakening the host's antiviral defenses^[13-17].

Metabolic dysregulation induced by hyperglycemia, particularly lipid peroxidation (LPO) resulting from abnormal lipid metabolism, directly suppresses T cell activation and function, leading to failure of the virus-specific immune response. The core mechanism involves a high-sugar environment triggering reactive oxygen species (ROS) accumulation and polyunsaturated fatty acid (PUFA) buildup within CD4⁺ T cells, initiating a chain reaction of LPO. The active aldehyde compounds produced by LPO (e.g., 4-HNE) carbonylate STAT4, a key transcription factor for Th1 cell differentiation, leading to its ubiquitination and degradation. The loss of STAT4 impairs downstream T-bet expression and drastically reduces IFN- γ production, ultimately causing the complete collapse of the Th1 differentiation program^[17].

Concurrently, high glucose induces acetyl-CoA accumulation and excessive histone acetylation, disrupting antigen presentation by dendritic cells (DCs) and indirectly weakening T cell activation^[15]. These metabolic-immune crosstalk dysregulations collectively cause failure of virus-specific immune responses, delaying viral clearance and exacerbating disease severity in infected individuals.

3.3. Dysfunction of the immune-endocrine regulatory circuit

During the initial phase of severe viral infection, the body initiates a finely tuned “immune-endocrine” regulatory circuit to coordinate systemic metabolism and optimize antiviral defense^[16]. Its core mechanism involves the rapid activation of $\gamma\delta$ T cells residing in tissues such as the lungs and splenic red pulp, which become an important early source of interferon- γ (IFN γ). Systemically released IFN γ strongly stimulates insulin synthesis and secretion by activating IFN γ receptors on pancreatic β -cell surfaces and their downstream JAK-STAT signaling pathways. The abrupt elevation of insulin levels exerts potent hypoglycemic effects: it inhibits hepatic gluconeogenesis and glycogenolysis while promoting glucose uptake and utilization in peripheral tissues, leading to transient physiological hypoglycemia.

This self-induced “glucose restriction” environment provides dual critical protective effects for the host as follows:

- (1) It directly limits the replication of many viruses highly dependent on glycolysis for energy, cutting off their energy and biosynthetic raw material supply;
- (2) It alleviates lactic acid accumulation caused by excessive glycolysis, thereby releasing the inhibition of key innate signaling pathways like interferon regulatory factor 3 (IRF3) and nuclear factor κ B (NF- κ B).

This significantly enhances the production of type I interferons (IFN-I), establishing a more robust systemic antiviral state. However, in diabetic patients—particularly those with type 1 diabetes or advanced type 2 diabetes where β -cell function is nearly depleted—this protective circuitry fails completely. The core defect lies in pancreatic β -cells' inability to respond to IFN γ signals and secrete sufficient insulin. Without insulin—the critical effector molecule—the liver's glucose output remains unchecked. Persistently elevated blood glucose levels prevent the induction of a beneficial “hypoglycemic window.” This not only provides ample fuel for viral replication, leading to substantially increased viral load, but also perpetuates lactate-mediated immunosuppression. Ultimately, this results in impaired IFN-I responses, uncontrolled viral replication, and a heightened susceptibility to severe disease progression.

3.4. Tissue barrier disruption and inflammatory storm

Hyperglycemia directly impairs tissue barrier function through multiple pathways. Persistent hyperglycemia induces “glucotoxicity” in vascular endothelial cells and alveolar epithelial cells, triggering excessive production of mitochondrial reactive oxygen species (mtROS). This leads to cellular DNA damage and apoptosis, subsequently compromising the

integrity of intercellular junctions and basement membranes^[17]. This compromised barrier function facilitates viral invasion and spread while exacerbating tissue edema and inflammatory exudation.

Concurrently, dysfunctional innate immune cells (e.g., alveolar macrophages) undergo severe metabolic-immune dysregulation under hyperglycemic stimulation. They exhibit “glycolytic dominance”, a metabolic reprogramming that drives their differentiation toward a dysfunctional inflammatory phenotype^[13]. Its core characteristics include high production of reactive oxygen species (ROS) and excessive pro-inflammatory cytokines (e.g., IL-6, IL-1 β , TNF- α), yet an inability to effectively initiate critical antiviral programs.

This is primarily due to high glucose/glycolysis-derived lactate accumulation, which directly inhibits the activation of IRF3 and NF- κ B signaling pathways. This leads to severe insufficiency in the production of core antiviral cytokines, including type I interferons (IFN-I) and type III interferons (IFN- λ). This “dysregulated inflammatory response” forms a vicious cycle^[13]. On one hand, excessive ineffective proinflammatory factors recruit more immune cells to the lesion site, triggering a “cytokine storm.” This excessive inflammation causes secondary damage to alveolar epithelium and vascular endothelium, dramatically increasing vascular permeability and leading to massive protein-rich fluid leakage—the classic pathological basis of acute respiratory distress syndrome (ARDS).

On the other hand, the absence of IFN-I fails to effectively suppress viral replication and dissemination within host cells, further exacerbating tissue damage. Ultimately, this immune disorder—incapable of clearing the virus while inflicting severe damage on the body’s own tissues—can rapidly spread from the lungs to the entire body, leading to multiple organ dysfunction syndrome (MODS)^[13].

4. Clinical characteristics and interactions: The bidirectional vicious cycle between diabetes and viral pneumonia

4.1. Diabetes exacerbates the severity of viral pneumonia

Across multiple viral pandemics, diabetes has consistently been identified as a key factor significantly increasing the risk of severe illness and death among patients^[18]. Historical data indicate this association persists across diverse viral infections. During the SARS-CoV-1 outbreak (2002–2003), type 2 diabetes was an independent predictor of acute complications and mortality^[19]. Subsequently, during the 2009 H1N1 influenza pandemic, T2DM patients faced a fourfold higher risk of ICU admission compared to non-diabetic individuals^[20]. In COVID-19, diabetic patients not only face a higher risk of developing severe disease but also exhibit significantly increased mortality rates. Multiple studies have further elucidated the role of diabetes in exacerbating viral infections at both mechanistic and clinical levels.

Lin et al. demonstrated through meta-analysis that age, blood glucose levels, lymphocyte counts, and diabetes are independent risk factors for severe COVID-19, with diabetes carrying the highest risk ratio^[21]. Du et al. used logistic regression analysis to emphasize that the mechanism behind worsening disease in elderly diabetic patients with concurrent infection may be related to lipid metabolism disorders caused by long-term hyperglycemia^[22].

Under the inflammatory storm triggered by COVID-19, this metabolic background makes patients more susceptible to rapid progression to severe or critical illness, significantly increasing mortality risk. Regarding influenza, multiple studies consistently report higher infection-related risks among diabetic patients. Compared to non-diabetic individuals, T2DM patients exhibit significantly higher rates of influenza events requiring medical intervention (1.96% vs. 1.37%, $p < 0.001$). This group also demonstrates higher vaccination and antiviral medication usage rates, indirectly corroborating their recognized high-risk status^[23].

Monitoring of hospitalized patients aged 65 years and older revealed a significantly increased risk of influenza-related hospitalization among diabetic patients (RR = 1.57)^[24]. Furthermore, during the influenza infection period (6 weeks before and after diagnosis), the risk of pneumonia co-occurrence in diabetic patients surged to 7.4 times the baseline level, with a significantly higher gain score for new-onset pneumonia compared to non-diabetic controls (4.76% vs. 3.06%)^[23]. More critically, diabetic patients exhibited markedly elevated risks of ICU admission due to influenza (RR = 1.84), mechanical

ventilation requirement (RR = 1.95), and in-hospital mortality (RR = 1.48), further underscoring diabetes' role in driving influenza severity ^[24].

In summary, whether during coronavirus or influenza outbreaks, diabetes serves as a significant independent risk factor that substantially increases the risk of severe illness, healthcare demands, and mortality among infected individuals. The underlying mechanisms are closely associated with hyperglycemia-mediated metabolic disorders and immune dysregulation.

4.2. Viral pneumonia leads to glucose metabolic disorders

Viral respiratory infections (such as COVID-19) may exacerbate glucose metabolic disorders through inflammatory responses and hormonal changes. Previous observations of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) also indicate that inflammatory cell infiltration can impair hepatic insulin signaling, suppress insulin-mediated glucose uptake, and result in hyperinsulinemia and hyperglycemia ^[25].

Diabetic patients infected with SARS-CoV-2 are more prone to entering a high-stress state, triggering massive release of hyperglycemic hormones (such as glucocorticoids and catecholamines), which in turn causes significant hyperglycemia and abnormal blood glucose variability ^[26]. Multiple clinical studies provide population-based evidence linking viral pneumonia to glucose metabolism abnormalities.

An investigation of 551 hospitalized COVID-19 patients in Italy found that 46% developed elevated blood glucose levels despite no prior history of diabetes; follow-up revealed that 35% of recovered patients still exhibited persistent hyperglycemia six months later ^[27]. Another large-scale study further indicated that COVID-19 patients face approximately a 40% increased risk of developing new-onset diabetes one year post-infection compared to healthy individuals ^[28]. Disease severity positively correlates with diabetes risk: patients requiring hospitalization or intensive care treatment exhibited roughly a threefold elevated risk compared to controls, while even mild cases without hospitalization showed increased susceptibility.

5. Prevention and future outlook

5.1. Vaccination

Vaccination serves as an effective means of preventing viral pneumonia, particularly for high-risk groups prone to complications, such as individuals with diabetes and the elderly. Studies indicate that vaccination reduces the risk of severe influenza cases progressing to pneumonia by approximately 15% ^[29]. Furthermore, another study on respiratory syncytial virus (RSV) demonstrated that during epidemic seasons, vaccination provided protection against RSV-related hospitalizations and severe in-hospital outcomes ^[30]. Specifically, efficacy against acute respiratory failure was 73% (95% CI: 50%–86%), while efficacy against invasive mechanical ventilation or death was 72% (95% CI: 7%–91%).

Further analysis of breakthrough infections with the Delta variant (VOC) suggested that prior vaccination significantly mitigated the severity of pneumonia caused by heterologous SARS-CoV-2 infection and reduced the virus-induced inflammatory response ^[31]. These findings indicate that current vaccination strategies not only help control transmission of known viral strains but may also enhance cross-protection against heterologous SARS-CoV-2 variants, thereby reducing the risk of severe symptoms following infection across the entire population. Consequently, advancing vaccination programs holds positive and far-reaching significance for establishing herd immunity barriers and reducing the burden of severe illness and mortality associated with viral pneumonia.

5.2. Glycemic control

Glycemic control is a critical component of comprehensive treatment for viral pneumonia, helping to reduce infection risk, improve prognosis, minimize complications, and enhance immune responses. Hyperglycemia impairs pulmonary immune function, particularly the antigen-presenting capacity of dendritic cells, leading to weakened immune responses and

increased susceptibility to viral pneumonia^[15]. Controlling blood glucose maintains normal function of pulmonary immune cells, thereby lowering infection risk. Patients with well-controlled blood glucose (fluctuating within 3.9–10.0 mmol/L) exhibit significantly lower mortality rates from viral pneumonia.

For instance, studies on COVID-19 patients with diabetes show mortality rates of only 1.1% among those achieving target glycemic control, compared to 11% in those with poor control^[32]. Hyperglycemia exacerbates inflammatory responses, leading to multi-organ dysfunction. Effective glycemic control helps mitigate inflammation, reduce damage to the lungs and other organs, and promote recovery. Stable blood glucose prevents suppression of immune cell functions, such as lymphocyte activity and phagocyte function. This enhances the body's ability to recognize and eliminate viruses, shortening the disease course^[26,33,34].

5.3. Future outlook

The population of individuals with diabetes complicated by viral pneumonia warrants attention. Future research and management of this condition require establishing a multidimensional prevention and control system spanning molecular mechanisms to public health policies. Epidemiologically, studies must move beyond risk association confirmation to develop dynamic predictive models integrating real-time blood glucose, complications, and immune biomarkers, while elucidating the bidirectional causal relationship between infection and diabetes. Although it is well established that hyperglycemia impairs antigen-presenting function in dendritic cells and causes T-cell cytotoxicity exhaustion, the upstream signaling pathways and cell-specific metabolic mechanisms driving these effects remain unknown.

Further research in this area is needed, with validation in human populations, to address the vulnerability of vulnerable populations—such as individuals with diabetes—to viral infections. Preventive measures should incorporate vaccines and precision glycemic control. Ultimately, interdisciplinary collaboration must accelerate the translation of fundamental discoveries into clinical applications, alongside public health policies ensuring drug and vaccine accessibility. The goal is to significantly reduce related mortality rates and break the vicious cycle linking infection to metabolic disorders.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Naghavi M, Ong K, Aali A, et al., 2024, Global Burden of 288 Causes of Death and Life Expectancy Decomposition in 204 Countries and Territories and 811 Subnational Locations, 1990-2021: A Systematic Analysis for the Global Burden of Disease Study 2021. *Lancet*, 403(10440):2100–2132.
- [2] Li Y, Hao E, Liu J, et al., 2021, Research Progress on Pharmacological Effects of Traditional Medicines in China and ASEAN Countries in Treatment of Diabetes and Its Complications. *Chinese Traditional and Herbal Drugs*, 52(4): 1165–1176.
- [3] Ong K, Stafford L, McLaughlin S, et al., 2023. Global, Regional, and National Burden of Diabetes from 1990 to 2021, with Projections of Prevalence to 2050: A Systematic Analysis for the Global Burden of Disease Study 2021. *Lancet*, 402(10397): 203–234.
- [4] Zhou Y, Liu J, Zhao Z, et al., 2025, The National and Provincial Prevalence and Non-Fatal Burdens of Diabetes in China from 2005 to 2023 with Projections of Prevalence to 2050. *Mil Med Res*, 12(1):28.
- [5] Liu J, Liu M, Chai Z, et al., 2023, Projected Rapid Growth in Diabetes Disease Burden and Economic Burden in China: A Spatio-Temporal Study from 2020 to 2030. *Lancet Reg Health West Pac*, 3(33):100700.

- [6] Qu J, Zhou M, 2020, Diagnosis and Treatment Pathway for Pneumonia in Patients with Diabetes Mellitus: A Chinese Experts' Consensus. *Chin J Endocrinol Metab*, 36(8):635–642.
- [7] Apicella M, Campopiano M, Mantuano M, et al., 2020, COVID-19 in People with Diabetes: Understanding the Reasons for Worse Outcomes. *Lancet Diabetes Endocrinol*, 8(9):782–792.
- [8] Shi Q, Zhang X, Jiang F, et al., 2020, Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients With Diabetes in Wuhan, China: A Two-Center, Retrospective Study. *Diabetes Care*, 43(7):1382–1391.
- [9] Brufsky A, 2020, Hyperglycemia, Hydroxychloroquine, and the COVID-19 Pandemic. *J Med Virol*, 92(7):770–775.
- [10] Means C, 2020, Letter to the Editor: Mechanisms of Increased Morbidity and Mortality of SARS-CoV-2 Infection in Individuals with Diabetes: What This Means for an Effective Management Strategy. *Metabolism*, 2020(108):154254.
- [11] Wang J, Meng W, 2020, COVID-19 and Diabetes: The Contributions of Hyperglycemia. *J Mol Cell Biol*, 12(12):958–962.
- [12] Liu W, Li H, 2020, COVID-19: Attacks the 1-Beta Chain of Hemoglobin and Captures the Porphyrin to Inhibit Human Heme Metabolism. *ChemRxiv*. <https://doi.org/10.26434/chemrxiv.11938173.v9>
- [13] Codo A, Davanzo G, Monteiro L, et al., 2020, Elevated Glucose Levels Favor SARS-CoV-2 Infection and Monocyte Response Through a HIF-1 α /Glycolysis-Dependent Axis. *Cell Metab*, 32(3):437–446
- [14] Herder C, Roden M, Venteclef N, et al., 2024, Diabetes and Pulmonary Infection: How Hyperglycaemia Shapes the Immune System. *Signal Transduct Target Ther*, 9(1):67.
- [15] Gray V, Chen W, Tan R, et al., 2024, Hyperglycemia-Triggered Lipid Peroxidation Destabilizes STAT4 and Impairs Anti-Viral Th1 Responses in Type 2 Diabetes. *Cell Metab*, 36(12):2511–2527.
- [16] Šestan M, Mikašinović S, Benić A, et al., 2024, An IFN γ -Dependent Immune-Endocrine Circuit Lowers Blood Glucose to Potentiate the Innate Antiviral Immune Response. *Nat Immunol*, 25(6):981–993.
- [17] Nobs S, Kolodziejczyk A, Adler L, et al., 2023, Lung Dendritic-Cell Metabolism Underlies Susceptibility to Viral Infection in Diabetes. *Nature*, 624(7992):645–652.
- [18] Singh A, Khunti K, 2022, COVID-19 and Diabetes. *Annu Rev Med*, 2022(73):129–147.
- [19] Yang J, Feng Y, Yuan M, et al., 2006, Plasma Glucose Levels and Diabetes are Independent Predictors for Mortality and Morbidity in Patients with SARS. *Diabet Med*, 23(6):623–8.
- [20] Allard R, Leclerc P, Tremblay C, et al., 2010, Diabetes and the Severity of Pandemic Influenza A (H1N1) Infection. *Diabetes Care*, 33(7):1491–1493.
- [21] Lin X, Zhang C, Kong H, et al., 2022, Analysis on Impacts of Diabetes on the Severity and Mortality of Patients with COVID-19: A Meta-Analysis. *Clinical Focus*, 37(5):389–399.
- [22] Du Y, Guo Y, Jiang L, 2022, Influence of Chronic Complications of Type 2 Diabetes on the Condition of COVID-19 in the Elderly. *Chin J Public Health Eng*, 21(5):846–847.
- [23] Samson S, Konty K, Lee W, et al., 2021, Quantifying the Impact of Influenza Among Persons With Type 2 Diabetes Mellitus: A New Approach to Determine Medical and Physical Activity Impact. *J Diabetes Sci Technol*, 15(1):44–52.
- [24] Owusu D, Rolfes M, Arriola C, et al., 2022, Rates of Severe Influenza-Associated Outcomes Among Older Adults Living With Diabetes-Influenza Hospitalization Surveillance Network (FluSurv-NET), 2012-2017. *Open Forum Infect Dis*, 9(5):131.
- [25] Kazakou P, Lambadiari V, Ikonomidis I, et al., 2022, Diabetes and COVID-19: A Bidirectional Interplay. *Front Endocrinol (Lausanne)*, 2022(13):780663.
- [26] Wang A, Zhao W, Xu Z, et al., 2020, Timely Blood Glucose Management for the Outbreak of 2019 Novel Coronavirus Disease (COVID-19) is Urgently Needed. *Diabetes Res Clin Pract*, 2020(162):108118.
- [27] Montefusco L, Ben M, D'Addio F, et al., 2021, Acute and Long-Term Disruption of Glycometabolic Control After SARS-CoV-2 Infection. *Nat Metab*, 3(6):774–785.

- [28] Xie Y, Al-Aly Z, 2022, Risks and Burdens of Incident Diabetes in Long COVID: A Cohort Study. *Lancet Diabetes Endocrinol*, 10(5): 311–321.
- [29] Godoy P, Soldevila N, Martínez A, et al., 2024, Effectiveness of Influenza Vaccination and Early Antiviral Treatment in Reducing Pneumonia Risk in Severe Influenza Cases. *Vaccines (Basel)*, 12(2):173.
- [30] Surie D, Self W, Yuengling K, et al., 2025, RSV Vaccine Effectiveness Against Hospitalization Among US Adults Aged 60 Years or Older During 2 Seasons. *JAMA*, 2025:e2515896.
- [31] Fan Q, Shi J, Yang Y, et al., 2022, Clinical Characteristics and Immune Profile Alterations in Vaccinated Individuals with Breakthrough Delta SARS-CoV-2 Infections. *Nat Commun*, 13(1):3979.
- [32] Zhu L, She Z, Cheng X, et al., 2020, Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-Existing Type 2 Diabetes. *Cell Metab*, 31(6):1068–1077.
- [33] Ceriello A, 2020, Hyperglycemia and COVID-19: What Was Known and What is Really New? *Diabetes Res Clin Pract*, 167:108383.
- [34] Ma W, Ran X, 2020, The Management of Blood Glucose Should Be Emphasized in the Treatment of COVID-19. *J Sichuan Univ (Med Sci Ed)*, 51(2):146–150.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on the Mechanism of Action of Traditional Chinese and Western Medicine and the Course of Treatment for Shenrongbian Pills in the Treatment of Impotence and Premature Ejaculation

Chunlei Chen^{1*}, Wei Yang², Bei Zhang³, Zheng Li⁴

¹Department of Surgery IV, Shanghai Municipal Hospital of Traditional Chinese Medicine Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 200071, China

²Department of Integrated Traditional Chinese and Western Medicine, People's Hospital of BiYang County, Zhumadian 463700, Henan, China

³Health Management Center, Shanghai Municipal Hospital of Traditional Chinese Medicine Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 200071, China

⁴Department of Inpatient and Medical Record Management, The Eighth Medical Center of the Chinese PLA General Hospital, Beijing 100091, China

**Author to whom correspondence should be addressed.*

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Objective: To investigate the clinical efficacy, mechanism of action of traditional Chinese and Western medicine, and reasonable treatment regimen of Shenrongbian pills in the treatment of impotence and premature ejaculation caused by kidney-Yang deficiency. Methods: A total of 160 patients with impotence and premature ejaculation caused by kidney-Yang deficiency admitted to our hospital from January 2023 to January 2024 were randomly divided into an observation group (80 cases) and a control group (80 cases). The observation group was treated with Shenrongbian pills; the control group was treated with sildenafil citrate tablets combined with dapoxetine. The International Index of Erectile Function (IIEF-5), intravaginal ejaculatory latency time (IELT), traditional Chinese medicine kidney-Yang deficiency syndrome score, overall clinical response rate, and safety were compared between the two groups before and after treatment. Results: There was no significant difference in the IIEF-5 scores and IELT between the two groups before treatment ($P > 0.05$). After 3 months and 6 months of treatment, both indicators improved significantly in both groups ($P < 0.05$), and the improvement in the observation group was more significant than that in the control group, with a more pronounced difference at 6 months ($P < 0.001$); there was no significant difference in the total traditional Chinese medicine syndrome scores between the two groups before treatment ($P > 0.05$). After 3 and 6 months of treatment, the traditional Chinese medicine (TCM) syndrome scores in the observation group were significantly lower than those in the control group ($P < 0.05$), and continued to decrease with prolonged treatment duration. The improvement in scores in the control group was not significant ($P > 0.05$). After 6 months of treatment, the overall response rate in the observation group was 93.75%, significantly higher than the 81.25% in the control group ($\chi^2 = 5.714$, $P = 0.017 < 0.05$). In the observation group, there was 1 case of dizziness and 2 cases of gastric discomfort, with an adverse reaction rate of 3.75%. In the control group, there were 4 cases of headache, 2 cases of facial flushing, and 1 case of abnormal vision, with an incidence rate of 12.5%. Conclusion: Shenrongbian pill, through

mechanisms such as warming and tonifying the kidney-Yang, harmonizing Yin and Yang, improving microcirculation, and regulating endocrine function, can significantly improve sexual function and systemic symptoms in patients with impotence and premature ejaculation due to kidney-Yang deficiency. It is highly safe, with a recommended treatment duration of 3–6 months, and its efficacy shows an increasing trend with prolonged treatment.

Keywords: Impotence; Kidney-Yang deficiency; Mechanism of action; Premature ejaculation; Shenrongbian pill; Treatment duration

Online publication: September 26, 2025

1. Introduction

Erectile dysfunction (ED) and premature ejaculation (PE) are the most prevalent sexual dysfunction disorders among men, with their incidence rates showing a yearly upward trend due to increased social pressure and lifestyle changes. These conditions not only directly affect sexual quality but also trigger psychological issues such as anxiety and low self-esteem in patients, leading to strained marital relationships and even family breakdown, thereby causing multidimensional damage to patients' physical and mental health and social functioning^[1].

Modern medicine posits that their onset is closely related to psychological factors, neurovascular dysfunction, and endocrine disorders. Treatment primarily involves medications such as PDE5 inhibitors (phosphodiesterase type 5 inhibitors, PDE5), but these have limitations including multiple adverse reactions and the need for on-demand use. Long-term use may also result in adverse reactions such as headaches and flushing^[2]. Topical anesthetics can prolong ejaculatory latency but often lead to a loss of sexual pleasure. These treatment approaches mostly focus on symptom relief and are difficult to fundamentally improve the overall functional state of patients, especially those with chronic conditions accompanied by systemic symptoms.

In traditional Chinese medicine, these conditions are classified under the categories of “impotence” and “PE,” with the core pathological mechanism being the decline of kidney-Yang. Treatment focuses on warming and tonifying kidney-Yang, as well as replenishing essence and marrow^[3]. Shenrongbian pill originates from the “Shenrong Decoction” in Wu Jutong's “Differentiation and Treatment of Warm Diseases” from the Qing Dynasty. After centuries of inheritance, it has become a classic original prescription. Its formulation features four types of animal penises (ox penis, donkey penis, dog penis, and mink penis) as the principal ingredients, supplemented by precious medicinal herbs such as red ginseng and deer antler. It exerts the effects of “nourishing and replenishing with the shapes of four animal penises.” Paired with two Yin-nourishing herbs (wolfberries and prepared rehmannia root) and two cooling herbs (asparagus root and lycium root bark), it achieves a “warming yet non-drying” effect. This herbal remedy not only improves sexual dysfunction but also alleviates symptoms of kidney-Yang deficiency, such as soreness and weakness in the lower back and knees, aversion to cold, and cold limbs, reflecting the characteristic of “addressing both symptoms and root causes.”

This study systematically explores the efficacy and mechanism of action of Shenrongbian pill in treating impotence and premature ejaculation due to kidney-Yang deficiency, aiming to provide a basis for clinical medication.

2. Materials and methods

2.1. General information

A total of 160 patients diagnosed with impotence and PE due to kidney-Yang deficiency at the andrology clinic of our hospital were randomly divided into an observation group (80 cases) and a control group (80 cases). The observation group had an age range of 25–55 years, with an average age of (38.62 ± 7.21) years; the disease duration ranged from 6 months to 10 years, with an average of (3.22 ± 1.83) years. The control group had an age range of 26–54 years, with an average age of $(37.95$

± 6.89) years; the disease duration ranged from 8 months to 9 years, with an average of (3.12 ± 1.69) years. There were no statistically significant differences in baseline data between the two groups ($P > 0.05$), indicating comparability.

The inclusion criteria are as follows:

- (1) Meeting the aforementioned diagnostic criteria of both traditional Chinese and Western medicine (Western medicine diagnosis: in accordance with the “Guidelines for the Diagnosis and Treatment of Erectile Dysfunction” (2016 edition) and the “Guidelines for the Diagnosis and Treatment of Premature Ejaculation” (2018 edition); IIEF-5 score ≤ 21 ; IELT ≤ 2 minutes; traditional Chinese medicine diagnosis: based on the “Diagnostic Efficacy Criteria for Traditional Chinese Medicine Syndromes,” diagnosed as kidney-Yang deficiency syndrome: primary symptoms include impotence and premature ejaculation; secondary symptoms include soreness and cold pain in the lower back and knees, aversion to cold, cold limbs, morning diarrhea, frequent nocturia (≥ 2 times/night), pale tongue with white coating, and deep, thin, and weak pulse);
- (2) Aged between 20 and 60 years;
- (3) Informed consent from the patient and their spouse.

The exclusion criteria are as follows:

- (1) Sexual dysfunction caused by organic lesions (such as diabetes, lumbar spine lesions, etc.);
- (2) Use of similar medications in the past month;
- (3) Allergy to the components of this medication;
- (4) Patients with mental disorders.

2.2. Therapeutic methods

The control group received treatment with sildenafil citrate tablets (50 mg per tablet) combined with dapoxetine (30 mg per tablet), taken one hour before sexual activity, with a maximum of one dose per day. The treatment was continuously observed for six months. The observation group was administered Shenrongbian pills (specification: 2.3 g per 10 pills), with a dosage of 10 pills taken twice daily, 1 to 2 hours before breakfast and dinner, accompanied by light salt water or plain water^[4]. Each treatment course lasted 15 days, followed by a 2-day break before the next course, continuing for a total of six months.

2.3. Observation indicators

The observation indicators are as listed:

- (1) International Index of Erectile Function (IIEF-5), encompassing five items such as erectile confidence and erectile maintenance, with a total score of 25 points. Higher scores indicate better function;
- (2) Intravaginal Ejaculatory Latency Time (IELT), the time from insertion to ejaculation was recorded by the spouse using a stopwatch;
- (3) TCM syndrome score, where six secondary symptoms, including lumbar and knee weakness, aversion to cold, and cold limbs, were scored (0-3 points per item). Higher total scores indicate more severe symptoms;
- (4) Clinical efficacy was determined based on improvements in IIEF-5 scores and IELT. Recovery: IIEF-5 score ≥ 22 points, IELT ≥ 3 minutes; Marked effectiveness: IIEF-5 score increased by ≥ 10 points, IELT increased by ≥ 2 minutes; Effective: IIEF-5 score increased by 5 to 9 points, IELT increased by 1 to 1.9 minutes; Ineffective: Did not meet the aforementioned criteria. The total effective rate = (number of recovered cases + number of markedly effective cases + number of effective cases) / total number of cases $\times 100\%$;
- (5) Safety Indicators such as adverse reactions (dizziness, headache, gastrointestinal discomfort, facial flushing, visual abnormalities, etc.) were monitored.

2.4. Statistical methods

SPSS 27.0 software was used. Continuous data were expressed as mean \pm standard deviation (SD), and comparisons

between groups were made using the t-test. Categorical data were expressed as [n (%)], and comparisons were made using the χ^2 test. A P -value of < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of main symptom indicators before and after treatment between the two groups

Before treatment, there were no significant differences in IIEF-5 scores and IELT between the two groups ($P > 0.05$). After 3 and 6 months of treatment, both indicators significantly improved in both groups ($P > 0.05$), with the observation group showing a greater degree of improvement than the control group, and the difference being more pronounced at 6 months ($P < 0.001$). See **Table 1**.

Table 1. Comparison of IIEF-5 Scores and IELT before and after treatment between the two groups (mean \pm SD)

Indicator	Group	Before Treatment	At 3 Months	At 6 Months
IIEF-5 (points)	Experimental (n=80)	11.21 \pm 2.55	17.81 \pm 2.91	22.35 \pm 3.12
	Control (n=80)	10.82 \pm 2.32	15.32 \pm 2.62	18.67 \pm 2.85
	t-value	1.012	5.689	7.789
	p-value	0.313	0.000	0.000
IELT (min)	Experimental (n=80)	1.21 \pm 0.52	3.51 \pm 1.12	5.28 \pm 1.36
	Control (n=80)	1.19 \pm 0.42	2.32 \pm 0.81	3.15 \pm 0.92
	t-value	0.268	7.701	11.603
	p-value	0.789	0.000	0.000

3.2. Comparison of TCM syndrome scores before and after treatment between the two groups

Before treatment, there was no significant difference in the total TCM syndrome scores between the two groups ($P > 0.05$). After 3 and 6 months of treatment, the TCM syndrome scores in the observation group were significantly lower than those in the control group ($P < 0.05$) and continued to decrease with prolonged treatment; the improvement in the control group was not significant ($P > 0.05$). See **Table 2**.

Table 2. Comparison of total TCM syndrome scores before and after treatment between the two groups

Group	Before Treatment	At 3 Months	At 6 Months
Experimental (n=80)	12.45 \pm 3.20	6.82 \pm 2.13	3.24 \pm 1.56
Control (n=80)	12.38 \pm 3.09	9.51 \pm 2.52	7.81 \pm 2.02
t-value	0.141	7.292	16.015
p-value	0.889	0.000	0.000

3.3. Comparison of clinical efficacy between the two groups

After 6 months of treatment, the overall response rate in the observation group was 93.75%, significantly higher than that in the control group at 81.25% ($\chi^2 = 5.714$, $P = 0.017 < 0.05$). See **Table 3**.

Table 3. Comparison of clinical efficacy between the two groups [n (%)]

Group	Cured	Markedly Effective	Effective	Ineffective	Total Effective Rate
Experimental (n=80)	35 (43.75%)	29 (36.25%)	11 (13.75%)	5 (6.25%)	75 (93.75%)
Control (n=80)	16 (20.00%)	20 (25.00%)	29 (36.25%)	15 (18.75%)	65 (81.25%)
χ^2					5.714
<i>p</i> -value					0.017

3.4. Comparison of adverse reaction incidence rates between the two groups

In the observation group, there was 1 case of dizziness and 2 cases of gastric discomfort, with an adverse reaction incidence rate of 3.75%; in the control group, there were 4 cases of headache, 2 cases of facial flushing, and 1 case of visual abnormalities, with an incidence rate of 12.5%. See **Table 4**.

Table 4. Comparison of adverse reaction incidence rates between the two groups

Adverse Reaction	Dizziness	Gastric Discomfort	Headache	Facial Flushing	Visual Disturbance	Total Incidence Rate
Experimental (n=80)	1 (1.25%)	2 (2.50%)	-	-	-	3 (3.75%)
Control (n=80)	-	-	4 (5%)	5 (6.25%)	1 (1.25%)	10 (12.5%)
χ^2						4.103
<i>p</i> -value						0.043

4. Discussion

Shenrongbian pills are derived from the “Shenrong Decoction” in Treatise on Differentiation and Treatment of Epidemic Febrile Diseases, with over 200 years of clinical validation. Wu Jutong believed that “in cases of Yang deficiency, Yang fails to transform Yin, leading to the predominance of Yin pathogens,” and thus proposed warming Yang and dispersing cold as the therapeutic principle^[5]. The modern formula adds four types of animal penises (ox penis, donkey penis, dog penis, and mink penis) to the original prescription, adhering to the “like cures like” theory to directly replenish kidney essence and invigorate Yang to treat impotence. Among them, ox penis and donkey penis enter the kidney meridian, capable of “tonifying kidney Qi and nourishing essence” (Compendium of Materia Medica); dog penis “enhances Yang and nourishes blood vessels” (Famous Physicians’ Records); mink penis is warm and potent, with a particularly strong Yang-boosting effect.

The synergistic action of the four penises directly targets the pathogenesis of kidney-Yang deficiency, providing a fundamental treatment for “impotence and spermatorrhea.” The formula also incorporates asparagus root, lycium root bark (cold in nature), wolfberry fruit, and prepared rehmannia root (Yin-nourishing) to counteract the warming and drying properties of the animal penises, ensuring that “tonifying Yang does not harm Yin”^[6]. In addition to improving sexual function, Shenrongbian pills significantly reduce symptom scores for soreness and weakness of the lower back and knees and frequent nocturia, reflecting the principle of “treating the root cause of the disease”. By tonifying kidney-Yang and consolidating kidney Qi, the formula strengthens “bones and tendons when kidney-Yang is sufficient and stabilizes the bladder,” achieving simultaneous improvement in local and systemic symptoms^[7].

From a Western medicine perspective, Shenrongbian pills can elevate serum testosterone levels, promote luteinizing

hormone (LH) secretion, and improve gonadal function, providing an endocrine basis for erectile and ejaculatory control^[8]. The IIEF-5 scores in the observation group significantly increased, confirming its role in improving vascular function. Additionally, it reduces serotonin (5-HT) reuptake, prolonging the ejaculatory latency period, while increasing dopamine levels to enhance sexual excitation transmission, thus providing bidirectional regulation of the ejaculatory reflex.

The results of this study showed that as the duration of treatment increases, the therapeutic effects of Shenrongbian pills gradually manifest and intensify. After three months of treatment, the IIEF-5 score, IELT, and TCM syndrome score for kidney-Yang deficiency in the observation group all demonstrated significant improvement. After six months of treatment, all indicators showed further enhancement. This indicates that Shenrongbian pills require a certain treatment duration to achieve optimal efficacy, with a recommended treatment course of 3–6 months. The reason may be that kidney-Yang deficiency syndrome is a chronic debilitating disease that requires long-term conditioning for recovery^[9].

As a traditional Chinese herbal preparation, Shenrongbian pills have a mild yet lasting effect, gradually replenishing kidney essence and warming kidney-Yang to achieve therapeutic goals. The dosing regimen of “15 consecutive days of administration followed by a 2-day break before continuing with the second course” ensures drug efficacy while minimizing drug accumulation in the body and reducing the risk of adverse reactions.

In contrast, the control group showed rapid onset but required on-demand administration and demonstrated limited improvement in systemic symptoms of kidney-Yang deficiency. Shenrongbian pills offer several advantages, including lasting efficacy with sustained effects after discontinuation, comprehensive improvement of systemic symptoms, minimal adverse reactions and high safety and suitability for long-term conditioning to fundamentally improve physical constitution.

Shenrongbian pills exhibit definite therapeutic effects in treating impotence and premature ejaculation caused by kidney-Yang deficiency. The mechanism involves a dual approach combining TCM principles of “warming kidney-Yang, replenishing essence and marrow, and harmonizing Yin and Yang” with Western medicine mechanisms of “regulating endocrine function, improving microcirculation, and modulating neurotransmitters,” achieving both symptomatic relief and root cause treatment^[10].

The clinically recommended treatment course is 3–6 months, using a regimen of “15-day treatment followed by a 2-day break,” which significantly enhances sexual function, improves kidney-Yang deficiency symptoms such as lumbar and knee soreness, and maintains high safety. As a century-old classic formula characterized by “four-organ tonification and warming without dryness,” it provides an ideal therapeutic option for patients with chronic sexual dysfunction caused by kidney-Yang deficiency.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Liu Y, Wang F, Zeng Y, et al., 2023, Examples of Traditional Chinese Medicines to Be Used with Caution for Impotence, Premature Ejaculation, and Male Infertility. *Chinese Journal of Human Sexuality*, 32(11): 109–112.
- [2] He F, 2021, Analysis of the Effect of Shenrongbianwan Combined with PDE5 Inhibitors in the Treatment of Impotence. *World Latest Medicine Information*, 21(83): 461–462.
- [3] Zhang J, Li Q, Wang H, et al., 2022, Research on the Medication Rules of Traditional Chinese Medicine Compounds for the Treatment of Premature Ejaculation Based on the National Patent Database. *Chinese Journal of Andrology*, 36(04): 22–28.
- [4] Liu Y, 2021, Efficacy of Modified Chaihu Longgu Muli Decoction Combined with Sildenafil Citrate Tablets in the

- Treatment of Impotence. Continuing Medical Education, 35(4): 150–151.
- [5] Huang J, Ba Y, 2025, Analysis of the Thoughts of Ancient Physicians on the Etiology and Pathogenesis of Impotence. Hubei Journal of Traditional Chinese Medicine, 47(5): 56–59.
 - [6] He F, 2021, Observation of the Effect of Shenrongbianwan Combined with Dapoxetine in the Treatment of Premature Ejaculation. World Latest Medicine Information, 21(101): 253–254.
 - [7] Liu X, Zhang J, 2023, Research Progress in Traditional Chinese Medicine Treatment of Chronic Prostatitis Accompanied by Premature Ejaculation and Impotence. Clinical Personalized Medicine, 3(4): 2653–2659.
 - [8] Li Y, 2021, Application Effect of Shenrongbianwan in Kidney Deficiency. World Latest Medicine Information, 21(98): 541–542.
 - [9] Zhao W, Wang Z, Zhang Q, et al., 2018, Tracing the Source of Traditional Chinese Medicine Diagnosis and Treatment of Impotence. Clinical Journal of Traditional Chinese Medicine, 30(5): 875–877.
 - [10] Liu B, Hu B, Zhao H, et al., 2025, Analysis of Research Progress in Traditional Chinese Medicine Treatment of Impotence from the Perspective of Theory, Method, Prescription, and Medicine. Guangming Journal of Chinese Medicine, 40(2): 407–411.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Glymphatic System Impairment in Type 2 Diabetes Mellitus Associated with Cognitive Function

Jie Gao^{1†}, Peichun Pan^{2†}, Jing Li³, Bingqian Gao³, Dongsheng Zhang¹, Min Tang¹, Xuejiao Yan¹, Kai Ai⁴, Xiaoyan Lei¹, Zhongwei Liu⁵, Yuming Zhang⁶, Xiaoling Zhang^{1*}

¹Department of MRI, Shaanxi Provincial People's Hospital, Xi'an 710000, Shaanxi, China

²Department of Graduate, Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

³Department of Graduate, Xi'an Medical University, Xi'an 710000, Shaanxi, China

⁴Department of Clinical Science, Philips Healthcare, Xi'an 710000, Shaanxi, China

⁵Department of Cardiology, Shaanxi Provincial People's Hospital, Xi'an 710000, Shaanxi, China

⁶Department of Anesthesiology, Shaanxi Provincial People's Hospital, Xi'an 710000, Shaanxi, China

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

***Corresponding author:** Xiaoling Zhang, zxl.822@163.com

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Objective: This study aims to investigate human glymphatic function in type 2 diabetes mellitus (T2DM) using the index for diffusion tensor image analysis along the perivascular space (DTI-ALPS) and to explore the relationship between this proposed measure of glymphatic clearance and cognitive functions. Methods: A total of 17 patients with T2DM and 20 age- and sex-matched health controls (HCs) were included in this study. All participants underwent neurological MRI and cognitive assessments. Both the average and bilateral DTI-ALPS indices, clinical and cognitive measurements were compared between the two groups. The correlations between DTI-ALPS indices and cognitive measurements were analyzed. Results: The average and right DTI-ALPS indices were significantly lower in the T2DM group than them in HC group ($P = 0.011$, $P = 0.005$). In HC group, the right DTI-ALPS index was higher than the left ($P = 0.039$), whereas no hemispheric difference was observed in T2DM. In correlation analyses, a lower DTI-ALPS index was associated with poorer TMT-B performance in T2DM ($\beta = -0.502$, $P = 0.001$), while no other significant correlations were found between DTI-ALPS index and cognitive measures in either group. Conclusion: This study demonstrated impaired glymphatic system function in T2DM patients and it is associated with worse performance in executive functions. The impaired glymphatic function in patients with T2DM may provide a new perspective for understanding the pathophysiology of T2DM-associated cognitive impairment.

Keywords: Diffusion tensor imaging; Glymphatic system; MRI; Type 2 diabetes mellitus.

Online publication: September 26, 2025

1. Introduction

Type 2 diabetes (T2DM) is the most common metabolic disease with a high incidence worldwide ^[1]. Brain damage caused by persistent hyperglycemia, which includes changes in neurophysiology and brain structures as well as the resultant

cognitive impairment involving memory, attention and executive functions, has emerged as an important risk factor for mild cognitive impairment (MCI), Alzheimer's disease (AD) and dementia ^[2,3]. With the increasing prevalence of diabetes and an aging population, the incidence of cognitive impairment is expected to increase gradually, posing great challenges for future health effects. Thus, identifying T2DM patients with high-risk for cognitive impairment and providing a preventive treatment is needed. However, understandings of potential therapeutic targets and mechanisms underlying the cognitive impairment associated with T2DM remains incomplete.

Since 2012, the brain glymphatic system has been discovered and identified the important role for clearing abnormal proteins and metabolites and maintaining brain homeostasis ^[4]. The glymphatic system transships metabolic waste and toxic substances from the brain through the perivascular space (PVS) to the dural lymphatic vessels, and finally to the extracranial deep cervical lymph nodes ^[5]. Accumulating evidences have indicated that impaired glymphatic system function is one of the pathophysiological mechanisms mediating neurodegenerative diseases and accelerating their progression, which is also closely related to advanced cognitive functions ^[6]. It has been hypothesized that failure to clear soluble amyloid-beta from perivascular space contributes to the accumulation of amyloid plaques and the progression of AD. Therefore, glymphatic disruption is considered the final common pathway for dementia and the function of brain glymphatic system might be used as a potential biomarker of cognitive decline.

At present, dynamic contrast enhanced MRI (DCE-MRI) is mainly used to evaluate the function of the human brain glymphatic system. After injecting contrast agent into the sheath of the subjects, the glymphatic system function of different brain regions was evaluated by measuring the change of T1-weighted signals over time to calculate the time required to produce tracer clearance ^[7]. Similarly, positron emission tomography (PET) also can be used to study the removal and drainage of perivascular space fluids ^[8]. The above two methods can obtain dynamic visualized fluid images of the whole brain glymphatic system. However, the injection of imaging agents or radionuclides are invasive, and multiple imaging must be performed within a few hours to a few weeks after DCE-MRI injection of contrast agents, making it difficult to carry out widespread application. Furthermore, PET has limited anatomical resolution and can only describe cerebrospinal fluid movement at the macroscale.

Recently, Taoka et al. proposed a new non-invasive alternative called diffusion tensor image analysis along the perivascular space (DTI-ALPS) to evaluate the human glymphatic function on diffusion tensor imaging (DTI) and susceptibility weighted imaging (SWI) ^[9]. This method measured the diffusivity perpendicular to the ventricular wall at the lateral ventricle body level to represent the interstitial fluid flow along the PVS. The ALPS index was calculated to quantitatively evaluate the glymphatic function. So far, DTI-ALPS has been used to assess the function of the glymphatic system in a variety of neurological disorders, including AD, dementia, Parkinson's disease (PD), cerebral small vessel disease (CSVD), ischemic stroke, attention deficit/hyperactivity disorder and idiopathic normal pressure hydrocephalus ^[10-15].

So far, cumulative evidences have confirmed the presence of a mass of toxic substances in diabetic brain tissues, including amyloid- β , hyperphosphorylated Tau, and advanced glycation end products ^[16-20]. Yang et al. also demonstrated ALPS-index was associated with the severity of T2DM, which suggested that disruption of the glymphatic system was also existed in T2DM. However, there is still lack of evidence about mechanisms underlying the associations between glymphatic functions and cognitive decline within T2DM. Thus, this study aims to investigate glymphatic function in T2DM using the DTI-ALPS index and to explore the relationship between DTI-ALPS index and cognitive functions.

2. Materials and methods

2.1. Participants

The study was conducted in accordance with the Helsinki declaration. The Human Ethics Committee of Shaanxi Provincial Peoples Hospital approved all experimental procedures after receiving informed consent.

Patients with T2DM were recruited from the Department of Endocrinology of Shaanxi Provincial People's Hospital, and healthy controls (HCs) matched for age, sex, and education level were obtained from our health examination center.

All the participants were between 40 and 70 years of age, right-handed, and educated for at least six years. The T2DM patients met the standard criteria proposed by the American Diabetes Association and without a history of hypoglycemia or hyperglycemia^[21]. The other inclusion criteria in the HC group were as follows:

- (1) No symptoms or a family history of diabetes;
- (2) Fasting glucose < 7.0 mmol/L;
- (3) Glycosylated hemoglobin A1c (HbA1c) level < 6.0%.

The exclusion criteria for both groups were as follows:

- (1) History of neurological disorders, such as cerebral infarctions, brain tumors, vascular malformations, or traumatic brain injury;
- (2) Illicit substance abuse, alcohol abuse, or psychiatric disorders;
- (3) Any other systemic disease irrelevant to diabetes and affecting cognition;
- (4) Inability to complete MRI examinations or unsatisfactory MRI images.

2.2. Clinical data and cognitive assessments

All participants' clinical data, including information regarding their age, sex, educational level, blood pressure, height, weight, and body mass index (BMI), were obtained from medical records and questionnaires. Laboratory tests, including blood biochemical analysis and evaluation of fasting plasma glucose (FPG) and HbA1c levels were performed and their results were recorded.

All participants underwent the following series of neuropsychological assessments: Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) were used to assess general cognitive function; Trail-Making Test A (TMT-A) reflected cognitive processing skills (psychomotor speed, processing speed, and visuospatial skills) and attention; Trail-Making Test B (TMT-B) provided information regarding executive function; Auditory Verbal Learning Test (AVLT) was used to evaluate episodic memory; and Clock Drawing Test (CDT) was performed to evaluate visuospatial skills. Neuropsychological tests were performed by a psychiatrist trained in systematic testing.

2.3. Image acquisition

Conventional MRI and DTI data were obtained using a 3.0 T MR scanner (Ingenia, Philips Healthcare, the Netherlands) equipped with a 32-channel phase-array head coil. Conventional MRI, including sagittal three-dimensional T1-weighted imaging (repetition time [TR]/excitation time [TE] = 7.5/3.5 ms, field of view [FOV] = 250 × 250 mm², matrix = 256 × 256, slice thickness = 1 mm) and T2 FLAIR (TR/TE = 6000/150 ms, FOV = 230 × 230 mm², matrix = 320 × 320, slice thickness = 6 mm) were used to identify visible brain lesions. DTI was performed using the following parameters: 32 directions, b value = 0, 1000 s/mm², TR/TE=5000/150 ms, slice thickness= 2 mm, field of view = 256 mm × 256 mm, matrix = 128 × 128, spatial resolution = 2 × 2 × 2 mm³.

2.4. Data processing

Data pre-processing included the following steps:

- (1) The image format was converted from DICOM to NIFTI;
- (2) Non-brain tissues, such as the scalp and skull, were removed using the Brain Extraction Tool (BET), which was performed in FMRIB's Software Library (FSL);
- (3) The diffusion-weighted images were realigned to the non-weighted b0 images to correct head motion and eddy current-induced distortions (also a tool of FSL).

Evaluation of DTI-ALPS index was accordant with previous studies^[22]. Diffusivities maps were co-registered to the FA map template (<https://neurovault.org/images/1406/>) by spm12 package in MATLAB (R2014a). Four 5-mm-diameter ROIs were placed on bilateral projection fibers and association fibers on FA map template. Manual correction was adapted to confirm the accuracy of registration and the location of ROIs for each patient. Then we recorded the diffusivities of

ROIs and calculated the average DTI-ALPS index of bilateral sides. DTI-ALPS was computed as the ratio between the mean of x-axis diffusivity on the projection fibers (Dxproj) and association fibers (Dxassoc) and the mean of y-axis diffusivity on the projection fibers (Dyproj) and z-axis diffusivity on association fibers (Dzassoc).

2.5. Statistical analysis

Data were analyzed by using SPSS (SPSS version 20.0, IBM, USA). Intergroup comparisons of DTI-ALPS indices, clinical and cognitive measurements were performed using Student's *t* tests or χ^2 tests as appropriate. The correlations between the DTI-ALPS index and cognitive measurements were analyzed by using multiple linear regression analyses, with age, sex, and years of education as the covariates. The Bonferroni correction was applied to correct for multiple comparisons. All tests were taken to be significant at $P < 0.05$ (two-tailed).

3. Results

3.1. Clinical and neuropsychological data

A total of 17 patients with T2DM and 20 HCs were enrolled in this study. **Table 1** showed the demographic and clinical characteristics of the enrolled participants. There were no significant differences in age, sex, years of education, blood pressure, total cholesterol, triglycerides, low-density lipoprotein levels, MMSE, MoCA, TMT-A, AVLT and CDT between HCs and patients with T2DM. Compared with HCs, patients with T2DM showed a significantly worse cognitive domain in TMT-B ($P = 0.004$).

Table 1. The demographic and clinical characteristics of the enrolled participants

Clinic information	T2DM (n = 17)	HC (n = 20)	T/Z/ χ^2 value	P value
Gender (male/female)	14/3	13/7	1.403	0.288
Age (years)	49.41 ± 8.97	51.95 ± 7.57	0.934	0.357
Formal education (years)	13.35 ± 3.12	13.90 ± 2.59	0.582	0.564
BMI (kg/m ²)	24.87 ± 3.42	22.55 ± 3.17	-2.006	0.055
Total cholesterol (mmol/L)	4.92 ± 1.03	5.00 ± 0.97	0.23	0.819
Triglycerides (mmol/L)	1.82 ± 0.94	1.33 ± 0.77	-1.432	0.109
HDL (mmol/L)	1.14 ± 0.29	1.50 ± 0.51	2.476	0.020
LDL (mmol/L)	2.86 ± 0.76	2.94 ± 0.73	0.308	0.760
Fasting glucose (mmol/L)	7.26 ± 2.38	4.94 ± 0.56	-3.819	0.001
HbA1c (%)	7.51 ± 1.73	5.48 ± 0.46	-4.410	< 0.001
MMSE	27.88 ± 1.50	28.20 ± 1.64	0.611	0.545
MoCA	25.71 ± 2.54	26.25 ± 1.45	0.815	0.420
TMT-A(s)	105.29 ± 25.27	87.05 ± 25.54	-1.175	0.248
TMT-B(s)	189.71 ± 83.71	118.85 ± 36.28	-3.241	0.004
CDT	21.35 ± 7.11	24.88 ± 3.86	1.911	0.064
AVLT-total	46.50 ± 10.35	42.40 ± 13.36	-1.008	0.321
AVLT-delay	9.50 ± 3.60	7.90 ± 4.13	-1.222	0.230

Note: AVLT: Auditory verbal learning test; BMI, Body mass index; CDT, Clock drawing test; HDL, High density lipoprotein; LDL, Low density lipoprotein; HbA1c, Glycated hemoglobin; MMSE, Mini-mental state examination; MoCA: Montreal cognitive assessment; TMT-A, Trail making test A; TMT-B, Trail making test B.

3.2. Comparison of DTI-ALPS index between two groups

Compared with HCs, patients with T2DM showed a significantly lower average DTI-ALPS index (1.68 ± 0.15 vs. 1.54 ± 0.17 , $P = 0.011$) and right DTI-ALPS index (1.73 ± 0.19 vs. 1.53 ± 0.20 , $P = 0.005$), as shown in **Figure 1**. In HCs, the right DTI-ALPS index was significantly higher than the left DTI-ALPS index (1.73 ± 0.19 vs. 1.64 ± 0.16 , $P = 0.039$, shown in **Figure 2**). However, this difference was not found in T2DM group (1.53 ± 0.20 vs. 1.55 ± 0.16 , $P = 0.517$).

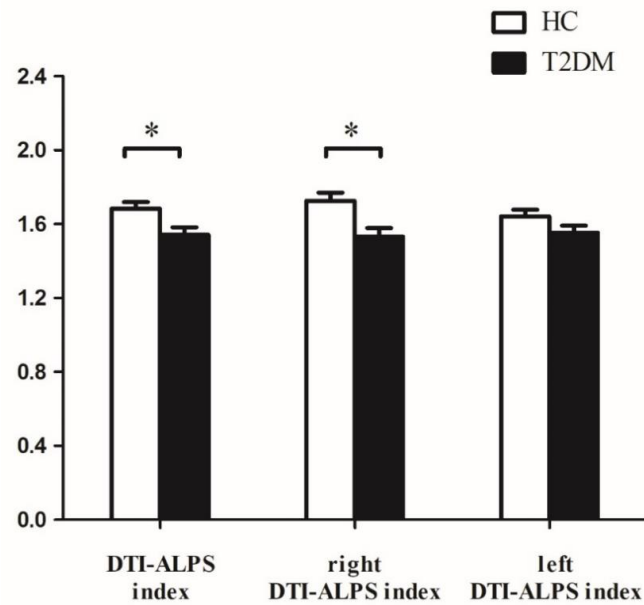


Figure 1. Group comparison of DTI-ALPS indices between patients with T2DM and healthy controls.

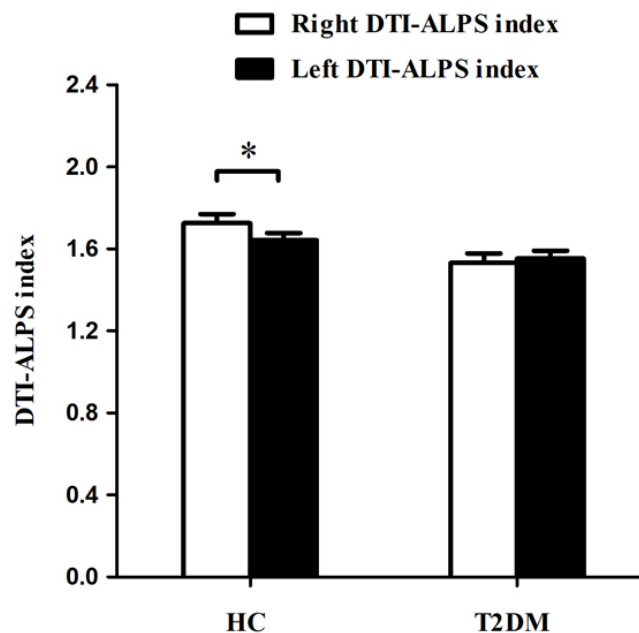


Figure 2. Interhemispheric differences in DTI-ALPS indices in healthy controls and patients with T2DM.

3.3. Relationship between DTI-ALPS index and cognitive impairment

The DTI-ALPS index showed significantly negative correlation with TMT-B ($\beta = -0.502$, $P = 0.001$), as shown in **Figure 3**, while DTI-ALPS index showed no significant correlation with any of other cognitive measures.

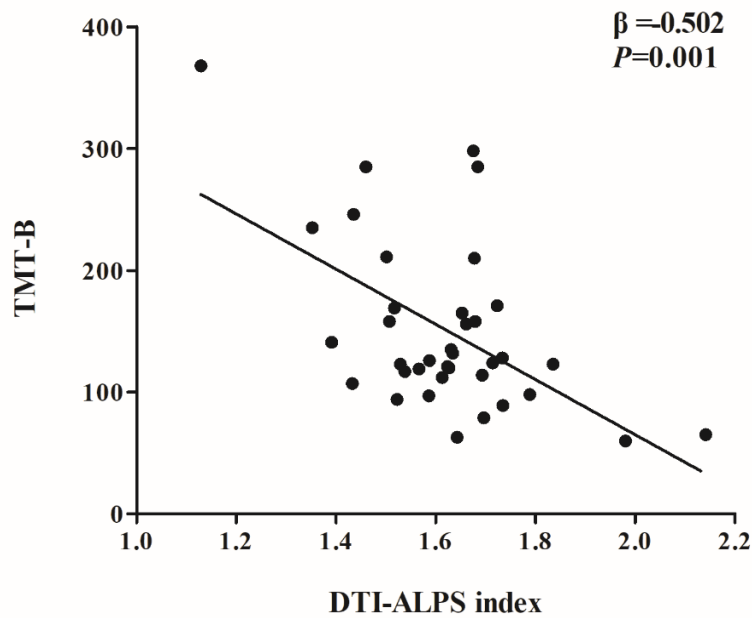


Figure 3. Negative correlation between DTI-ALPS index and TMT-B performance.

4. Discussion

In this study, we investigated *in vivo* glymphatic system function in T2DM patients using the DTI-ALPS index, a non-invasive diffusion-derived MRI index of diffusivity along the perivascular space. Our findings revealed that patients with T2DM exhibited significantly lower bilateral and right DTI-ALPS indices compared with HCs, indicating impaired glymphatic function associated with diabetes. Moreover, a right-greater-than-left hemispheric asymmetry of ALPS indices was observed in HCs but was absent in the T2DM group, suggesting that diabetes may disrupt the normal lateralization of glymphatic activity. Within the T2DM cohort, lower DTI-ALPS indices were significantly correlated with poorer TMT-B performance, implying that compromised interstitial fluid clearance may contribute to cognitive deficits, particularly executive dysfunction in this population.

Our observation of reduced DTI-ALPS indices in T2DM is consistent with recent studies reporting impaired perivascular or interstitial fluid transport in metabolic conditions ^[23,24]. Previous research in diabetic cohorts has similarly demonstrated lower ALPS values compared with healthy controls and linked these alterations to poorer cognitive performance, supporting the notion that glymphatic dysfunction constitutes an important mechanism underlying diabetes-related brain vulnerability. However, our findings not only corroborate but also extend previous evidence in several important respects.

For instance, we identified a hemispheric pattern in glymphatic function: healthy controls exhibited a right-greater-than-left ALPS asymmetry that disappeared in the T2DM group. This loss of lateralization suggests that diabetes may not only reduce global perivascular diffusivity but also disrupt the normal interhemispheric organization of glymphatic pathways, an aspect rarely examined in earlier studies. Given that prior reports seldom quantified hemispheric asymmetry, our results highlight lateralization metrics as potentially more sensitive markers of disease-related glymphatic disruption.

Furthermore, while earlier studies primarily emphasized global cognitive impairment, our results highlighted a domain-specific relationship between reduced ALPS index and cognitive performance in T2DM. This finding indicates that glymphatic dysfunction may not uniformly affect cognition but instead shows selective associations with certain domains. The observed pattern underscores the potential of ALPS as a sensitive imaging biomarker for subtle cognitive alterations in diabetes, warranting further investigation in larger and longitudinal cohorts.

On top of that, our associations remained significant after adjusting for age, sex, and years of education and survived multiple-comparison correction, further reinforcing the robustness and reproducibility of the ALPS-cognition relationship. Moreover, by explicitly separating average, right, and left ALPS indices, our side-resolved analysis revealed additional variance not captured by mean ALPS measures alone. This methodological refinement provides greater biological specificity and may help future studies achieve more consistent and physiologically meaningful results.

The present study further demonstrated that lower ALPS index was specifically associated with poorer TMT-B performance in patients with T2DM, which suggests that glymphatic dysfunction might preferentially affect cognitive domains related to information processing and executive control. Similar domain-specific associations have been observed in AD, where reductions in ALPS reductions were most strongly linked to processing speed and executive functions rather than global cognition^[25,26].

Executive and processing-speed deficits are typically mediated by fronto-subcortical circuits that rely on intact white-matter integrity, which are known to be particularly vulnerable in diabetes^[27]. Impaired glymphatic clearance may therefore contribute to cognitive dysfunction through disruption of these white-matter-based networks. Additionally, a recent study in stroke populations has shown that ALPS indices measured during the subacute phase were predictive of MoCA outcomes at 90 days, highlighting their potential as a prognostic biomarker for cognitive recovery^[28].

This convergent evidence supports our interpretation that altered perivascular clearance, reflected by a reduced ALPS index, might serve as an early neuroimaging indicator of cognitive vulnerability in T2DM. The absence of significant correlations between ALPS and global cognitive scales in our study may reflect limited statistical power, mild cognitive heterogeneity, and the multifactorial nature of cognitive impairment in diabetes, which involves vascular, metabolic, and inflammatory mechanisms acting in concert. Future longitudinal studies combining ALPS metrics with multimodal imaging and detailed cognitive profiling may clarify the temporal dynamics and mechanistic pathways linking glymphatic dysfunction to cognitive decline in this population.

The glymphatic system is a well-organized cerebrospinal-fluid-interstitial transport system that is responsible for clearing abnormal proteins and metabolites such as amyloid- β , phosphorylated tau, and advanced glycation end products (AGEs), which are known to accumulate in diabetic brains. Its function is impaired with aging and in pathological conditions^[29,30]. Failure of this clearance pathway may accelerate neurotoxic deposition, oxidative injury, and synaptic dysfunction, ultimately impairing cognition.

Several AD studies have shown that lower ALPS indices are associated with greater amyloid and tau burden on PET imaging^[25,31]. These findings raise the possibility that similar mechanisms operate in T2DM, linking impaired glymphatic drainage to the early development of diabetes-related cognitive decline. Chronic hyperglycemia, insulin resistance, and oxidative stress are hallmarks of T2DM and can directly impair microvascular integrity, endothelial function, and blood brain barrier (BBB) permeability^[32]. The pulsatile motion of cerebral arteries is a key driving force of perivascular cerebrospinal fluid (CSF) flow^[4,33].

Diminished vascular compliance in diabetes may therefore attenuate this driving pressure, slowing glymphatic transport and leading to decreased ALPS indices. Experimental studies provide convergent evidence, whereby diabetic rodent models show delayed CSF tracer clearance on DCE-MRI, consistent with reduced glymphatic efficiency^[34]. Endothelial dysfunction and basement membrane thickening in diabetes further narrow perivascular channels, exacerbating glymphatic stagnation. These mechanisms may underlie the observed glymphatic impairment in our cohort.

This study had several limitations:

- (1) This was a single-center study based on a Chinese population and only recruited inpatients with T2DM. The sample size was modest, which may have limited statistical power to detect weaker associations. Our results require validation in a larger and more diverse population;
- (2) The cross-sectional design precludes causal inference; whether reduced ALPS precedes or follows cognitive decline remains uncertain. Longitudinal data will be required to establish predictive validity;
- (3) The ALPS index reflects diffusivity perpendicular to projection and association fibers at a specific periventricular

level and may not represent global glymphatic efficiency. Its value can be affected by local white-matter microstructure, age, and disease-related demyelination, which is worth further study in the future;

- (4) Cognitive assessment in this study focused on conventional neuropsychological tests; incorporating task-based fMRI or network-connectivity analyses could provide a more comprehensive understanding of functional correlates.

5. Conclusion

This study demonstrated that patients with T2DM exhibit reduced DTI-ALPS indices, reflecting impaired glymphatic system function and an altered pattern of hemispheric asymmetry. The lower ALPS values were associated with poorer executive performance, suggesting that glymphatic dysfunction may be linked to specific aspects of cognitive control in T2DM. By applying a non-invasive diffusion-based imaging method, our findings provide supportive evidence that DTI-ALPS can serve as a potential imaging biomarker for assessing glymphatic function in metabolic disorders. Although further longitudinal and mechanistic studies are warranted, these results highlight a possible pathway through which vascular and metabolic disturbances may contribute to cognitive decline. Understanding glymphatic alterations in diabetes may aid in early identification of individuals at higher risk for cognitive impairment and promote the development of targeted prevention and intervention strategies.

Funding

National Natural Science Foundation of China (Project No.: 82170820); Social Development Science and Technology Research Project of Shaanxi Province of China (Project No.: 2023-YBSF-579)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Saeedi P, Petersohn I, Salpea P, et al., 2019, Global and Regional Diabetes Prevalence Estimates for 2019 and Projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract*, 2019(157): 107843.
- [2] Damanik J, Yunir E, 2021, Type 2 Diabetes Mellitus and Cognitive Impairment. *Acta Med Indones*, 53(2): 213–220.
- [3] Moran C, Beare R, Wang W, et al., 2019, Type 2 Diabetes Mellitus, Brain Atrophy, and Cognitive Decline. *Neurology*, 92(8): e823–e830.
- [4] Iliff J, Wang M, Liao Y, et al., 2012, A Paravascular Pathway Facilitates CSF Flow Through the Brain Parenchyma and the Clearance of Interstitial Solutes, Including Amyloid β . *Sci Transl Med*, 4(147): 147.
- [5] Hladky S, Barrand M, 2022, The Glymphatic Hypothesis: The Theory and the Evidence. *Fluids Barriers CNS*, 19(1): 9.
- [6] Bah T, Siler D, Ibrahim A, et al., 2023, Fluid Dynamics in Aging-related Dementias. *Neurobiol Dis*, 2023(177): 105986.
- [7] Lee S, Yoo R, Choi S, et al., 2021, Contrast-Enhanced MRI T1 Mapping for Quantitative Evaluation of Putative Dynamic Glymphatic Activity in the Human Brain in Sleep-Wake States. *Radiology*, 300(3): 661–668.
- [8] Benveniste H, Lee H, Ozturk B, et al., 2021, Glymphatic Cerebrospinal Fluid and Solute Transport Quantified by MRI and PET Imaging. *Neuroscience*, 2021(474): 63–79.

- [9] Taoka, T, Masutani Y, Kawai H, et al., 2017, Evaluation of Glymphatic System Activity with the Diffusion MR Technique: Diffusion Tensor Image Analysis Along the Perivascular Space (DTI-ALPS) in Alzheimer's Disease Cases. *Jpn J Radiol*, 35(4): 172–178.
- [10] Hsu J, Wei Y, Toh C, et al., 2021, Magnetic Resonance Images Implicate That Glymphatic Alterations Mediate Cognitive Dysfunction in Alzheimer Disease. *Ann Neurol*, 93(1): 164–174.
- [11] Toh C, Siow T, 2021, Glymphatic Dysfunction in Patients With Ischemic Stroke. *Front Aging Neurosci*, 2021(13): 756249.
- [12] Kikuta, J, Kamagata K, Taoka T, et al., 2022, Water Diffusivity Changes Along the Perivascular Space After Lumboperitoneal Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus. *Front Neurol*, 2022(13): 843883.
- [13] Song H, Ruan Z, Gao L, et al., 2022, Structural Network Efficiency Mediates the Association Between Glymphatic Function and Cognition in Mild VCI: A DTI-ALPS Study. *Front Aging Neurosci*, 2022(14): 974114.
- [14] Chen Y, Wang M, Su S, et al., 2023, Assessment of the Glymphatic Function in Children with Attention-Deficit/Hyperactivity Disorder. *Eur Radiol*, 34(3): 1444–1452.
- [15] Ma X, Li S, Li C, et al., 2021, Diffusion Tensor Imaging Along the Perivascular Space Index in Different Stages of Parkinson's Disease. *Front Aging Neurosci*, 2021(13): 773951.
- [16] Jayaraj R, Azimullah S, Beiram R, 2020, Diabetes as a Risk Factor for Alzheimer's Disease in the Middle East and its Shared Pathological Mediators. *Saudi J Biol Sci*, 27(2): 736–750.
- [17] Li H, Luo Y, Xu Y, et al., 2018, Meloxicam Improves Cognitive Impairment of Diabetic Rats through COX2-PGE2-EPs-cAMP/pPKA Pathway. *Mol Pharm*, 15(9): 4121–4131.
- [18] Tang Y, Yu C, Wu J, et al., 2018, Lychee Seed Extract Protects Against Neuronal Injury and Improves Cognitive Function in Rats with Type II Diabetes Mellitus with Cognitive Impairment. *Int J Mol Med*, 41(1): 251–263.
- [19] Jash K, Gondaliya P, Kirave P, et al., 2020, Cognitive Dysfunction: A Growing Link Between Diabetes and Alzheimer's Disease. *Drug Dev Res*, 81(2): 144–164.
- [20] Chen R, Shi J, Yin Q, et al., 2018, Morphological and Pathological Characteristics of Brain in Diabetic Encephalopathy. *J Alzheimers Dis*, 65(1): 15–28.
- [21] American Diabetes Association, 2013, Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, 36 Suppl 1(Suppl 1): S67–74.
- [22] Zhang W, Zhou Y, Wang J, et al., 2021, Glymphatic Clearance Function in Patients with Cerebral Small Vessel Disease. *Neuroimage*, 2021(238): 118257.
- [23] Roy B, Lubera V, Sing K, et al., 2025, Glymphatic System Impairment in Type II Diabetes Mellitus Adults. *Res Sq*. <https://doi.org/10.21203/rs.3.rs-6467065/v1>
- [24] Hu P, Zou Y, Zhou M, et al., 2025, Association of Diffusion Tensor Imaging Along the Perivascular Space Index with Cognitive Impairment in Type 2 Diabetes Mellitus. *Quant Imaging Med Surg*, 15(2): 1491–1504.
- [25] Chen Q, Ge D, Xu X, et al., 2025, Glymphatic Function Associates with Alzheimer's Disease-Signature Region Volumes, Plasma Biomarkers and White Matter Hyperintensity Progression in Cognitively Unimpaired Older Adults. *Age Ageing*, 54(6): afaf141.
- [26] Zhang X, Wang Y, Jiao B, et al., 2024, Glymphatic System Impairment in Alzheimer's Disease: Associations with Perivascular Space Volume and Cognitive Function. *Eur Radiol*, 34(2): 1314–1323.
- [27] Zhou C, Li J, Dong M, et al., 2021, Altered White Matter Microstructures in Type 2 Diabetes Mellitus: A Coordinate-Based Meta-Analysis of Diffusion Tensor Imaging Studies. *Front Endocrinol (Lausanne)*, 2021(12): 658198.
- [28] Wang Y, Yang M, Zeng X, et al., 2025, Glymphatic Dysfunction Assessed by DTI-ALPS Index Predicts Early Cognitive Impairment in Acute Subcortical Infarcts: A Prospective Clinical Cohort Study. *Front Neurol*, 2025(16): 1605889.
- [29] Rasmussen M, Mestre H, Nedergaard M, 2018, The Glymphatic Pathway in Neurological Disorders. *Lancet Neurol*,

17(11): 1016–1024.

- [30] Kamagata K, Andica C, Takabayashi K, et al., 2022, Association of MRI Indices of Glymphatic System With Amyloid Deposition and Cognition in Mild Cognitive Impairment and Alzheimer Disease. *Neurology*, 99(24): e2648–e2660.
- [31] Okazawa H, Nogami M, Ishida S, et al., 2024, PET/MRI Multimodality Imaging to Evaluate Changes in Glymphatic System Function and Biomarkers of Alzheimer’s Disease. *Sci Rep*, 14(1): 12310.
- [32] Lashkari A, 2025, The Effects of Diabetes on the Glymphatic System: Recent Advances and Mechanistic Insights. *Cardiovasc Diabetol Endocrinol Rep*, 11(1): 14.
- [33] Iliff J, Wang M, Zeppenfeld D, et al., 2013, Cerebral Arterial Pulsation Drives Paravascular CSF-Interstitial Fluid Exchange in the Murine Brain. *J Neurosci*, 33(46): 18190–9.
- [34] Jiang Q, Zhang L, Ding G, et al., 2017, Impairment of the Glymphatic System After Diabetes. *J Cereb Blood Flow Metab*, 37(4): 1326–1337.

Publisher’s note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Efficacy of External High-Frequency Hyperthermia Combined with Circulating Hyperthermic Perfusion Chemotherapy in the Treatment of Malignant Pleural and Peritoneal Effusions

Aerhengbieke·Tuhanbai, Zixuan Wang, Guohui Sun*

Department of Oncology, The Seventh Affiliated Hospital of Xinjiang Medical University, Urumqi 830028, Xinjiang, China

Copyright: © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To investigate the efficacy and safety of external high-frequency hyperthermia (HCPT) combined with circulating hyperthermic perfusion chemotherapy in the treatment of malignant pleural and peritoneal effusions. *Methods:* A retrospective analysis was conducted on 20 patients with malignant pleural effusions admitted to our hospital from January 2020 to December 2024 as the study group, and 20 patients before 2020 as the control group. Chemotherapy drugs such as doxorubicin hydrochloride injection, vinorelbine injection, and daunorubicin liposome were administered via circulating hyperthermic perfusion chemotherapy. The experimental group also received HCPT combined with hyperthermic perfusion chemotherapy once daily for three consecutive days, with the drug solution changed every three days. The improvement of clinical symptoms and the levels of blood tumor markers were observed. *Results:* The effective rate in the experimental group was 95%, significantly higher than 85% in the control group, but the difference was not statistically significant ($P > 0.05$). The levels of carcinoembryonic antigen (CEA), CA19-9, and CA72-4 significantly decreased compared to pre-treatment levels, with statistically significant differences ($P < 0.05$). Additionally, indicators such as serum lactate dehydrogenase (LDH), AST/ALT, and INR showed no correlation with changes in tumor marker levels ($P > 0.05$). *Conclusion:* HCPT combined with hyperthermic perfusion chemotherapy demonstrates favorable efficacy and safety in the treatment of malignant pleural and peritoneal effusions.

Keywords: External high-frequency hyperthermia; circulating hyperthermic perfusion chemotherapy; malignant pleural and peritoneal effusions

Online publication: September 26, 2025

1. Introduction

As living standards improve, the incidence of malignant tumors has been increasing year by year. Malignant pleural and peritoneal effusions are among the most common complications of malignant thoracic and peritoneal diseases. Pulmonary metastases account for approximately 40% of cases, with pleural effusions in non-small cell lung cancer patients often resulting from pulmonary overinflation due to pulmonary failure, pulmonary venous hypertension, and increased

capillary pressure^[1]. Metastases to organs such as the pancreas, bile ducts, prostate, and colorectum can lead to peritoneal effusions. Clinically, effusions are classified into primary and secondary categories based on their origin. Primary pleural and peritoneal effusions are primarily caused by tumors, while secondary effusions may be related to trauma, infection, autoimmune diseases, or genetic factors^[2]. Currently, there are multiple methods for treating malignant thoracic and abdominal cavity effusions, including chemotherapy, surgical resection, minimally invasive drainage, and percutaneous needle aspiration, among others. However, all these methods have certain drawbacks. For instance, they may fail to achieve effective therapeutic doses during treatment, leading to rapid proliferation of tumor cells^[3]. Traditional drainage methods often require repeated punctures, increasing the risk of infection. Additionally, aspiration may inadvertently remove tumor tissue, disrupting the tumor's immune microenvironment^[4]. Extracorporeal high-frequency hyperthermia (high-frequency focused therapy, HCPT) is a safe and effective physical treatment for malignant tumors. By heating the body externally to around 50°C, it induces tumor cell death and releases a large amount of heat shock proteins, activating lymphocytes and macrophages, enhancing the body's immune function, and thereby achieving the goal of killing tumor cells^[5]. This study explored the efficacy and safety of HCPT combined with cyclic hyperthermic perfusion chemotherapy in 20 patients with malignant thoracic and abdominal cavity effusions. The findings are reported as follows:

2. Materials and Methods

2.1. General Information

A retrospective analysis was conducted on 20 patients with malignant abdominal cavity effusions admitted to our hospital from January 2020 to December 2024, serving as the study group. This group included 12 males and 8 females, aged between 48 and 79 years, with an average age of (60.41±11.22) years. Another 20 patients treated before 2020 were selected as the control group, comprising 11 males and 9 females, aged between 46 and 71 years, with an average age of (61.01±11.11) years. All patients met the following criteria: ① Diagnosis of malignant thoracic and abdominal cavity effusions confirmed by chest CT and abdominal B-ultrasound; ② Confirmed by thoracic or abdominal cavity puncture aspiration. Exclusion criteria included: ① Patients with cardiopulmonary insufficiency; ② Patients with concurrent malignancies in other organs; ③ Pregnant or lactating women; ④ Patients with severe infections or other serious diseases.

2.2. Treatment Methods

① Control Group: Patients received cyclic hyperthermic perfusion chemotherapy using chemotherapeutic agents such as doxorubicin hydrochloride injection, vinorelbine injection, and daunorubicin liposome. ② Experimental Group: Under ultrasound guidance, a puncture needle was inserted into the patient's thoracic or abdominal wall skin, and effusion was aspirated for HCPT treatment. In the control group, after hyperthermic perfusion, patients received routine chemotherapy with chemotherapeutic drugs such as Doxorubicin Hydrochloride Injection, Vinorelbine Injection, and Daunorubicin Liposome, administered once daily for four consecutive weeks. In the experimental group, patients underwent HCPT combined with hyperthermic perfusion chemotherapy once daily for three consecutive days, with the medication changed every three days.

2.3. Observation Indicators

(1) Improvement in clinical symptoms: The degree of symptom improvement was evaluated based on the patients' clinical manifestations upon admission, categorized into three levels: improvement, stabilization, and worsening; (2) Blood tumor marker levels: Monitoring the changes in serum carcinoembryonic antigen (CEA), CA19-9, and CA72-4 markers before and after treatment, as well as LDH (U/L), AST/ALT, and INR, and comparing the differences between the two groups.

2.4. Statistical Methods

Data analysis was performed using SPSS software. Measurement data were expressed as mean ± standard deviation (\bar{x}

$\pm s$), and comparisons between the two groups were made using the t-test. Count data were expressed as frequencies and percentages, and comparisons between groups were made using the χ^2 test. A P-value < 0.05 was considered statistically significant.

3. Results

3.1. Clinical Efficacy Rate

The efficacy rate in the experimental group was 95%, significantly higher than the 85% in the control group, but the difference was not statistically significant ($P > 0.05$), as shown in **Table 1**.

Table 1. Comparison of Clinical Symptom Improvement Between the Two Groups [n(%)]

Group	n	Improved	Stable	Worsened	Effective Rate
Experimental Group	20	16 (80.00)	3 (15.00)	1 (5.00)	19 (95.00)
Control Group	20	10 (50.00)	7 (35.00)	3 (15.00)	17 (85.00)
χ^2					0.278
P-value					0.598

3.2. Serum Tumor Markers in Both Groups

The levels of carcinoembryonic antigen (CEA), CA19-9, and CA72-4 showed a significant decrease compared to pre-treatment levels, with statistically significant differences ($P < 0.05$). Additionally, serum lactate dehydrogenase (LDH), AST/ALT, INR, and other indicators showed no correlation with changes in tumor marker levels ($P > 0.05$). See **Table 2**.

Table 2. Serum Tumor Markers

Group		Experimental Group (n=20)	Control Group (n=20)	t	P
CEA($\mu\text{g/L}$)	Before treatment	28.56 \pm 12.34	27.89 \pm 11.97	0.194	0.847
	After treatment	8.23 \pm 3.45	15.67 \pm 6.78	4.672	<0.001
CA19-9(U/mL)	Before treatment	356.78 \pm 145.23	342.56 \pm 138.67	0.332	0.741
	After treatment	89.45 \pm 32.12	156.34 \pm 58.90	5.123	<0.001
CA72-4(U/mL)	Before treatment	45.67 \pm 18.34	43.89 \pm 17.56	0.321	0.750
	After treatment	12.34 \pm 5.67	22.45 \pm 9.12	4.289	<0.001
LDH(U/L)	Before treatment	285.34 \pm 76.45	278.90 \pm 72.34	0.287	0.775
	After treatment	240.12 \pm 65.78	255.67 \pm 68.90	0.756	0.453
AST/ALT	Before treatment	1.23 \pm 0.45	1.19 \pm 0.43	0.312	0.757
	After treatment	1.18 \pm 0.39	1.21 \pm 0.41	0.267	0.790
INR	Before treatment	1.05 \pm 0.12	1.03 \pm 0.11	0.602	0.550
	After treatment	1.02 \pm 0.10	1.04 \pm 0.09	0.712	0.480

4. Discussion

Malignant pleural and peritoneal effusion refers to the accumulation of fluid within the thoracic and abdominal cavities

caused by malignant tumors, which usually already exists when symptoms manifest. Malignant pleural effusion can present as unilateral or bilateral effusion, while peritoneal effusion manifests as fluid accumulation in multiple parts of the body. Patients often experience clinical symptoms such as chest tightness and shortness of breath, which severely impact their quality of life^[6]. Currently, the treatment methods for malignant pleural and peritoneal effusion include conservative and surgical approaches. Conservative treatment primarily involves diuresis, antibiotic therapy for infection control, thoracentesis for fluid drainage, and conservative medical supportive care. However, these methods often struggle to effectively control the volume and quantity of the effusion and may lead to complications^[7]. For certain patients, especially those with advanced-stage tumors, surgical resection of the tumor often fails to completely cure the disease, and the postoperative recurrence rate is high^[8]. Hyperthermia can inhibit tumor cell proliferation and induce apoptosis, while also creating a pronounced hypoxic microenvironment within the tumor tissue. This, in turn, reduces the tumor cells' resistance to chemotherapy drugs and enhances the efficacy of chemotherapy^[9]. The hypoxic effect induced by hyperthermia promotes endogenous angiogenesis, increases local blood perfusion, and improves microcirculation. It also stimulates the release of tumor necrosis factors, enhances the body's immune function, and promotes tumor cell apoptosis, thereby strengthening the body's anticancer capabilities^[10]. Therefore, combining hyperthermia with chemotherapy can improve treatment outcomes.

Currently, surgical treatment is the primary approach for malignant pleural and peritoneal effusion, but it can have varying impacts on postoperative recovery depending on the location of the tumor. In recent years, with advancements in imaging technology and minimally invasive treatment techniques, extracorporeal circulation perfusion combined with hyperthermia for the treatment of pleural and peritoneal effusion has garnered increasing attention. Hyperthermic chemoperfusion therapy (HCPT) is a treatment modality characterized by its broad therapeutic scope and favorable efficacy. Clinically, it can be applied to the treatment of various diseases, including pleural effusion or ascites caused by tumors^[11]. The results of this study indicate that compared to hyperthermic lavage alone, the combination of HCPT with chemotherapy significantly improves the effective rates for treating both pleural and peritoneal effusion, with statistically significant differences. This suggests that HCPT combined with hyperthermic perfusion chemotherapy exhibits high efficacy in the treatment of malignant pleural and peritoneal effusion.

This study found that compared with chemotherapy alone, the therapeutic effect of EHT combined with CTX hyperthermic perfusion chemotherapy was superior, possibly due to the following advantages of this therapy: ① The combined use of EHT and hyperthermic perfusion chemotherapy not only leverages the benefits of EHT treatment but also compensates for the shortcomings of chemotherapy alone, fully exerting its anti-tumor effects; ② Hyperthermia can increase drug concentration, enhance the efficacy of chemotherapy, and avoid the toxic side effects of chemotherapy; ③ EHT can increase vascular permeability, allowing drugs to penetrate into tissue spaces, while hyperthermic perfusion chemotherapy enhances drug penetration. The combined application of the two can improve the sensitivity of tumor cells to chemotherapy drugs and increase the effectiveness of chemotherapy; ④ Both EHT and hyperthermic perfusion chemotherapy can alleviate adverse reactions such as myelosuppression, nausea, and vomiting caused by chemotherapy, reducing the incidence of complications. The combined application of the two is beneficial for ensuring the smooth progress of chemotherapy.

Although EHT treatment offers numerous advantages, it also has certain limitations. For instance, the thermal effect is not adjustable, and temperatures that are too high or too low can affect the therapeutic outcome. Temperatures that are too low are not conducive to killing cancer cells, while temperatures that are too high can disrupt the body's internal environment. Therefore, it is necessary to select an appropriate temperature based on the patient's specific condition to achieve the best therapeutic effect. Additionally, the cost of this therapy is relatively high, and for patients with financial difficulties, careful consideration is required. Therefore, the clinical sector should strengthen the promotion of EHT technology and vigorously disseminate relevant knowledge to benefit a broader range of patients. Due to the small sample size in this study, further validation with an increased sample size is needed, as no significant differences in clinical effectiveness were observed.

In summary, malignant thoracic and abdominal effusions are a common clinical pathological condition with poor prognosis due to the lack of effective treatment options. Research has shown that EHT can enhance the sensitivity of tumor cells to chemotherapy drugs, improve patients' quality of life, and prolong survival.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Wang L Y, Fu X J, 2024, Comparative efficacy of cell block paraffin-embedded sections and cell smears in differentiating benign from malignant pleural and peritoneal effusions. *Guizhou Medical Journal*, 48(11): 1815-1817.
- [2] Wu Y R, Li J, Wang D K, 2024, Exploring the treatment of malignant pleural and peritoneal effusions from the perspective of the triple burner theory. *Henan Traditional Chinese Medicine*, 44(10): 1502-1506.
- [3] Zhou Y, 2024, Clinical efficacy analysis of Endostar and/or combined with cisplatin in the treatment of malignant pleural and peritoneal effusions. Jilin Province, Jilin Provincial People's Hospital.
- [4] Li H J, Liu L, Liao W L, 2023, Application of modified agar embedding method in the differential diagnosis of benign and malignant pleural and peritoneal effusions. *China Modern Medicine*, 30(36): 141-144.
- [5] Jiang X, Huang J H, 2023, Observation of the efficacy of hyperthermic perfusion, bevacizumab combined with cisplatin in the treatment of malignant pleural and peritoneal effusions in gynecological tumors. *Practical Journal of Gynecological Endocrinology Electronic Edition*, 10(24): 49-51.
- [6] Zhu S Q, 2023, Analysis of the application value of biochemical indicators and tumor marker tests in the diagnosis of pleural and peritoneal effusions. *China Modern Medicine Application*, 17(15): 73-76.
- [7] Li R L, Su Y, Lei L X, 2022, Current research status of external treatment methods of traditional Chinese medicine for malignant tumor-induced pleural and peritoneal effusions. *Medical Information*, 35(24): 183-185.
- [8] Wang T, Tian K, Liu Y T, 2022, Retrospective study on the treatment of malignant pleural and peritoneal effusions with *Pseudomonas aeruginosa* injection combined with deep hyperthermia. *Biomedical Translation*, 3(01): 70-74.
- [9] Mo G R, 2021, Efficacy and safety analysis of hyperthermic intraperitoneal chemotherapy in the treatment of patients with malignant pleural (peritoneal) effusions. *Medical Nutrition and Health*, 19(09): 44-45.
- [10] Li H C, Zhou L X, Zou H, 2021, Clinical efficacy and impact on quality of life of hyperthermic intraperitoneal chemotherapy (HGGZ-102 hyperthermic intraperitoneal chemotherapy machine) in patients with malignant pleural and peritoneal effusions. *Harbin Medical Journal*, 41(02): 71-72.
- [11] Zhang X J, 2017, Observation of the efficacy of external high-frequency deep hyperthermia combined with cyclic hyperthermic perfusion chemotherapy in the treatment of malignant pleural effusions. *Electronic Journal of Clinical Medical Literature*, 4(18): 3421.

Publisher's note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.