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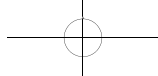
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Journal of Clinical and Nursing Research

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

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Analysis of the Effects of Combined Spinal-Epidural Anesthesia and Epidural Anesthesia in Appendicitis Surgery at Primary Hospitals

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Abstract: *Objective:* To analyze the effects of combined spinal-epidural anesthesia and epidural anesthesia in patients undergoing appendicitis surgery. *Methods:* Seventy-eight patients who underwent surgical treatment for appendicitis from February 2022 to February 2025 were selected as samples and randomly divided into two groups. The study group received combined spinal-epidural anesthesia, while the control group received epidural anesthesia. Anesthesia indicators, vital signs, and complication indicators were compared between the two groups. *Results:* The onset time of anesthesia in the study group was shorter than that in the control group, the visual analog scale (VAS) score was lower than that in the control group, and the highest plane of anesthesia block was lower than that in the control group ($P < 0.05$). At 15 minutes after anesthesia induction and at the end of surgery, the heart rate (HR), mean arterial pressure (MAP), and blood oxygen saturation (SPO2) in the study group were significantly different from those in the control group ($P < 0.05$). The complication rate in the study group was lower than that in the control group ($P < 0.05$). *Conclusion:* Combined spinal-epidural anesthesia for appendicitis surgery can reduce the impact of anesthesia on vital signs, shorten the onset time of anesthesia, and is highly effective and feasible.

Keywords: Appendicitis surgery; Epidural anesthesia; Combined spinal-epidural anesthesia; Pain

Online publication: July 2, 2025

1. Introduction

Appendicitis is a relatively common disease among surgical acute abdominal conditions, often presenting with metastatic right lower abdominal pain accompanied by symptoms such as nausea, vomiting, fever, and chills. It is associated with factors like infection and obstruction. Surgical treatment is frequently used for appendicitis, but invasive procedures can exacerbate pain, leading to reduced patient cooperation during surgery. Therefore, it is crucial to perform perioperative anesthesia effectively. Epidural anesthesia is a commonly used anesthetic technique in appendicitis surgery, but it has issues such as long block induction time and incomplete block^[1]. Combined spinal-epidural anesthesia, on the other hand, is a modern anesthetic technique that can shorten the onset time of anesthetics and maintain stable vital signs during surgery. Based on this, this study explores the

value of combined spinal-epidural anesthesia using a sample of 78 patients who underwent surgical treatment for appendicitis from February 2022 to February 2025.

2. Materials and methods

2.1. Materials

A total of 78 patients who underwent surgical treatment for appendicitis from February 2022 to February 2025 are selected as the sample and randomly divided into groups. The appendicitis data of the study group are compared with those of the control group ($P > 0.05$), as shown in **Table 1**.

Table 1. Analysis of appendicitis data

Group	n	Gender(%)		Age (years)		Weight(kg)		ASA Classification	
		Male	Female	Range	Mean	Range	Mean	Grade I	Grade II
Research Group	39	21 (53.85)	18 (46.15)	19–58	49.11 ± 2.09	56–72	66.18 ± 2.28	24(61.54)	15(38.46)
Control Group	39	22 (56.41)	17 (43.59)	19–57	49.18 ± 2.11	56–71	66.21 ± 2.31	25(64.10)	14(35.90)
χ^2/t	-	0.0518		0.1472		0.0577		0.0549	
P	-	0.8199		0.8834		0.9541		0.8148	

2.2. Inclusion and exclusion criteria

The inclusion criteria of the study are: (1) Acute appendicitis confirmed by ultrasound, CT, or pathology; (2) Signed informed consent by the patient or family members; (3) Presence of symptoms such as metastatic right lower abdominal pain, tenderness or rebound pain at McBurney's point; (4) Presence of surgical indications; (5) Adult patients aged ≥ 18 years.

Meanwhile, the exclusion criteria are: (1) Abnormal coagulation system; (2) Cardiovascular disease; (3) Liver and kidney disease; (4) Poor tolerance to ropivacaine; (5) Pregnancy or high surgical difficulty, combined with other infections; (6) Patients undergoing complex and non-surgical treatment.

2.3. Methods

2.3.1. Control group

The epidural puncture point is determined at the T12–L1 intervertebral space. After successful puncture and catheter placement, patients are placed in a supine position. A Around 3–5 ml of 2% lidocaine hydrochloride is injected. If no discomfort occurred after 5 minutes, 8–10 ml of 2% lidocaine is injected, and additional anesthetics are administered based on the surgical requirements for appendicitis.

2.3.2. Observation group

Combined spinal-epidural anesthesia is performed. Based on the epidural anesthesia procedure, a spinal needle is inserted through the L3–4 intervertebral space, and cerebrospinal fluid is allowed to flow out. A mixture of 2ml of 0.75% ropivacaine and 10% glucose solution is injected at a controlled injection speed of 0.2ml/s to maintain the T6 anesthesia level. The anesthetic dose is adjusted based on the surgical requirements for appendicitis.

2.4. Observation indicators

- (1) Anesthesia indicators: Record the onset time of anesthesia, VAS score (0 for no pain, 10 for severe pain, with the score proportional to the level of pain), and the highest plane of anesthesia blockade (determined by pinprick pain measurement before the start of surgical operation but after the onset of anesthesia).
- (2) Vital signs: Monitor HR, MAP, and SPO₂ indicators before anesthesia, 15 minutes after anesthesia, and at the end of surgery.
- (3) Complications: Record hypotension, lower back pain, nausea and vomiting, and headache.

2.5. Statistical analysis

SPSS 23.0 is used to process the data. The χ^2 test is used for counting data (recorded as %), and the t-test is used for measurement indicators (recorded as $\bar{x} \pm s$). Statistical significance is set at $P < 0.05$.

3. Results

3.1. Anesthesia indicators

The study group had a shorter onset time of anesthesia, lower VAS score, and lower highest plane of anesthesia blockade compared to the control group, with $P < 0.05$. The result is shown in **Table 2**.

Table 2. Anesthesia indicators ($\bar{x} \pm s$)

Group	Anesthesia onset time (min)	VAS score (points)	Maximum anesthesia block level (cm ²)
Research group ($n=39$)	2.12 ± 0.42	2.14 ± 0.48	5.64 ± 0.21
Control group ($n=39$)	5.11 ± 0.69	4.33 ± 0.69	7.11 ± 0.36
t	23.1160	16.2712	22.0267
P	0.0000	0.0000	0.0000

3.2. Vital signs indicators

At 15 minutes after anesthesia and at the end of surgery, there were differences in HR, MAP, and SPO₂ indicators between the study group and the control group. The study group showed smaller changes and more stable vital signs, with $P < 0.05$. The results are shown in **Table 3**.

Table 3. Vital signs indicators ($\bar{x} \pm s$)

Group	HR(times/min)			MAP(mmHg)			SPO ₂ (%)		
	Pre-anesthesia	15 min after anesthesia	End of surgery	Pre-anesthesia	15 min after anesthesia	End of surgery	Pre-anesthesia	15 min after anesthesia	End of surgery
Research group ($n=39$)	76.29 ± 1.25	68.41 ± 1.05	69.11 ± 1.11	93.18 ± 2.43	81.46 ± 1.25	83.16 ± 1.42	97.48 ± 1.81	93.41 ± 1.57	95.42 ± 1.72
Control group ($n=39$)	76.31 ± 1.26	75.25 ± 1.13	78.43 ± 1.32	93.21 ± 2.45	86.49 ± 1.68	89.62 ± 1.78	97.52 ± 1.83	90.18 ± 1.36	93.68 ± 1.44
t	0.0704	27.6920	33.7475	0.0543	15.0010	17.7174	0.0971	9.7111	4.8441
P	0.9441	0.0000	0.0000	0.9568	0.0000	0.0000	0.9229	0.0000	0.0000

3.3. Complication indicators

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

Table 4. Complication indicators (n,%)

Group	Hypotension	Lower back pain	Nausea and vomiting	Headache	Incidence rate
Research group ($n=39$)	1(2.56)	0(0.00)	0(0.00)	0(0.00)	1(2.56)
Control group ($n=39$)	2(5.13)	2(5.13)	1(2.56)	1(2.56)	6(15.38)
X^2	-	-	-	-	3.9235
P	-	-	-	-	0.0476

4. Discussion

The inducements of appendicitis are mainly related to factors such as bacterial infection, obstruction of the appendiceal lumen, and congenital malformations of the appendix. It often occurs acutely, and its pathological feature is severe lower abdominal pain. In addition, if acute appendicitis is not treated early, it can progress to chronic appendicitis. Surgery is often used to treat appendicitis clinically, but surgical resection can exacerbate the patient's pain and even cause a series of discomforting symptoms. Therefore, attention should be paid to the management of anesthesia for appendicitis, and anesthetic methods should be reasonably selected to alleviate the patient's pain. Epidural anesthesia has a high application rate in appendicitis surgery. Injecting anesthetic drugs through the dura mater into the yellow ligament space can anesthetize the nerve roots in the target area. Moreover, the epidural space and cranial cavity in the human body are not connected, so the injection of anesthetic drugs will not cause paralysis of the medulla oblongata^[2].

However, it should be noted that patients receiving epidural anesthesia may experience myocardial inhibition and vasodilation due to the anesthetic effect on sympathetic nerves, increasing the risk of intraoperative bradycardia and hypotension. Additionally, epidural anesthesia alone cannot block the vagus nerve. Therefore, surgical exploration of the appendix can stimulate the muscles, leading to problems such as increased muscle tone, pain, and vomiting. To ensure the smooth progress of surgical operations, the dosage of anesthetic drugs should be increased, highlighting the limitations of epidural anesthesia alone^[3]. Subarachnoid anesthesia refers to the injection of anesthetic drugs into the subarachnoid space before appendicitis surgery to block nerve tissue, which can shorten the onset time of anesthesia.

However, during lumbar anesthesia, there is a risk of cerebrospinal fluid leakage due to the puncture of the dura mater, increasing the risk of post-anesthesia headache. Additionally, it is not possible to adjust the drug dosage intraoperatively according to the patient's actual needs during lumbar anesthesia alone^[4]. In recent years, combined spinal-epidural anesthesia has gradually been used in perioperative anesthesia for appendicitis, integrating the advantages of both techniques. This approach can enhance the anesthetic effect, reduce the drug dosage, shorten the onset time of anesthetic blockade, and ensure high safety. It can also avoid the problem of physiological muscle tone increase caused by intraoperative traction. Furthermore, during combined spinal-epidural anesthesia, anesthetic drugs quickly reach the spinal nerve roots to provide analgesia, shortening the onset time of anesthesia. It can also relax abdominal muscles and muscles adjacent to the appendix, facilitating surgical operations and reducing unnecessary intraoperative injuries^[5].

Based on the data analysis in this paper, the anesthesia onset time of the study group was shorter than

that of the control group, the VAS score was lower than that of the control group, and the highest level of anesthesia block was lower than that of the control group, with $P < 0.05$. The reason for this is that patients with appendicitis receiving epidural anesthesia alone can experience analgesia after the injection of anesthetics, but it can easily induce vasodilation issues. Additionally, under the influence of myocardial depression, problems such as bradycardia and hypotension are likely to occur. Moreover, epidural anesthesia does not block the vagus nerve, so when the surgeon explores the appendix, it can increase reflex muscle tone, leading to a weakening of the analgesic effect, requiring continuous addition of anesthetics to ensure the smooth progress of the surgical operation. The combination of spinal and epidural anesthesia integrates the advantages of both methods.

During spinal anesthesia, the anesthetic enters the subarachnoid space and directly contacts nerve fibers to exert its effect, which can reduce the onset time of the anesthetic ^[6]. The subarachnoid space is relatively closed, allowing the anesthetic to quickly spread to adjacent nerve fibers after injection. Furthermore, due to the fluidity of cerebrospinal fluid, the anesthetic can spread with it, further reducing the onset time. Additionally, during combined spinal and epidural anesthesia, the active ingredients of the anesthetic directly block the spinal nerve roots, enhancing the analgesic effect in the surgical area. The surgeon can flexibly adjust the level of anesthesia by adjusting the dose and administration speed of the anesthetic, which can avoid the risk of complications caused by excessively high anesthesia levels ^[7]. Another set of data showed that at 15 minutes after anesthesia and at the end of the surgery, there were significant differences in HR, MAP, and SPO2 between the study group and the control group ($P < 0.05$), indicating more stable vital signs in the combined spinal and epidural anesthesia group. This is because combined spinal and epidural anesthesia has a high application rate in spinal block, facilitating anesthesiologists to adjust the anesthesia level and enhance the analgesic effect.

Additionally, the combined block has a slight sympatholytic effect, which facilitates surgical operations and results in more stable patient vital signs. During combined spinal and epidural anesthesia, ropivacaine is often chosen for anesthesia. Its chemical structure is similar to that of bupivacaine, but it has a more durable anesthetic effect. As an amide local anesthetic, it can exert a sensory-motor blockade effect, which is beneficial for reducing complications in the circulatory and respiratory systems, resulting in higher medication safety ^[8]. Finally, data showed that the postoperative complication rate of appendicitis in the study group was lower than that in the control group ($P < 0.05$). The reason for this is that combined spinal and epidural anesthesia allows surgeons to flexibly adjust the anesthesia level, reducing the incidence of hypotension caused by abnormal increases in anesthesia level. The active ingredients of the combined anesthesia exert their effects at the spinal cord and spinal nerve roots, which can reduce traction on nerve roots during appendectomy and relax muscles, thereby reducing the risk of lower back pain. The rapid onset of combined anesthesia can also reduce stress responses, stabilize the neuroendocrine system, and slow down gastrointestinal contractions, thereby reducing the incidence of nausea and vomiting ^[9].

In addition, combined anesthesia can reduce cerebrospinal fluid loss and stabilize intracranial pressure, thereby reducing postoperative headache. Furthermore, the low dose of medication used in combined spinal and epidural anesthesia can reduce the paralysis of sympathetic nerves caused by induction drugs, further reducing the risk of anesthetic adverse reactions and enhancing the safety of appendicitis surgery ^[10]. However, regardless of the anesthesia method chosen, there are anesthesia risks involved in appendicitis surgery. In this study, one patient in the combined spinal and epidural anesthesia group experienced hypotension. This occurred when lidocaine was injected into the subarachnoid space, resulting in a rapid decrease in blood pressure. The injection of the anesthetic was immediately suspended, and the patient was treated with vasopressors and fluid replacement, resulting in

gradual stabilization of blood pressure. After reducing the dose of lidocaine, the anesthesia was completed without further hypotension issues. This case of hypotension may be related to an excessively high anesthesia level, where the active ingredients of lidocaine rapidly spread with the cerebrospinal fluid, leading to widespread sympathetic nerve block, abnormal cardiovascular compensation, subsequent bradycardia, and rapid blood pressure decrease.

To ensure the effectiveness of combined spinal and epidural anesthesia, it is necessary to guide patients with appendicitis to fast for 6–8 hours before surgery to prevent perioperative aspiration and vomiting events. Anesthesia operations should be performed following aseptic principles to prevent perioperative infections. Gentle and slow puncture operations should be performed to protect nerve roots and the spinal cord as much as possible, and the depth and direction of the puncture needle should be adjusted based on actual conditions to ensure that the anesthetic reaches the subarachnoid space and epidural space smoothly. After completing the anesthesia operation, electrocardiographic monitoring should be performed, and changes in HR, MAP, SPO₂, and other indicators should be recorded.

5. Conclusion

In summary, the use of combined spinal and epidural anesthesia in patients undergoing appendicitis surgery can stabilize vital signs, shorten the onset time of anesthesia, enhance the analgesic effect, and reduce anesthetic adverse reactions, making it worthy of promotion.

Disclosure statement

The author declares no conflict of interest.

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Analysis of the Impact of Predictive Rehabilitation Nursing Model on the Quality of Emergency Transport for Patients with Acute Cerebral Hemorrhage

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Abstract: *Objective:* To analyze the impact of the predictive rehabilitation nursing model on the quality of emergency transport and rehabilitation outcomes for patients with acute cerebral hemorrhage (ICH). *Methods:* A total of 62 patients with acute cerebral hemorrhage admitted to the hospital from January 2022 to December 2024 were selected as the study subjects. The observation group ($n = 31$) received conventional nursing combined with the predictive rehabilitation nursing model during the emergency process, while the control group ($n = 31$) received conventional nursing. The recovery conditions (Fuel-Meyer Assessment (FMA) score, Barthel Index (BI)), incidence of complications, nursing satisfaction, and time to regain consciousness were compared between the two groups. *Results:* After the intervention, the FMA and BI scores of the observation group were significantly higher than those of the control group, with statistically significant differences. The incidence of complications in the observation group was significantly lower than that in the control group. In terms of nursing satisfaction, the scores of various indicators in the observation group were higher than those in the control group, with statistically significant differences. The time to regain consciousness in the observation group was (48.72 ± 11.76) minutes, compared to (64.29 ± 14.58) minutes in the control group, with the observation group regaining consciousness earlier than the control group. *Conclusion:* The application of the predictive rehabilitation nursing model in the emergency transport process of patients with acute cerebral hemorrhage can reduce the incidence of complications, shorten the duration of consciousness disorder, improve the quality of transport, and enhance functional rehabilitation levels.

Keywords: Predictive rehabilitation nursing model; Acute cerebral hemorrhage; Functional rehabilitation; Quality of transport; Nursing satisfaction

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1. Introduction

Acute cerebral hemorrhage (ICH) is a sudden and severe cerebrovascular disease characterized by high incidence, high mortality, and high disability rates^[1]. Patients in the early stages of onset require prompt professional medical treatment to reduce the risk of death and disability^[2, 3]. Timely and safe transport to medical institutions with appropriate treatment capabilities is crucial in the management of patients with acute cerebral hemorrhage^[4]. Various risks and complications may arise during the transport process, necessitating close monitoring and timely intervention by professional nursing staff^[5–7]. The predictive nursing model is a patient-centered approach that emphasizes assessment and intervention before patient needs arise, aiming to prevent potential problems and complications, thereby improving transport quality and patient satisfaction^[8].

Acute cerebral hemorrhage is a severe medical condition that requires rapid and accurate diagnosis and treatment, as well as high-quality early rehabilitation and nursing intervention^[9]. During the emergency transport of patients with acute cerebral hemorrhage, the predictive rehabilitation nursing model may positively impact the quality of transport, patient nursing satisfaction, and subsequent functional rehabilitation^[10, 11]. Based on this, this study selected 62 patients with acute cerebral hemorrhage within the time frame from January 2022 to December 2024, aiming to analyze the impact of applying the predictive rehabilitation nursing model in the emergency process of patients with acute cerebral hemorrhage.

2. Materials and methods

2.1. General information

From January 2022 to December 2024, sixty-two patients with acute cerebral hemorrhage who are admitted to the emergency department of the hospital are selected as study subjects. They are divided into two groups based on whether the predictive rehabilitation nursing model is applied. The control group consisted of 31 patients (18 males and 13 females) aged between 50 and 73 years (mean age 61.28 ± 2.83 years) with hematoma volumes ranging from 22 to 37 mL (mean volume 30.28 ± 2.81 mL). The observation group also consisted of 31 patients (19 males and 12 females) aged between 51 and 74 years (mean age 61.47 ± 2.62 years) with hematoma volumes ranging from 21 to 36 mL (mean volume 30.13 ± 2.62 mL). The baseline characteristics (gender, age, hematoma volume) of the two groups are comparable ($P > 0.05$). This study complies with the Helsinki Declaration and has been approved by the Medical Ethics Committee of the hospital (2020023I-C2).

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Diagnosed with intracerebral hemorrhage (ICH) by cranial MRI.
- (2) Onset time ≤ 72 hours.
- (3) Informed consent from the patient's family.

2.2.2. Exclusion criteria

- (1) Cerebral hemorrhage caused by non-vascular factors such as vascular malformations.
- (2) Presence of mental illness or cognitive impairment.
- (3) Incomplete clinical data.

2.3. Methods

2.3.1. Control group

Patients in the control group received routine nursing care. Assist patients to turn over every 2–4 hours without pulling or dragging them. Massage limbs and provide oxygen therapy, adjusting the oxygen flow rate as needed. Clear respiratory secretions to ensure smooth breathing. Monitor blood oxygen saturation, blood pressure, heart rate, and body temperature. If the patient has a fever, use physical cooling methods such as a warm water bath. If ineffective, administer antipyretic drugs. Observe for abnormal pulse, elevated blood pressure, and abnormal pupils, and provide dehydration and intracranial pressure reduction treatment if necessary. During the acute phase, patients should consume low-fat, high-calorie, and high-quality protein foods, with strict control of sodium intake. If the patient is comatose, provide nasogastric feeding. Observe the color and characteristics of vomit and stool, assess skin condition, and clean the skin with warm water. Properly secure drainage tubes, check for patency, and record the characteristics of the drainage fluid. If the patient is agitated, provide sedation. Educate the family about cerebral hemorrhage using simple language and appropriate images, explain the rescue process, soothe family emotions, inform them of the patient's condition, and provide case studies.

2.3.2. Observation group

In addition to routine care, patients received predictive rehabilitation nursing intervention. Pre-emergency risk assessment and contingency planning. For consciousness status, the Glasgow Coma Scale (GCS) is commonly used to quickly assess the degree of consciousness impairment by observing the patient's eye-opening, verbal, and motor responses. Vital signs monitoring focuses on blood pressure, heart rate, respiratory rate, and body temperature, with sudden or unstable blood pressure and abnormal heart rate indicating the severity of the condition. The assessment of bleeding volume can be preliminarily judged through on-site symptoms and subsequent imaging examinations, such as severe headache and frequent vomiting, often indicating a large amount of bleeding.

Personalized transport plans need to be designed based on the assessment results. If the patient is unconscious and has unstable breathing, a portable ventilator is required; if there are significant blood pressure fluctuations, antihypertensive or pressor medications should be prepared. Emergency transport process optimization and complication prevention. Preparatory work before transport is the foundation for ensuring patient safety. Equipment checks include various instruments in the ambulance, such as ECG monitors, defibrillators, and suction devices, to ensure their good performance. Medication preparation should be comprehensive, including hemostatic drugs, antihypertensive drugs, and dehydrating agents.

Airway management is crucial. According to cardiopulmonary rehabilitation principles, the patient's head should be turned to one side, and oral secretions should be cleared in time to prevent aspiration. If necessary, an oropharyngeal airway or endotracheal intubation should be placed. Intracranial pressure control can be achieved by elevating the head of the bed by about 30° and administering dehydrating agents such as mannitol to reduce intracranial pressure. There are many risks during transport, such as sudden brain herniation and asphyxia. For brain herniation, if the patient exhibits symptoms like unilateral pupil dilation and worsening consciousness impairment, rapid intravenous infusion of mannitol should be administered, and transport speed should be increased. For asphyxia risk, continuous monitoring of the patient's breathing is necessary, and if asphyxia occurs, suction and cardiopulmonary resuscitation should be performed promptly.

A detailed framework for multi-system collaborative rehabilitation nursing should emphasize coordinated

care across key physiological systems. Respiratory support, circulatory monitoring, and skin protection need to be coordinated. Respiratory support involves adjusting the oxygen delivery method and concentration based on the patient's respiratory status, and mechanical ventilation may be used if necessary; circulatory monitoring involves continuous attention to blood pressure, heart rate, and blood oxygen saturation, with timely adjustments to the dosage of vasoactive drugs. Skin protection involves measures such as regular turning and using pressure-relieving mattresses to prevent pressure ulcers.

Nutritional support combined with psychological intervention significantly enhances patient compliance. Early administration of nasal feeding or intravenous nutrition ensures sufficient energy and nutrient intake to promote physical recovery. Psychological intervention involves proactive communication between nursing staff and patients and their families, patiently answering questions to alleviate their anxiety and tension. Comparative data show that after implementing multi-system collaborative rehabilitation nursing, patient compliance significantly improved. Interdisciplinary collaboration plays a crucial role in this process, with doctors, rehabilitation therapists, and nurses jointly participating to formulate comprehensive nursing plans, significantly enhancing patient care quality and functional rehabilitation outcomes.

2.4. Evaluation indicators

2.4.1. Functional rehabilitation indicators

The Fugl-Meyer Assessment (FMA) is used to evaluate limb motor function, with a score range of 0–100 points. The Barthel Index (BI) is used to quantify daily living abilities, also with a score range of 0–100 points. Standardized double-blind assessments are conducted, and reliability and validity are verified by retesting every 24 hours.

2.4.2. Complication rate

The incidence of neurological complications during hospitalization, such as lung infections and deep vein thrombosis, is recorded based on ICD-11 standards. Real-time records are maintained through the medical record system. The total incidence rate (number of cases/total number of cases \times 100%) is calculated and compared between groups using the chi-square test.

2.4.3. Satisfaction evaluation

Satisfaction is evaluated across five dimensions: nursing response, operational standards, health guidance, humanistic care, and environmental comfort. Each dimension is scored out of 20 points, with a total score of 100 points. An anonymous third-party questionnaire survey is conducted before discharge, and reliability is tested using Cronbach's α . The average scores are compared and analyzed.

2.4.4. Time to consciousness

Consciousness is defined as a Glasgow Coma Scale (GCS) score of ≥ 13 maintained for 24 hours. The time from onset to consciousness (in hours) is recorded. Kaplan-Meier survival analysis and Log-rank tests are used to compare differences between groups, calculating the median time to consciousness and the 95% confidence interval (CI).

2.5. Statistical analysis

Statistical analysis is conducted using GraphPad Prism 10.0 software. Categorical data are expressed as rates and

percentages, and the chi-square test is used for comparisons. Continuous data that follow a normal distribution are expressed as mean \pm standard deviation ($\bar{x} \pm s$) and analyzed using the t-test. A P -value of < 0.05 indicates a statistically significant difference.

3. Results

3.1. The functional rehabilitation conditions of the two groups of patients before and after the intervention

Before the intervention, there was no statistically significant difference in FMA and BI scores between the two groups ($P > 0.05$). After the intervention, the FMA and BI scores in the observation group were significantly higher than those in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of recovery status

Group	FMA		BI	
	Before intervention	After intervention	Before intervention	After intervention
Control($n=31$)	40.27 \pm 2.83	64.28 \pm 2.34 ^a	33.91 \pm 5.38	54.81 \pm 7.23 ^a
Observation($n=31$)	40.73 \pm 2.47	72.13 \pm 5.38 ^a	33.48 \pm 5.23	70.23 \pm 7.46 ^a
t	0.681	13.095	0.319	8.264
P	0.498	0.000	0.750	0.000

*Note: Compared with the same group before intervention, $P < 0.05$.

3.2. Incidence of complications in both groups

The incidence of complications in the observation group was lower than that in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of complication incidence

Group	Urinary tract infection	Pulmonary infection	Gastrointestinal bleeding	Complication
Control ($n=31$)	1(3.23)	2(6.45)	1(3.23)	4(12.90)
Observation ($n=31$)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
χ^2	-	-	-	4.275
P	-	-	-	0.038

3.3. Nursing satisfaction in both groups

The nursing satisfaction indicators in the observation group were higher than those in the control group, with a statistically significant difference ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of satisfaction scores

Group	Nursing attitude	Operational skills	Psychological counseling	Health guidance	Nurse-Patient communication
Control(<i>n</i> =31)	83.27 ± 2.83	86.65 ± 2.45	85.27 ± 2.16	84.12 ± 2.51	85.71 ± 2.45
Observation(<i>n</i> =31)	89.71 ± 2.46	92.84 ± 2.54	93.72 ± 2.47	92.43 ± 2.46	93.13 ± 2.50
<i>t</i>	9.562	9.765	14.338	13.164	11.802
<i>P</i>	0.000	0.000	0.000	0.000	0.000

3.4. Analysis of consciousness recovery time in both groups

Comparison of consciousness recovery time: the observation group had a significantly shorter recovery time of (48.72 ± 11.76) minutes compared to the control group, which had a recovery time of (64.29 ± 14.58) minutes. The difference was statistically significant ($t = 13.2561$, $P < 0.05$).

4. Discussion

Acute cerebral hemorrhage is a severe cerebrovascular disease primarily caused by the rupture of cerebral blood vessels, leading to blood influx into the brain parenchyma^[12]. The pathological characteristics of this condition include a sudden onset and rapid progression, often resulting in a sharp increase in intracranial pressure within a short period^[13]. This increased pressure compresses the surrounding brain tissue, causing a series of severe neurological dysfunctions^[14]. These sudden changes present numerous challenges for emergency treatment^[6]. On one hand, the condition of patients with cerebral hemorrhage changes rapidly, with complex and diverse symptoms, requiring medical personnel to make accurate judgments and decisions in a short time^[7, 15]. On the other hand, due to the special nature of brain tissue, any slight mishap during treatment can lead to severe complications, further exacerbating the patient's condition and increasing the risk of death and disability^[16, 17].

The predictive rehabilitation nursing model plays a crucial role in the treatment of acute cerebral hemorrhage^[18, 19]. By anticipating and assessing the patient's condition in advance, rehabilitation therapists and nurses can take targeted measures during the golden hour of emergency care, effectively shortening the emergency response time^[20]. For example, by preparing the necessary emergency equipment and medications in advance, they can ensure that treatment can be promptly initiated upon the patient's arrival at the hospital^[21]. Additionally, predictive rehabilitation nursing can preemptively address potential complications of cerebral hemorrhage, such as lung infections and pressure sores, by formulating preventive measures in advance^[22]. This reduces the incidence of complications, thereby alleviating the patient's suffering and lowering the mortality and disability rates^[23].

The data from this study indicate that, after the intervention, the recovery scores for FMA and BI were significantly higher in the observation group compared to the control group, with a statistically significant difference ($P < 0.05$). For the time to regain consciousness, the observation group had a mean time of (48.72 ± 11.76) minutes, whereas the control group had a mean time of (64.29 ± 14.58) minutes, showing a significantly shorter time in the observation group ($P < 0.05$). The reason lies in the fact that predictive rehabilitation nursing, through early assessment and preparation, effectively shortens the emergency response time and the time taken for CT diagnosis. This provides more rescue time for patients, thereby increasing the success rate of emergency interventions. Consequently, it shortens the patient's awakening time and improves their prognosis and rehabilitation outcomes.

The results indicate that the incidence of complications in the observation group is lower than that in the control group, with a statistically significant difference ($P < 0.05$), fully demonstrating the effectiveness of predictive rehabilitation nursing. For pulmonary infection, measures such as cardiopulmonary rehabilitation management before transport and respiratory support during transport reduce the risk of aspiration and lower the likelihood of pulmonary infection. For pressure ulcers, regular turning and skin protection measures effectively prevent prolonged pressure on local skin. For deep vein thrombosis, appropriate limb positioning and activity reduce the possibility of blood stasis leading to thrombosis. It is evident that targeted rehabilitation nursing measures closely correspond to the mechanisms of complication occurrence, effectively preventing complications. Comparing the scores of nursing satisfaction indicators, the observation group scores are higher than those of the control group, with a statistically significant difference ($P < 0.05$).

5. Conclusion

In conclusion, the application of predictive rehabilitation nursing in the emergency transport of patients with acute cerebral hemorrhage can reduce the incidence of complications, shorten the duration of consciousness impairment, and improve the quality of transport and functional rehabilitation levels. This study provides new insights for enhancing the emergency transport and rehabilitation levels of patients with acute cerebral hemorrhage.

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Disclosure statement

The authors declare no conflict of interest.

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Effects of Healthcare Failure Mode and Effect Analysis on the Prevention of Deep Venous Thrombosis in Elderly Patients Undergoing Femoral Fracture Surgery

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Abstract: *Purpose:* To evaluate the effects of healthcare failure mode and effect analysis (FMEA) on the prevention of deep venous thrombosis (DVT) in elderly patients undergoing femoral fracture surgery. *Methods:* Eighty elderly patients undergoing femoral fracture surgery who did not apply FMEA in Suzhou BenQ Medical Center from June 1, 2022 to May 31, 2023 were selected as the control group. According to the equal group experiment method, 80 elderly patients who were managed using FMEA from June 1, 2023 to May 31, 2024 were selected as the FMEA group. The control group received traditional nursing management, while the FMEA group applied FMEA to analyze failure causes, calculate Risk Priority Numbers (RPNs), identify failure modes with higher RPNs, analyze the influencing factors, develop improvement measures, and optimize processes. The RPN values and the incidence of DVT, as well as nursing satisfaction scores, were compared in the two groups. *Results:* Compared with the control group, the total RPN values of the FMEA group decreased significantly, with a reduction rate of 87.0%. Besides, the incidence of DVT was 1.3% in the FMEA group, lower than 10.0% in the control group (8/80). What's more, the patients in the FMEA group were more satisfied with the nursing service compared with the patients in the control group. *Conclusion:* The application of the FMEA in elderly patients undergoing femoral fracture surgery has demonstrated its potential to prevent the incidence of DVT, lower RPN values, and improve nursing satisfaction.

Keywords: Healthcare failure mode and effect analysis; Venous thrombosis; Femoral fracture

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1. Introduction

Deep venous thrombosis (DVT) is a prevalent complication among patients who have undergone surgery or have been bedridden for extended periods ^[1]. When DVT occurs, it can significantly impair the functionality of the lower limbs, ranging from reduced work capacity in mild cases to life-threatening Pulmonary Embolism (PE) in severe instances ^[2]. DVT is particularly common in individuals who have suffered major trauma or are elderly, especially during the immobilization period following major orthopedic surgeries ^[3]. Consequently, the prevention and management of DVT have emerged as crucial aspects of orthopedic clinical nursing.

Failure Mode and Effects Analysis (FMEA) is a proactive methodology that anticipates problems, assesses high-risk healthcare processes, pinpoints potential hazards, and implements preventive risk management strategies ^[4-6]. This study integrates FMEA into the postoperative nursing management of elderly patients with femoral fractures. Through the quantification of risk indicators and the formulation of tailored preventive measures, the aim is to significantly reduce the occurrence of DVT, ultimately facilitating a smoother recovery process for patients.

2. Methods

2.1. General information

Eighty elderly patients undergoing femoral fracture surgery who did not apply FMEA in Suzhou BenQ Medical Center from June 1, 2022 to May 31, 2023 are selected as the control group. According to the equal group experiment method, eighty elderly patients who are managed using FMEA from June 1, 2023 to May 31, 2024 are selected as the FMEA group. Inclusion criteria: (1) Patients aged ≥ 60 years; (2) Patients who met the indications for surgery; (3) Patients with normal cognitive and communicative functions; (4) Able to undergo rehabilitation training; (5) Willing to join in the study and sign the informed consent. Exclusion criteria: (1) Suffer from serious heart, brain, lung, and kidney diseases; (2) Unwilling to join in the study.

2.2. Ethics statement

This study is approved by the Institutional Review Board of the XX Medical Center (Approval No. SZMJYY20XXXX1401).

2.3. Establishment of FMEA team

The FMEA team consisted of 12 members, including one chief physician, one deputy chief physician, one deputy chief nurse, four supervisor nurses, and six senior nurses. All selected members received FMEA training for at least one month. The department held meetings regularly to brainstorm and analyze the main causes of hospital-acquired infections and lower limb deep venous thrombosis in elderly patients undergoing femoral fracture surgery in the control group, thus to assess risks and analyze mechanisms, and efficacy. After then, the risk priority number (RPN) is calculated using three dimensions, including severity (S), occurrence (O), and detection (D). In brief, $RPN = S \times O \times D$. Use numbers 1 to 10 to represent the degree of each dimension, with a larger number indicating a higher likelihood or severity of occurrence. Accordingly, the lowest RPN score is 1 point, and the highest score is 1000 points. The higher the score, the greater the risk of the failure mode. Calculating RPN values can help FMEA team members identify high-value failure modes that require priority attention. Sort the calculated RPN values from high to low, identify the top 4 failure modes, analyze and identify them using FMEA, identify hazardous

factors, improve techniques, and prevent failure from occurring according to the literature and clinical experience, as shown in **Table 1** ^[7, 8].

Table 1. Causes of failure modes and improvement measures in elderly patients undergoing femoral fracture surgery

Failure mode	Causes	Improvement measures	S	O	D	PRN
Improper organizational system management	Lack of risk management awareness; incomplete risk classification; Lack of guidelines and standards for patient education	Improve the risk classification management system. Using the Wells DVT score ^[7] patients with a thrombosis risk score greater than or equal to 3 should take anti thrombotic measures and ensure that the measures are implemented effectively; Develop management education standards and guidelines for DVT prevention to assist nurses in implementing phased preoperative and postoperative nursing guidance and education for patients.	7	7	6	294
Irregularities in medical care procedures	Inadequate education and lack of effective communication with patients; Failure to observe the condition in a timely manner and failure to predict changes in risk factors; New nurses lack assessment ability	Strengthen communication with patients; Nurses are required to pay attention to observing the peripheral circulation of the patient's limbs dynamically, such as skin color, temperature, pain, swelling, numbness, presence of arterial pulsation, sensory abnormalities, venous filling, etc; Establish a unified DVT assessment standard guideline within the department, using the Autar scale for clinical risk assessment ^[8] . The research group conducts extensive professional training for nurses, organizing one DVT theoretical learning and operational exercise for general nursing staff every week. The training exercises are conducted in the form of lectures, demonstrations, exercises, and random exams to prevent thrombosis.	7	7	8	392
Patient and family factors	Elderly and weak individuals often have underlying diseases and are prone to sudden changes in their condition; Poor compliance and lack of cooperation with anticoagulant therapy; Lack of assistance from family members in postoperative rehabilitation exercise for patients	Nurses are required to pay more attention to elderly and weak individuals with underlying diseases, once abnormal changes occur, immediately identify the cause and take early intervention measures; For patients who do not cooperate with anticoagulant therapy, it is necessary to promptly clarify the reasons and provide corresponding explanations; For patients who lack assistance in postoperative rehabilitation training, arrange for dedicated personnel to assist.	6	6	7	252
Equipment and environment	Incomplete physical therapy equipment and outdated auxiliary tools	Apply to purchase physical therapy equipment and update auxiliary tools	5	7	3	105

*Abbreviations: DVT for Deep Venous Thrombosis; S for severity; O for occurrence; D for detection; RPN for the risk priority number.

2.4. Observed indexes

The RPN value for each failure mode is calculated and compared in the two groups. The reduction rate = (RPN in control group – RPN in FMEA group / RPN in control group × 100%. The occurrence of DVT in the lower limbs is determined using Doppler ultrasound examination and compared in the two groups. Besides, the nursing satisfaction questionnaire designed by the researcher includes three aspects: Disease explanation (5 items), Postoperative functional exercise guidance (10 items), and Communication effectiveness (5 items), which is used to assess patients' satisfaction. Each item was divided into 5 grades from “very dissatisfied” to “very satisfied”, with a score of 1–5, and a total score of 100 points. The higher the score, the higher the patient satisfaction.

2.5. Statistical analysis

SPSS 22.0 is used to analyze the data. The measurement data are expressed as mean \pm SD and analyzed with a t-test, and the counting data are expressed in rate (%) and analyzed with a chi-square test. $P < 0.05$ meant the difference is statistically significant.

3. Results

3.1. Comparison of general information between the two groups

There were no significant differences between the two groups in age, gender, married status, or education level (all $P > 0.05$), as shown in **Table 2**, which meant that the two groups were comparable.

Table 2. Comparison of general information between the two groups

General information	Control group (n=80)	FMEA Group (n=80)	t/χ^2	p
Age (y)	69.63 \pm 6.04	69.94 \pm 6.73	0.31	0.758
Gender			0.43	0.511
Male (%)	31 (38.8)	27 (33.8)		
Female (%)	49 (61.3)	53 (66.3)		
Married status			0.23	0.629
Married (%)	49 (61.3)	46 (57.5)		
Other (%)	31 (38.8)	34 (42.5)		
Years of education (y)			1.44	0.486
≤6 (%)	53 (66.3)	56 (70.0)		
6-12 (%)	19 (23.8)	20 (25.0)		
≥12 (%)	8 (10.0)	4 (5.0)		

*Abbreviations: FMEA for Failure Mode and Effects Analysis.

3.2. FMEA reduced RPN values

Compared with the control group (total RPN values = 1043), the total RPN values of the FMEA group (total RPN values = 136) decreased significantly, with a reduction rate of 87.0%, indicating a significant improvement, as shown in **Table 3**.

Table 3. FMEA model reduced RPN values

Item	Control group (n=80)	FMEA group (n=80)	The reduction rate (%)
Improper organizational system management	294	36	87.8
Irregularities in medical care procedures	392	56	85.7
Patient and family factors	252	32	87.3
Equipment and environment	105	12	88.6
Total scores	1043	136	87.0

*Abbreviations: FMEA for Failure Mode and Effects Analysis.

3.3. FMEA reduced the incidence of DVT

The incidence of DVT was 1.3% in the FMEA group (1/80), lower than 10.0% in the control group (8/80) ($P < 0.05$), indicating that FMEA could help reduce the incidence of DVT in elderly patients undergoing femoral fracture surgery, as shown in **Table 4**.

Table 4. FMEA model reduced the incidence of DVT

Group	<i>n</i>	DVT	DVT incidence rate (%)	<i>p</i>
Control group	80	8	10.0	0.034
FMEA group	80	1	1.3	

*Abbreviations: FMEA for Failure Mode and Effects Analysis; DVT for Deep Venous Thrombosis.

3.4. FMEA improved nursing satisfaction scores

The patients in the FMEA group were more satisfied with the nursing service compared with the patients in the control group, and the difference was statistically significant (all $P < 0.05$), as shown in **Table 5**.

Table 5. Comparison of nursing satisfaction score between the two groups

Group	Disease explanation	Postoperative functional Exercise guidance	Communication effectiveness	Overall satisfaction
Control group (<i>n</i> =80)	20.71 ± 2.17	43.79 ± 3.56	22.00 ± 1.81	86.50 ± 4.98
FMEA group (<i>n</i> =80)	22.70 ± 1.72	46.96 ± 2.28	22.95 ± 1.62	92.61 ± 3.18
<i>t</i>	6.42	6.72	3.50	9.26
<i>p</i>	< 0.001	< 0.001	0.001	< 0.001

*Abbreviations: FMEA for Failure Mode and Effects Analysis.

4. Discussion

Elderly individuals, due to their weaker physical capabilities and limited mobility, are highly susceptible to femoral fractures resulting from falls, external impacts, and conditions like osteoporosis^[9]. For these elderly patients with femoral fractures, prompt surgical treatment is essential to achieve favorable outcomes, shorten the duration of bed rest, and minimize the risks of disability and mortality^[9]. However, during femoral fracture surgeries, elderly patients tend to have poor surgical tolerance, experience more intense stress reactions, and require longer periods of rehabilitation. These factors can contribute to coagulation disorders, slow down deep venous blood flow in the lower extremities, exacerbate venous dilation, blood stasis, and damage to venous wall endothelial cells, thereby increasing the risk of developing DVT^[10, 11]. Consequently, preventing DVT holds significant importance in improving the prognosis of elderly patients undergoing femoral fracture surgery^[11].

FMEA is a robust and proactive analytical tool that anticipates and assesses the likelihood of medical events, implementing preventive measures tailored to the level of risk to minimize their occurrence^[12]. Xu applied the FMEA framework to oral and maxillofacial surgery, and they found that FMEA for oral and maxillofacial surgery could prevent MDRO infections, improve the implementation of preventive and control measures, as well as oral self-care ability^[13]. Besides, Davide found that the FMEA could reduce the risk of human error during laparoscopic surgery and improve patient safety^[6].

FMEA perfectly encapsulates the essence of high-quality nursing models by meticulously tackling every

aspect of management, establishing standardized and streamlined frameworks, and guiding the implementation of targeted and efficient nursing plans tailored to patients' needs ^[14, 15]. In the current study, the FMEA team convened meetings to scrutinize possible factors for postoperative DVT in elderly patients undergoing femoral fracture surgery. The analysis uncovered four high-risk indicators, including improper organizational system management, irregularities in medical care procedures, patient and family factors, and equipment and environment. Upon recognizing the failure modes and their underlying causes, targeted interventions were devised, resulting in a notable reduction in the RPNs across all four indicators. The overall RPN reduction rate reached 87.0%, underscoring the profound effectiveness of the implemented measures and the successful mitigation of risks. Notably, while 8 cases of DVT occurred in the control group, only 1 case was reported in the FMEA group. This underscores the effectiveness of utilizing FMEA principles in nursing management, where quantifying risk indicators and formulating preventive measures can drastically reduce the incidence of DVT, ensuring the smooth recovery of elderly patients undergoing femoral fracture surgery, thus improving nursing satisfaction.

5. Conclusion

In summary, the application of the FMEA in elderly patients undergoing femoral fracture surgery has demonstrated its potential to prevent the incidence of DVT, lower RPN values, and improve nursing satisfaction. However, the applicability of this model necessitates further analysis, given the constraints posed by limited follow-up time and sample size.

Disclosure statement

The author declares no conflict of interest.

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Reviewing the Role of Oral Microbiota in Cognitive Impairment from Microbiota Homeostasis and Pathogenic Bacteria

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Abstract: Cognitive impairment is a common symptom of various neurodegenerative diseases. In recent years, an increasing body of research has focused on the relationship between oral microbiota and cognitive impairment. This review aims to explore the microbial homeostasis of oral microbiota and its interactions and mechanisms with the host, as well as the impact of specific pathogenic bacteria on cognitive function. By summarizing existing studies, this review aims to provide a theoretical basis for the pathogenesis, risk assessment, and early intervention and treatment strategies for cognitive impairment.

Keywords: Cognitive impairment; Oral microbiota; Alzheimer's disease; neurodegenerative diseases

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1. Introduction

Cognitive impairment (CI) refers to a decline in cognitive function caused by various factors, including impairments in perception, memory, attention, and executive function, independent of normal aging processes. It encompasses multiple types, such as mild cognitive impairment (MCI), Alzheimer's disease (AD), and cerebrovascular diseases. With the intensification of global population aging, the number of CI patients worldwide is projected to reach 130 million by 2050^[1]. In recent years, a substantial body of research has demonstrated significant associations between oral health and a variety of systemic diseases^[2-4]. Additionally, oral health has been linked to neurological conditions, with dental issues exhibiting a bidirectional relationship with

cognitive impairment. Poor oral health is a risk factor for cognitive dysfunction, and conversely, diminished cognitive abilities can exacerbate oral health decline ^[5, 6]. The correlation between oral health issues and cognitive impairment has emerged as a subject of global research interest. Therefore, this review aims to explore the relationship between oral microbiota and CI, with a particular focus on elucidating the potential impact mechanisms of specific oral pathogens on cognitive function. The goal is to provide a theoretical foundation for the development of preventive and therapeutic strategies for individuals with CI.

2. Microbial homeostasis of oral microbiota and host interactions

The oral microbiota of healthy individuals maintains microbial homeostasis through interspecies cooperation and competition, host immune modulation, and environmental adaptability. The microbiota in the oral cavity is diverse, including bacteria, archaea, fungi, viruses, and protozoa ^[7]. These microorganisms interact and cooperate to stabilize the biofilm, playing a crucial role in protecting host health. For instance, *Streptococcus mutans* secretes extracellular polysaccharides to enhance the structural stability of the biofilm, creating a favorable environment for the coexistence of multiple bacterial species ^[8]. Meanwhile, *Streptococcus sanguinis* degrades glycerol to maintain its persistence and competitiveness while producing hydrogen peroxide to inhibit the growth of competing bacterial strains ^[9, 10]. Furthermore, some bacteria can adjust their growth and metabolic strategies through quorum sensing to achieve coexistence in resource-limited environments ^[11].

The physical and chemical conditions of the oral environment, such as temperature, humidity, and pH, have a significant impact on the composition of the microbial community. Saliva in the oral cavity not only mechanically removes food debris and microorganisms but also promotes microbial balance by maintaining an optimal pH level. Saliva buffers the acidic substances from the diet and acids produced by the fermentation of carbohydrates by bacteria, maintaining its pH level within a relatively stable range of 6.5 to 7 ^[12, 13]. This is crucial for promoting and maintaining a healthy microbial composition in the oral cavity and helps regulate the microbial homeostasis between microbes and the host. Additionally, saliva provides essential nutrients to oral bacteria through enzymatic breakdown of dietary starches, proteins, and salivary glycoproteins ^[13].

The relationship between the host's immune system and the oral microbiota is also of critical importance. Under healthy conditions, the host's immune system maintains the dynamic balance of the microbiota and prevents pathogen invasion through the cooperation of innate and adaptive immunity. When immune function is normal, the oral microbiota can sense signaling molecules released by the host and adjust its growth and metabolism to minimize harm to the host ^[14]. For example, in the case of elevated lactate levels, the oral microbiota in periodontitis patients influences macrophage polarization and promotes osteoblast differentiation, suppressing inflammation and aiding tissue repair ^[15]. Of course, oral microbiota can also release inflammatory cytokines or stimulate specific immune cells, activating the host's immune system, thereby affecting the ratio and composition of immune cells to induce local or distant diseases. For example, oral microbiota promotes colitis by activating inflammatory caspases in colonic mononuclear phagocytes and inducing migratory Th17 cells ^[16].

The balance between oral microbiota and immune activity maintains systemic homeostasis. Disrupting this balance can lead to oral and systemic diseases, such as cognitive dysfunction, cardiovascular diseases, pneumonia, rheumatoid arthritis, and digestive system cancers ^[17]. J. R. Gabaldón, T. contributors<auth-address>Barcelona Supercomputing Centre (BCS-CNS. The metabolic products of oral microbiota not only impact oral health through local pathways but also regulate the host's immune system and

systemic inflammatory responses through distant actions. These discoveries highlight the significance of oral microbiota in overall health and offer new directions for future disease prevention and treatment.

3. Mechanisms of oral microbiota impact on CI

Oral microbiota can influence the central nervous system (CNS) through multiple mechanisms, thereby affecting cognitive function. First, the proximity of the oral cavity to the brain and the rich neural connections provide the basis for direct interaction between oral microbiota and the brain^[18]. Oral microbiota can invade the brain through neural pathways, particularly the trigeminal nerve and olfactory nerve. In 2002, Riviere *et al.* first observed that the colonization rate of oral spirochetes in the cerebral cortex, brainstem, and trigeminal ganglion of AD patients was significantly higher than that of cognitively normal elderly individuals^[19]. This finding suggests that oral microbiota may enter the brain through neural pathways, influencing cognitive function. In 2020, Sundar *et al.* further discovered that *Chlamydia pneumoniae* could enter the olfactory cortex and hippocampus via the olfactory bulb, providing additional evidence for the relationship between oral microbiota and cognitive function^[20].

Secondly, oral microbiota may affect brain function by inducing inflammatory responses. For example, the toxic protein gingipain produced by *Porphyromonas gingivalis* (*P. gingivalis*) can trigger brain inflammation, thereby promoting the deposition of β -amyloid protein and exacerbating CI^[21, 22]. In addition, the oral microbiota may exert influence on the brain via the circulatory system. On one hand, oral microbes can enter the brain by traversing the blood-brain barrier (BBB) or the circumventricular organs and choroid plexus through the bloodstream^[23]. On the other hand, once these oral microbes infiltrate the cerebral blood vessels, they can induce arteriosclerosis, potentially leading to inadequate cerebral blood flow, neuronal damage, and ultimately, the onset or exacerbation of AD^[24]. Furthermore, oral microbiota may influence cognitive function through the regulation of gene expression, especially the TREM-2 gene in microglial cells, which triggers neuroinflammation and accelerates neuronal apoptosis^[25].

Lastly, the interaction between dysbiosis of the oral and gut microbiota is also considered an important mechanism influencing cognitive function. Research indicates that significant dysbiosis of the oral and gut microbiota is associated with progressive cognitive decline in periodontitis mice, and its mechanism is probably related to microbiota-gut-brain axis disorders^[26]. Oral microbiota influence cognitive function through neural pathways, inflammatory responses, blood circulation, gene expression regulation, and interactions with the oral and gut microbiota. These mechanisms suggest a complex relationship between oral health and cognitive function, providing theoretical foundations for the prevention and treatment of related diseases in the future.

4. The role of major oral pathogenic bacteria in the formation of CI

4.1. *Porphyromonas gingivalis*

P. gingivalis is one of the most significant periodontal pathogens and is also one of the most extensively studied, playing a pivotal role in the association between periodontitis and brain aging/neurodegeneration. *P. gingivalis* is an anaerobic, Gram-negative bacterium with various virulence factors that can trigger persistent, nonspecific inflammatory responses by modulating the host's immune response. This inflammation not only damages periodontal tissues but can also spread to distant organs through compromised epithelial barriers^[27]. Gingipains, the primary virulence factors of *P. gingivalis*, have been found to be significantly more abundant in the brains

of AD patients compared to non-AD individuals, and the gingipain load was also positively correlated with the expression of tau protein ^[23]. Research has discovered that gingipains are present in the hippocampus and cerebral cortex of AD patients, and colocalized with the AD pathology hallmarks of tau tangles and intraneuronal β -amyloid (A β) ^[21]. These findings suggest that the oral bacterium *P. gingivalis* can enter the brain and is associated with AD pathological changes. Several animal studies have provided direct evidence of *P. gingivalis* invading the brain. After oral colonization with *P. gingivalis* in mice, increased levels of *P. gingivalis* mRNA and Pg-LPS were detected in the hippocampus, confirming that *P. gingivalis* from the oral cavity can reach brain tissue ^[28].

Furthermore, *P. gingivalis* is also closely associated with neurodegenerative diseases such as Parkinson's disease (PD) and multiple sclerosis (MS). Research on PD mouse models found that *P. gingivalis* leads to a reduction of dopaminergic neurons in the substantia nigra and an increase in activated microglial cells ^[29]. MS is characterized by demyelination of nerve cell fibers and infiltration of inflammatory cells, often resulting in severe physical and cognitive impairments ^[30]. A meta-analysis indicated that individuals with MS are 1.93 times more likely to be diagnosed with periodontitis compared to healthy controls, suggesting a significant association between periodontitis and MS ^[31]. Interestingly, the detection rate of *P. gingivalis* in healthy individuals was also 43.33%, and in patients with moderate to severe periodontitis and those with AD complicated by periodontitis, the detection rates were 76.67% and 100%, respectively ^[32]. This result suggests that while *P. gingivalis* can exist in the oral cavity of healthy individuals, whether it can cause disease under normal conditions still requires further investigation.

4.2. Spirochetal

Spirochetal are highly active Gram-negative bacteria that include various pathogens related to oral and periodontal infections. Among them, *Treponema denticola* (*T. denticola*) is one of the primary pathogens of periodontitis. Spirochetal exhibit significant neurotropism and can spread through the lymphatic system along nerve fibers ^[33]. Studies have detected spirochetal in the trigeminal nerve and trigeminal ganglia, with *T. denticola* and *Borrelia burgdorferi* being the most frequently detected species ^[34]. *T. denticola* is capable of bypassing the blood-brain barrier, entering the brainstem's mesencephalic nucleus of the trigeminal nerve (Vmes) and the locus coeruleus, triggering inflammatory responses that lead to neurodegenerative changes and norepinephrine imbalance, ultimately resulting in cognitive dysfunction ^[35]. Multiple laboratory studies have indicated an association between spirochetal and AD ^[36, 37]. Moreover, spirochetal may also enter the central nervous system via the olfactory nerve fibers and olfactory tract, affecting brain function ^[20]. However, the specific mechanisms involved require further investigation and validation.

4.3. Candida albicans

Recent studies have indicated that *Candida albicans*, a common opportunistic fungus in the oral cavity, is associated with neurodegenerative diseases ^[38]. *Candida albicans* is the most commonly isolated fungal species from the oral swabs of AD patients, and its prevalence is significantly higher in AD patients compared to non-AD patients ^[39]. Research has shown that after causing oral ulcers, *Candida albicans* can cross the blood-brain barrier, leading to asymptomatic fungal infections in the cerebral cortex, and form granulomas similar to AD plaques, thereby causing transient memory impairment ^[40]. More importantly, *Candida albicans* infection may compromise the integrity of the blood-brain barrier in elderly individuals, making it easier for pathogens and virulence factors to invade the nervous system ^[41]. Animal experiments have also confirmed this mechanism.

Based on previous research, Wu *et al.* established a fungal encephalitis mouse model and found that the spatial memory of the mice was significantly impaired. Anatomical analysis revealed spherical lesions in the mouse brain, with *Candida albicans* at the core, surrounded by astrocytes and microglial cells. Therefore, it is hypothesized that these granulomas may activate immune-related NF- κ B signaling pathways, promote the secretion of cytokines such as IL-6 and IL-18, and increase the levels of amyloid precursor protein (APP) and A β , thus accelerating the progression of neurodegenerative lesions ^[42].

4.4. *Streptococcus mutans*

Streptococcus mutans (*S. mutans*) is a Gram-positive bacterium commonly found in the oral cavity and is a major pathogen responsible for dental caries ^[43]. Although *S. mutans* is primarily associated with dental caries, it can also induce local and systemic inflammatory responses, leading to increased levels of inflammatory factors in the brain. Moreover, the acidic metabolic products and other toxins produced by *S. mutans* can cross the BBB, directly or indirectly damaging neuronal cells, thereby affecting cognitive function. In a 2016 study, Watanabe *et al.* demonstrated in a mouse model that Cnm-positive *S. mutans* is associated with cognitive impairment, accompanied by an increase in cerebral microbleeds (CMBs) ^[44]. Notably, previous studies have established that CMBs are an independent risk factor for cognitive decline ^[45]. Cnm is a collagen-binding protein, 120-kDa in size, encoded by the *cnm* gene on the surface of *S. mutans* cells ^[46]. Recent multicenter prospective studies have further revealed the longitudinal association between Cnm-positive *S. mutans* and CMBs, and comprehensive oral examinations have confirmed the relationship between Cnm-positive *S. mutans* and the development of CMBs, as well as the increased risk of cognitive decline ^[47].

The impact of Cnm-positive *S. mutans* on cognitive impairment may be related to the following mechanisms: First, Cnm-positive *S. mutans* strongly binds to dentin, which is composed of type I collagen, promoting the development of caries in the periodontal space and facilitating the entry of *S. mutans* into the bloodstream ^[48]. Second, Cnm-positive *S. mutans* attracts circulating neutrophils to the site of injury, where they activate local inflammation and secrete matrix metalloproteinase (MMP)-9, ultimately increasing the permeability of the BBB. Dysfunction of the BBB disrupts the brain's homeostasis, reducing the supply of glucose and other nutrients, and impairing the elimination of waste products and metabolic byproducts, all of which can contribute to cognitive dysfunction ^[49].

5. Conclusion

The oral cavity serves as a reservoir for various microorganisms, and the balance of these microorganisms is crucial for maintaining overall health. Poor oral health can significantly impact cognitive function, with a bidirectional relationship between the two. Oral microorganisms not only reside in the oral cavity but can also enter the brain, increasing with age and neurodegeneration. The relationship between oral health issues and cognitive dysfunction is invaluable for the early detection and prevention of oral risk factors associated with cognitive impairment. Therefore, it is essential to comprehensively investigate the connection between oral health and cognitive dysfunction to effectively prevent or identify potential risk factors for cognitive impairment at an early stage.

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Application of 4R Crisis Management Theory in the Management of Incontinence-Associated Dermatitis in ICU Patients with Fecal Incontinence

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Abstract: *Objective:* To analyze the preventive and management effects of the 4R crisis management theory on incontinence-associated dermatitis (IAD) in ICU patients with fecal incontinence. *Methods:* A hundred patients with fecal incontinence who were admitted to the ICU for treatment between January 2024 and December 2024 were selected and randomly divided into two groups using a random number table. The observation group received 4R crisis management theory, while the control group received routine management. The IAD risk score, incidence of IAD, severity of IAD, and formation and healing time of IAD were compared between the two groups. *Results:* After management, the IAD risk score of the observation group was lower than that of the control group ($P < 0.05$). The incidence of IAD in the observation group was lower than that in the control group, the proportion of mild IAD was higher than that in the control group, the formation time of IAD was later than that in the control group, and the healing time was shorter than that in the control group ($P < 0.05$). *Conclusion:* Adopting the 4R crisis management theory for ICU patients with fecal incontinence can reduce the risk of IAD occurrence, effectively prevent IAD, reduce its severity, delay its formation time, and promote good healing.

Keywords: 4R crisis management theory; ICU fecal incontinence; Incontinence-associated dermatitis; Management

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1. Introduction

Incontinence-associated dermatitis (IAD) is a common complication of fecal incontinence, with an incidence rate of approximately 30% in ICU patients^[1]. This disease continuously reduces patients' immunity, leading to adverse events such as secondary infections, and affects the tolerance of skin cells to external pressure, increasing the probability of pressure injuries. To effectively prevent IAD in ICU patients with fecal incontinence and ensure

patient safety during treatment, comprehensive nursing management services are needed. Routine management can comprehensively evaluate patients' IAD risks and provide systematic care. However, its management system lacks scientific rigor and is difficult to maximize IAD prevention^[2]. The 4R crisis management theory is subdivided into four stages, which interact and influence each other, optimizing the management system, fully identifying risk issues, and implementing targeted and comprehensive management. Therefore, this study selected 100 patients with fecal incontinence admitted to the ICU to evaluate the intervention effect of the 4R crisis management theory.

2. Materials and methods

2.1. General information

A hundred patients with fecal incontinence who were admitted to the ICU for treatment between January 2024 and December 2024 are selected and randomly divided into two groups using a random number table. The observation group consisted of 50 patients, including 27 males and 23 females, with an age range of 40–75 years and a mean age of (53.25 ± 4.18) years. The frequency of incontinence was ≤ 7 times per day in 31 cases and ≥ 8 times per day in 19 cases. The control group consisted of 50 patients, including 29 males and 21 females, with an age range of 37–76 years and a mean age of (53.37 ± 4.23) years. The frequency of incontinence was ≤ 7 times per day in 32 cases and ≥ 8 times per day in 18 cases. There was no statistically significant difference in basic information between the two groups ($P > 0.05$). Inclusion criteria are: Adult patients; Admitted to the ICU department for ≥ 24 hours; incontinence frequency of ≥ 3 times per day; Presence of loose or watery stools; Complete basic information. Meanwhile, the exclusion criteria include: Presence of IAD upon admission to the ICU; Pressure injury in the sacrococcygeal region; Infectious diseases or skin diseases in IAD high-risk areas; Concomitant urinary incontinence; Withdrawal from the study.

2.2. Methods

The control group received routine management: nursing staff strictly washed their hands, wore masks, verified patients' identity information, evaluated the causes of fecal incontinence, assessed the basic information such as perineal skin condition, and understood the patients' current self-care abilities. They prepared gloves, cotton swabs, warm water, and feces collectors, explained the purpose and process of nursing management for fecal incontinence to the patients to obtain their cooperation. The patients are kept in a supine position, with soft cloth covering their private areas, and warm nursing care is provided. The local skin is moderately cleaned to ensure that no feces or urine remained in the skin folds, and the skin was patted dry with a paper towel. Targeted treatment is applied to skin defects. A moderate amount of emollient and skin protectant is applied, and the patients are returned to a supine position. Education on fecal incontinence and IAD knowledge is provided to enable patients to acquire basic nursing skills.

The observation group adopted the 4R crisis management theory: 16 experts, including dermatologists and wound care nurses, with a familiarity of 0.74 and an authority level of 0.82, are consulted. Based on the results of the first round of consultation, the experts conducted literature reviews, consulted frontline medical staff, and developed a consultation form after multiple discussions. This included the "Basic Information Form for Experts" and the "Accuracy Expert Consultation Form for IAD Crisis Management Plan Items for Critically Ill Patients in the ICU", etc. The results of the first round of consultation are revised to form professional nursing management content, specifically:

(1) Reduction stage

The goal is to eliminate hidden factors of IAD and skin damage, effectively prevent the disease, and reduce its harm. Specific measures include conducting a detailed examination of the patient's skin condition within 2 hours of entering the ICU department. The Perineal Assessment Tool (PAT) is used to comprehensively evaluate the patient's risk of IAD, understand the patient's stool characteristics (liquid or formed stool), skin manifestations in the perineal area, duration of skin exposure to the external environment, and diarrhea-related factors such as hypoproteinemia or *Clostridium* infection. With 7 points as the standard value, those scoring below 7 are classified as low-risk, while those scoring 7 or above are classified as high-risk. The first PAT assessment is performed within 2 hours of the patient's admission to the department. For high-risk patients, immediate assessment is required after each bowel movement, while low-risk patients are strictly assessed during shift changes. Timely re-evaluation is needed for new risk factors.

(2) Readiness stage

The goal is to improve the ability of ICU medical staff to identify and respond to IAD, enhancing their readiness. Specific measures include establishing a management team led by an experienced chief nursing officer and consisting of senior nursing staff. The team leader conducts knowledge training once a week, explaining IAD high-risk factors, severity classification methods, assessment frequency, daily assessment opportunities, and other knowledge through workshops, on-site demonstrations, or theoretical courses. At the same time, they provide information on the selection and usage precautions of skin care products, and outline structured measures for skin care management. After the training, assessments are conducted through theoretical exams and practical operations to ensure that each team member has risk prevention and control abilities and professional nursing skills. Team members are responsible for regularly checking patients' disease conditions, summarizing skin problems, providing IAD warnings, and implementing corresponding nursing management processes.

(3) Response stage

After a patient is diagnosed with IAD, their severity is assessed, and systematic nursing management is implemented. A skin cleanser that is rinse-free, gentle, and slightly acidic is selected. A stool collector is reasonably chosen based on the patient's stool characteristics and volume. If the patient belongs to a difficult case, a stoma specialist is invited to participate in the department consultation to provide efficient nursing management methods.

(4) Recovery stage

After a patient develops IAD, it is necessary to evaluate the psychological changes of the nursing staff, prohibit the use of accusatory language, and promptly carry out remedial plans in collaboration with the nursing staff to effectively control the patient's condition. A group meeting is held once a week to summarize the incidence and causes of IAD, deeply analyze management deficiencies, and list improvement suggestions.

2.3. Observation indicators

- (1) IAD risk score: The PAT assessment method is selected, which includes duration of irritants, related influencing factors, intensity of irritants, and perineal skin condition, each with a score of 1–3, totaling 4–12 points. The risk level is positively correlated with the score.

- (2) IAD incidence rate: Observe the proportion of IAD cases in each group.
- (3) Severity of IAD: The IAD Severity Assessment Scale is selected, which includes dimensions such as rash, skin color, and defects, with a total of 13 areas evaluated. Among them, mild refers to pink skin, no blisters, intact and dry, blurred boundaries, elevated skin temperature on palpation, accompanied by stinging or burning sensation; moderate refers to bright red skin, local exudation or damage, accompanied by pain; severe refers to skin defects and redness, accompanied by bleeding and exudation.
- (4) Formation and healing time of IAD: Observe the time from fecal incontinence to the appearance of IAD; the time from the appearance of IAD to healing.

2.4. Statistical analysis

Data processing software is SPSS 28.0. Measurement data is expressed as $[\pm s]$, and t-value comparison and testing are performed. Count data is expressed as $[n/\%]$, and χ^2 value comparison and testing are performed. Statistical significance is indicated by $P < 0.05$.

3. Results

3.1. Comparison of IAD risk scores between the two groups

Before management, there was no difference in IAD risk scores between the two groups ($P > 0.05$). After management, the IAD risk score of the observation group was lower than that of the control group ($P < 0.05$). The results are shown in **Table 1**.

Table 1. Comparison of IAD risk scores between the two groups [$\bar{x} \pm s$, points]

Group	Number of cases	Irritant duration (min)		Related factors	
		Before intervention	After intervention	Before intervention	After intervention
Observation group	50	2.07 ± 0.31	1.41 ± 0.29	2.04 ± 0.38	1.71 ± 0.30
Control group	50	2.09 ± 0.33	1.82 ± 0.34	2.06 ± 0.40	1.98 ± 0.35
<i>t</i>	-	0.312	6.488	0.256	4.142
<i>P</i>	-	0.755	< 0.001	0.798	< 0.001

Group	Number of cases	Irritant intensity		Perineal skin status	
		Before intervention	After intervention	Before intervention	After intervention
Observation group	50	1.84 ± 0.33	1.90 ± 0.28	1.90 ± 0.28	1.40 ± 0.28
Control group	50	1.86 ± 0.32	1.91 ± 0.24	1.91 ± 0.24	1.68 ± 0.27
<i>t</i>	-	0.308	0.192	0.192	5.090
<i>P</i>	-	0.759	0.848	0.848	< 0.001

3.2. Comparison of IAD incidence between two groups

The incidence of IAD in the observation group was 18.00% (9/50), while the incidence in the control group was 36.00% (18/50) ($\chi^2 = 4.110$, $P = 0.043$).

3.3. Comparison of IAD severity between two groups

Based on **Table 2**, the proportion of mild IAD in the observation group was higher than that in the control group ($P < 0.05$).

Table 2. Comparison of IAD severity between two groups [n/%]

Group	Number of cases	Mild n (%)	Moderate n (%)	Moderate n (%)
Observation group	9	7(77.78)	2(22.22)	0
Control group	18	6(33.33)	11(61.11)	1(5.56)
χ^2	-	4.747	3.635	0.519
P	-	0.029	0.057	0.471

3.4. Comparison of IAD formation and healing time between two groups

The formation time of IAD in the observation group was later than that in the control group, and the healing time was shorter than that in the control group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of IAD formation and healing time between two groups [$\bar{x} \pm s$, d]

Group	Number of cases	IAD onset time (days)	IAD healing time (days)
Observation group	9	3.58 ± 0.41	7.42 ± 1.76
Control group	18	2.91 ± 0.38	9.20 ± 1.83
t	-	4.210	2.412
P	-	< 0.001	0.024

4. Discussion

IAD mainly occurs in ICU patients with fecal incontinence. Its predisposing factors include the negative impact of enteral nutrition on the intestinal tract, decreased gastrointestinal barrier function, and abuse of antibacterial drugs. Excessive relaxation of the anal sphincter muscle in patients can increase bowel frequency [3]. The persistence of this disease can increase the incidence of stress injuries and lead to complications such as urinary tract infections, thereby increasing the patient's disease burden and treatment costs. Clinical medicine believes that regularly assessing patients' fecal incontinence and IAD risk can effectively prevent the disease. However, the current evaluation system is not perfect, and prevention and control management content is limited, making it difficult to significantly reduce the incidence of IAD [4].

The 4R crisis management theory is a relatively new theory that can develop a continuous and sustainable management system based on the current status of IAD nursing management ($P < 0.05$). It emphasizes risk process management, values prior control, allows for targeted management during events, and enables the development of post-event management content, thereby improving nursing management quality [5]. This theory covers four stages, which are independent and closely related to each other. It enables dynamic, comprehensive, and systematic circular management of patients, implemented throughout the entire management process, to prevent crisis events [6].

The results showed that after management, the IAD risk score of the observation group was significantly

lower than that of the control group ($P < 0.05$). The incidence of IAD in the observation group was 18.00%, while that in the control group was 36.00%. The proportion of mild IAD in the observation group was 77.78%, while that in the control group was 33.33%. The comparison between the two sets of data yielded $P < 0.05$. The reason for this is that the 4R crisis management theory considers skin care as the core of management. It enables timely screening and evaluation of skin problems, allowing for the development of standardized and individualized skin care content to prevent IAD^[7, 8]. This theory facilitates circular nursing for existing nursing management problems, making the management process dynamic and minimizing disease progression, thereby reducing its severity^[9]. The formation time of IAD in the observation group was later than that in the control group, and the healing time was shorter than that in the control group ($P < 0.05$). The reason is that this theory cultivates nursing staff's risk awareness, improves their ability to manage IAD, allows them to take proactive measures, actively screens patients for risk factors, and follows a scientific management process, thereby delaying IAD formation and promoting faster healing^[10].

5. Conclusion

In summary, adopting the 4R crisis management theory for ICU patients with fecal incontinence can prevent IAD, reduce its severity, and accelerate the healing of dermatitis, demonstrating significant management advantages.

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Disclosure statement

The authors declare no conflict of interest.

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The Significance of the Expression Level of Carbohydrate Antigen 125 (CA125) in Threatened Miscarriage

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Abstract: *Objective:* To investigate the expression level of carbohydrate antigen 125 (CA125) in threatened miscarriage and explore its significance in the auxiliary diagnosis of threatened miscarriage. *Method:* Pregnant women who underwent prenatal examinations in the hospital from June 2023 to June 2024 were collected. Among them, 66 cases were clinically diagnosed with threatened miscarriage and 74 cases had early normal pregnancies. The expression levels of CA125 in the serum of the above research subjects and the HCG levels of pregnant women with different pregnancy conditions were compared. *Result:* The expression level of CA125 in the threatened abortion group (119.0 ± 23.37) was significantly higher than that in the normal pregnancy group (57.15 ± 5.554), and the difference was significant ($p < 0.05$). Clinical data analysis showed that the expression level of human chorionic gonadotropin (HCG) in the threatened abortion group (11690 ± 2337) was significantly lower than that in the normal pregnancy group (36130 ± 6855), and there was a significant difference between the two ($p < 0.05$); The expression level of progesterone (P) in the threatened abortion group was also significantly lower than that in the normal pregnancy group ($P < 0.05$). *Conclusion:* CA125 is abnormally expressed in the serum of pregnant women with threatened miscarriage and can be used as a molecular marker for the auxiliary diagnosis of threatened miscarriage. Regular detection of the concentration of CA125 in the serum of pregnant women can provide a reference for clinical assessment of decidual damage and can be used as an auxiliary basis for predicting the risk of threatened miscarriage.

Keywords: Threatened miscarriage; Carbohydrate antigen 125; Molecular markers

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1. Introduction

Threatened abortion refers to the condition where there is a small amount of vaginal bleeding, often dark red or bloody leucorrhea, before 28 weeks of gestation, without the expulsion of pregnancy tissue, followed by paroxysmal lower abdominal pain or back pain. Gynecological examination shows that the cervix is not open, the membranes are not ruptured, and the uterus size corresponds to the gestational week. The incidence rate is 20–25% ^[1]. Depending on the time of occurrence, it can be divided into two types: early threatened abortion, which occurs before 12 weeks of gestation, and late threatened abortion, which occurs at or after 12 weeks. Nearly 50% of pregnant women are forced to terminate their pregnancies, severely affecting their physical and mental health as well as their family's quality of life ^[2].

Currently, the clinical diagnosis of threatened abortion mainly relies on the clinical manifestations of pregnant women, such as irregular vaginal bleeding, abdominal pain, sound monitoring, and detection of human chorionic gonadotropin (HCG) in peripheral blood ^[3]. However, this method often considers ultrasound and peripheral blood testing only after pregnant women consciously experience corresponding clinical manifestations, and thus cannot play an early “warning” role. Therefore, finding markers for the auxiliary diagnosis of threatened abortion has become a top priority. According to literature studies, carbohydrate antigen 125 (cancer antigen 125, CA125), as an emerging biomarker, has received increasing attention in the field of early threatened abortion. This indicator may have potential value in predicting and diagnosing early threatened abortion.

CA125 is a glycoprotein derived from the coelomic epithelium during embryonic development. It is low or even not expressed in normal ovarian tissue but is highly expressed in the peripheral blood of patients with ovarian tumors. Currently, CA125 has been widely used as a molecular marker for ovarian tumors in clinical practice for many years. In recent years, studies have found abnormal expression of CA125 in tumor diseases such as rectal cancer and breast cancer ^[4, 5]. However, its role in threatened abortion is less understood.

2. Materials and methods

2.1. Materials

A total of 140 pregnant women undergoing prenatal examination in our hospital from June 2023 to June 2024 are collected, including 66 cases clinically diagnosed with threatened abortion with an average age of 33.5 years (range: 20–46 years), and 74 cases of early normal pregnancy with an average age of 31.5 years (range: 20–43 years). All pregnant women and their families are informed of the purpose and significance of this study and volunteer to participate.

The inclusion criteria are:

- (1) The diagnosis of threatened abortion meets the relevant standards, that is, a small amount of vaginal bleeding occurs before 28 weeks of gestation, often dark red or bloody leucorrhea, without the expulsion of pregnancy tissue, followed by paroxysmal lower abdominal pain or back pain. Gynecological examination shows that the cervix is not open, the membranes are not ruptured, and the uterus size corresponds to the gestational week.
- (2) Natural pregnancy
- (3) Human chorionic gonadotropin in the serum and urine of all pregnant women is positive
- (4) Ultrasound shows intrauterine singleton pregnancy
- (5) No drug or surgical embryo killing was performed before detection.

The exclusion criteria include:

- (1) Ectopic pregnancy
- (2) Clinically diagnosed with tumors or severe liver, kidney, and other organ diseases.

2.2. Methods

On the day of testing, 5 mL of blood is collected from the elbow vein on an empty stomach in the morning and placed in a biochemical tube. After standing, the supernatant serum is collected by centrifugation at 4000r for 20 minutes. The expression level of CA125 is examined using a chemiluminescence method. The CA125 reagent is an Abbott CA125 chemiluminescent microparticle immunoassay kit, and the instrument is Abbott I2000.

2.3. Statistical analysis

Data analysis is performed using GraphPad Prism 5.0 software. The expression levels of CA125 in the threatened abortion group and the normal pregnancy control group are analyzed using a non-parametric test for two independent samples. A *P*-value less than 0.05 is considered statistically significant.

3. Results

3.1. Comparison of CA125 between the two groups ($\pm S$)

The expression level of CA125 in the threatened abortion group was 119.0 ± 23.37 , while the expression level of CA125 in the normal pregnancy group was 57.19 ± 5.554 . The level of CA125 in the threatened abortion group was significantly higher than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 1** (unit: U/ml).

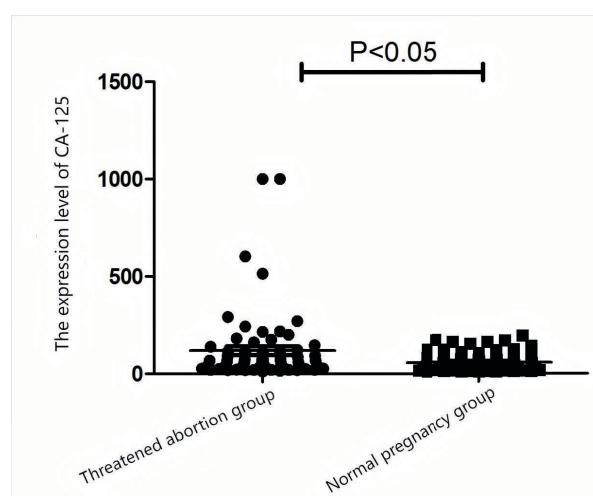


Figure 1. Expression levels of CA125 in maternal serum between threatened abortion and normal pregnancy groups

3.2. Comparison of HCG and P between the two groups ($\pm S$)

Based on the analysis of clinical case data, the expression level of HCG in the threatened abortion group was 11690 ± 2337 , while that in the normal pregnancy group was 36130 ± 6855 . The HCG level in the threatened abortion group was significantly lower than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 2** (unit: U/L). The expression level of P in the threatened abortion group was 42.82 ± 4.383 , while that in the normal

pregnancy group was 63.81 ± 4.151 . The P level in the threatened abortion group was significantly lower than that in the normal pregnancy group ($P < 0.05$), as shown in **Figure 3** (unit: nmol/L).

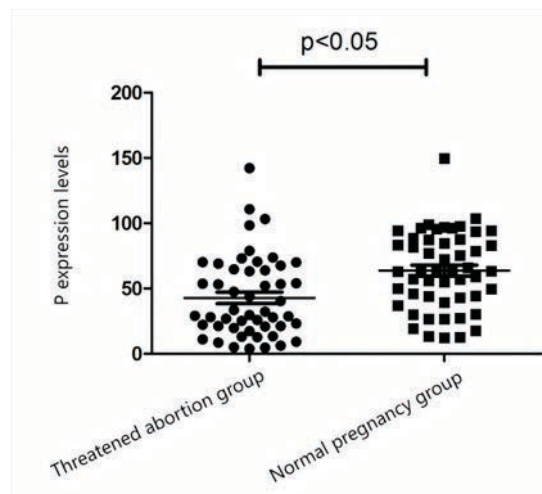


Figure 2. Expression levels of CA125 in the serum of pregnant women in the threatened abortion group and the normal pregnancy group

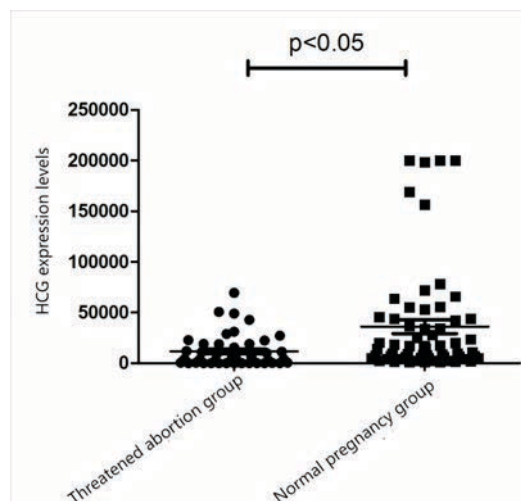


Figure 3. Expression levels of progesterone in maternal serum between threatened abortion and normal pregnancy groups

3.3. Analysis of the effectiveness of CA125 as a molecular marker for auxiliary diagnosis of threatened abortion

Using GraphPad Prism 5.0 software, a ROC curve was plotted to analyze the expression level of CA125 in 66 pregnant women with threatened abortion and 74 pregnant women with normal pregnancies (**Figure 4**). The area under the curve was 0.6144 (95% CI: 0.52–0.70).

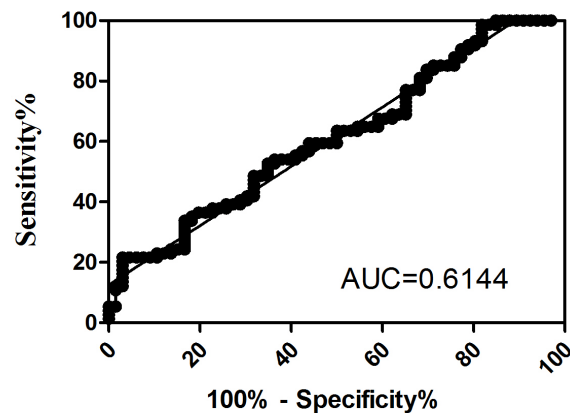


Figure 4. CA125 ROC curve

4. Discussion

Research indicates that the pathogenesis of threatened abortion involves multiple factors, which can be primarily attributed to embryonic chromosomal abnormalities, maternal health issues, infectious etiologies, and immune dysfunction. From the chromosomal perspective, common types of abnormalities include trisomy syndromes, polyploidy variations, X chromosome monosomy, and specific chromosomal structural aberrations. Maternal influencing factors can be divided into two categories: one is organic lesions of the reproductive system, such as congenital uterine malformations, cervical or uterine cavity adhesions, and uterine fibroids; the other is pregnancy comorbidities, including gestational diabetes, gestational hypertension syndrome, pelvic inflammation, and thyroid dysfunction. Infectious factors include bacterial vaginosis, toxoplasmosis, listeriosis, and other pathogenic microorganisms. Complex factors such as antiphospholipid antibody syndrome, autoimmune system diseases, and allogeneic immune abnormalities in immune mechanisms may also trigger the risk of abortion. Additionally, the physical condition and psychological trauma of pregnant women significantly affect the development process of threatened abortion, and the high incidence of this disease severely impacts the physical and mental health of pregnant women.

Currently, clinical diagnostic criteria often rely on blood and imaging tests after pregnant women experience abnormal symptoms, which often misses the optimal time for preserving the pregnancy ^[6]. Investigations have shown that patients with threatened abortion presenting with irregular vaginal bleeding during early pregnancy often exhibit subchorionic hematoma characteristics on ultrasonography. Studies have pointed out that there is a positive correlation between serum CA125 concentration and the amount of vaginal bleeding, suggesting that the degree of elevation of this marker can serve as an important reference for evaluating the risk of abortion. CA125, as a tumor-associated glycoprotein antigen, is mainly produced in epithelial tissues of body cavities, mucosal tissues of the genital tract, and epithelial cells of the ovary. Although traditionally used as a marker for ovarian cancer diagnosis, research has revealed its specificity in biological behavior during pregnancy, with significant concentrations present in amniotic fluid, decidual tissue, and chorion. Increasing studies have demonstrated its abnormal expression in other tumors or tumor-related diseases, but there are limited reports on its role in threatened abortion ^[7]. Regarding the mechanism of elevated maternal blood CA125 during early pregnancy, existing research focuses on two directions: first, it is believed that decidua-derived CA125 enters the maternal circulatory system

through the fallopian tubes in a reverse direction, leading to increased serum levels via peritoneal lymphatic absorption. As the pregnancy progresses, the fallopian tube endometrium merges to form a physiological barrier, resulting in a decrease in CA125 concentration. Second, it is advocated that early pregnancy villus invasion, i.e., damage to decidual cells during placental formation, allows CA125 to enter the maternal bloodstream. In cases of threatened abortion, destruction of decidual tissue or separation of the trophoblast-decidua interface triggers the massive release of CA125. Therefore, dynamic monitoring of CA125 level changes can effectively evaluate the degree of damage to decidual and chorionic cells and disease progression.

HCG is an important glycoprotein hormone secreted by placental syncytiotrophoblast cells. In normal healthy pregnancies, HCG starts to double from 40 days after the last menstrual period, peaks between the 8th and 10th weeks, and then begins to decline after 12 weeks. When placental dysfunction or ectopic pregnancy occurs, the rate of HCG increase is far less than that in normal pregnancies. Therefore, clinically, HCG levels are often measured to confirm pregnancy, understand placental function, and detect ectopic pregnancies ^[8]. Meanwhile, P is a crucial steroid hormone produced by the placenta and corpus luteum. In pregnant women, serum P levels continuously increase from the 5th week until slightly decreasing before delivery and rapidly decreasing after placental expulsion. It plays a significant role in maintaining pregnancy, influencing menstruation, and promoting breast development. Clinically, it is commonly used to assess placental and corpus luteum function ^[9, 10]. In this study, serum samples from women with threatened abortion and normal pregnancies were collected to detect CA125 expression levels. Statistical analysis revealed that CA125 was highly expressed in the serum of women with threatened abortion, with statistical significance, and the area under the ROC curve was 0.6144. Clinical case data analysis showed that HCG and P were low in the serum of women with threatened abortion, consistent with their physiological roles during human pregnancy. These data confirm that abnormally elevated serum CA125 levels in early threatened abortion patients are significantly associated with poor pregnancy outcomes. For pregnant women with symptoms of threatened abortion, CA125 level determination has significant clinical predictive efficacy in judging the possibility of pregnancy continuation. However, due to limited time and insufficient sample size, this study did not include detection and correlation analysis of more indicators, and further research will be conducted with an expanded sample size.

5. Conclusion

In conclusion, CA125 can serve as a molecular marker for the auxiliary diagnosis of threatened abortion, providing value for clinical diagnosis and further demonstrating the predictive value of this indicator.

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Disclosure statement

The authors declare no conflict of interest.

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Evidence-Based Strategies for the Prevention and Management of Intradialytic Hypotension in Maintenance Hemodialysis Patients

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Abstract: *Objective:* To summarize evidence on the prevention and management of intradialytic hypotension in maintenance hemodialysis patients, providing reference for clinical practice. *Method:* Chinese and English databases, guideline websites, and professional society websites were systematically searched for literature on intradialytic hypotension guidance, including clinical decisions, guidelines, evidence summaries, systematic reviews, and expert consensus, from database inception to October 1, 2024. Evidence was extracted after literature quality evaluation. *Results:* A total of 11 publications were included: 2 clinical decisions, 7 guidelines, 1 systematic review, and 1 expert consensus. 38 pieces of evidence were summarized across 4 themes: pre-dialysis assessment and prevention, monitoring and management during dialysis, medication use, and patient self-management. *Conclusion:* The best evidence for prevention and management of intradialytic hypotension in maintenance hemodialysis patients is scientific and comprehensive. Healthcare professionals are advised to apply this evidence judiciously in conjunction with clinical realities to ensure patient safety.

Keywords: Hemodialysis; Intradialytic hypotension; Evidence summary; Evidence-based nursing

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1. Introduction

Intradialytic hypotension (IDH) is the most common acute complication in maintenance hemodialysis (MHD) patients, with an incidence of 20–40%^[1, 2]. Currently, most studies recognize the definition of IDH in The European Best Practice Guidelines (EBPG): a decrease in systolic blood pressure of ≥ 20 mmHg (1 mmHg = 0.133 kPa) and a decrease in mean arterial blood pressure of ≥ 10 mmHg on dialysis with symptoms of hypotension,

which requires the administration of interventions^[3, 4]. IDH causes clinical symptoms such as nausea and vomiting, muscle cramps, dyspnea, and transient syncope^[5, 6], which not only results in inadequate dialysis, decreased residual renal function, and occlusion of endovascular fistulae, but also causes cardiovascular and cerebral vascular diseases, and even leads to the death of patients^[7, 9]. At present, there is a lack of standardized and systematic guidance on the prevention and management of hypotension in MHD patients on dialysis in China. This study summarizes the evidence on the prevention and management of IDH in MHD patients, aiming to provide an evidence-based basis for clinical healthcare professionals to develop management programs.

2. Materials and methods

2.1. Literature retrieval strategy

Following the “6S” pyramid model, top-down searches are performed on BMJ Best Practice, UpToDate, Cochrane Library, JBI, National Institute for Health and Clinical Excellence (NIHCE) (UK), Ontario Nursing Association (Canada), International Guidelines Collaboration (IGCC), DynaMed Evidence-Based Knowledge Base, U.S. National Guidelines Repository, Scottish Interhospital Guidelines Network, American College of Physicians Guidelines Repository, Nursing Practice Guidelines Web site, American Society of Diagnostic Interventional Nephrology, National Kidney Foundation, and the British Society of Nephrology Web sites, the websites of professional societies, such as the European Renal Association-European Dialysis and Transplantation Association, the Japan Dialysis Society, and the Chinese Society of Medicine Nephrology Section^[10]. Supplementary searches are performed on databases such as PubMed, Embase, Medline, CINAHL, Web of Science, China Biomedical Database, CNKI, Wanfang Database, VIP Database, and Yimaitong. Chinese keywords such as “hemodialysis / renal dialysis /hemodialysis purification /hypotension in dialysis /complications” and “systematic evaluation / systematic review /evidence-based /guidelines /summary of evidence /recommendations /consensus /statements”. English keywords included “renal dialysis /maintenance hemodialysis /maintained hemodialysis /hemopurification /HD /haemodialysis /blood purification” and “hypotension /IDH /adverse events in dialysis /intradialytic hypotension /low blood purification.” The search was performed from the time of construction to October 1, 2024. This study is registered with the Center for Evidence-Based Nursing at Fudan University under registration number on ES20257587.

2.2. Literature inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Publicly available literature in Chinese and English
- (2) The study subjects are MHD patients
- (3) The study is on the prevention, treatment, and care of IDH
- (4) The type of study is on clinical decision making, guideline, evidence summary, systematic evaluation, and expert consensus

2.2.2. Exclusion criteria

- (1) Full text is not available
- (2) Guidelines and expert consensus that had been updated
- (3) Research proposal or report, abstract

(4) Low quality evaluation, incomplete information, duplicate publication, or translated version

2.3. Literature quality evaluation

- (1) Guideline evaluation is performed using the appraisal of guidelines for research and evaluation II, AGREE II ^[11].
- (2) Expert consensus is evaluated using the JBI expert consensus evaluation tool ^[12].
- (3) Systematic evaluations are evaluated using the measure tool to assess systematic reviews, AMSTAR 2 ^[13].
- (4) Critical appraisal for summaries of evidence (CASE) to evaluate the quality of inclusion in clinical decision making ^[14].

2.4. Evidence extraction, integration, and evaluation

The evaluation of guidelines is done independently by four researchers, and the rest of the literature is done independently by two researchers. In case of disagreement, it was discussed and adjudicated by the research team. When evidence from different sources conflicted, the inclusion of evidence followed the principle of prioritizing the most recently published, authoritative sources, and evidence-based evidence ^[15]. Inclusion is done using the JBI Evidence Pre-grading and Evidence Recommendation Level System (2014) to evaluate the inclusion of evidence and categorize it into levels 1 to 5, where 1a is the highest level and 5c is the lowest level ^[16].

3. Results

3.1. General characteristics of the included literature

A total of 690 documents were retrieved, and 38 documents were obtained after initial screening by de-emphasizing, reading titles and abstracts, and further re-screened by reading the full text and quality evaluation, and finally 11 documents were obtained, including 2 clinical decision-making, 7 guidelines, 1 systematic evaluation, and 1 expert consensus ^[17–25, 26, 28]. The basic characteristics of the literature are shown in **Table 1**.

Table 1. Basic characteristics of included literature ($n = 11$)

Literature	Publication time (year)	Literature sources	Document type	Subject
Jennifer <i>et al.</i> ^[17]	2023	Uptodate	Clinical decision	Intradialytic hypotension in an otherwise stable patients
Thomas <i>et al.</i> ^[18]	2022	Uptodate	Clinical decision	Emergency hemodialysis prescription
Kooman <i>et al.</i> ^[19]	2007	European Renal Association -- European Dialysis and Transplantation Association	Guide	Guidelines for the management of patients with hemodynamic instability
National Kidney Foundation ^[20]	2015	Cochrane	Guide	KDOQI Clinical practice guidelines for hemodialysis adequacy: 2015 update
Ashby <i>et al.</i> ^[21]	2019	British Renal Association Network	Guide	Hemodialysis Clinical Practice Guidelines
Watanabe <i>et al.</i> ^[22]	2015	Uptodate	Guide	Dialysis prescription for maintenance hemodialysis
Hirakata <i>et al.</i> ^[23]	2012	Japanese Society for Dialysis Therapy	Guide	Guidelines for Management of Cardiovascular Diseases in Patients on Chronic Hemodialysis

Table 1 (Continued)

Literature	Publication time (year)	Literature sources	Document type	Subject
Chen XM ^[24]	2021	Pulse of Medicine (TCM)	Guide	Standard Operating Procedures for Blood Purification
Liu WH <i>et al.</i> ^[25]	2015	Wanfang (China)	Guide	Clinical Practice Guidelines for Hemodialysis Adequacy in China
Mustafa <i>et al.</i> ^[26]	2016	PubMed	Systematic review	Dialysate temperature reduction for intradialytic hypotension for people with chronic kidney disease requiring haemodialysis
Li WG <i>et al.</i> ^[28]	2022	Wanfang (China)	Expert consensus	Expert consensus on prevention and treatment of hypotension in hemodialysis

3.2. Results of literature quality evaluation

Two clinical decisions were included in this study, all of which were evaluated as “yes” except for the entry “whether potential bias was avoided”, which was evaluated as “partially yes”^[17, 18]. Seven guidelines were recommended at grade B or higher^[19–25]. Two systematic evaluations were evaluated in this study, one of which was included in the literature, and one of which was traced back to the original literature through clinical decision-making derived from UpToDate^[26, 27]. Literature was rated as “yes” for all entries except entry 4, “Systematic evaluation of whether authors used a comprehensive search strategy”, which was rated as “partially yes”; and literature was rated as “partially yes” except for entry 4 evaluated as “partially yes” and entry 10 “Systematic evaluation of whether authors reported funding sources for individual studies” evaluated as “no”, all other entries in literature were evaluated as “Yes” for all entries^[26, 27]. One expert consensus was included, and all entries were evaluated as “yes”^[28].

3.3. Summary of evidence

Through evidence extraction and integration, 38 pieces of evidence were summarized and formed in 4 areas: pre-dialysis assessment and prevention, monitoring and management, medication use, and patient self-management, as shown in **Table 2**.

Table 2. Summary of the best evidence for the prevention and management of hypotension in hemodialysis patients during dialysis

Category of evidence	Content of evidence	Level of evidence
Assessment and prevention	1.It is recommended that the target weight be assessed once a month and again when the clinical situation changes ^[17,21-22,28]	1a
	2.The use of objective measurements is recommended to supplement the assessment of the patient's fluid status after an ambiguous clinical assessment or after the occurrence of a complication ^[17,21-24]	2b
	3.Evaluate patient's cardiac function and maintain patient's cardiac status ^[17,19,23-24,28]	1a
	4.Evaluate primary causes of hypotension e.g. pericardial effusion, amyloidosis, systemic infection, air embolism ^[17,24]	1a
	5.It is recommended that the ultrafiltration rate be controlled at or below 13 ml/kg-h in dialysis ^[23, 28]	2a
	6.Reduction of IDH using a simple ultrafiltration model ^[28]	2b
	7.Ultrafiltration programs (curves) are not recommended to prevent IDH ^[17-19,28]	3b
	8.In patients with frequent IDH, a dialysate with a calcium concentration of no less than 1.5 mmol/L is recommended ^[18-19,24]	2b
	9.Avoid magnesium dialysate ≤ 0.25 mmol/L, especially in combination with low-calcium dialysates ^[19]	2b
	10.It is not recommended to increase the sodium concentration to reduce the incidence of hypotension in dialysis, and if it is needed, it is not recommended to set the dialysate with a sodium concentration of >144 mmol/L and try not to increase the sodium concentration 1 h before going off the machine ^[28]	2a
	11.Use of low-temperature dialysis fluid, dialysis fluid temperature ≤ 36 °C and ≥ 35 °C ^[17-20,23-24,26-28]	2a
	12.Recommendations for prolonging dialysis duration and/or increasing dialysis frequency ^[17-20,23-24,28]	2b
	13.In patients with frequent IDH or IDH that is not easily corrected, a change in dialysis modality, such as hemodialysis filtration, peritoneal dialysis, daily dialysis, or nocturnal dialysis, is recommended ^[17,19,23-24,28]	2b
	14.The use of dialysis devices with continuous blood pressure monitoring and biofeedback mechanisms and automatic ultrafiltration control is recommended for the prevention of IDH. ^[28]	3c
	15.Automated Volume Control Feedback Can Be Tried as a Second-Line Option for Patients with Refractory IDH ^[17,19]	3c
Monitoring and processing	16.It is recommended that blood pressure and heart rate should be measured frequently during dialysis to predict the onset of IDH ^[19]	5c
	17.Reduce ultrafiltration rate or stop ultrafiltration ^[17,19,24,28]	1a
	18.Reduced blood flow <200 ml/min and dialysate flow rate <350 ml/min ^[24]	2a
	19.Recommended head-down supine position or elevated lower extremities (passive leg raising test) ^[17,24,28]	1a
	20.Recommended 50% dextrose injection 40~100ml IV, isotonic/hypertonic saline 100~200ml rapid IV infusion ^[17,23-24,28]	1a
	21.For those whose blood pressure has not recovered, a rapid intravenous infusion of 100-200 ml of 20% mannitol solution and a rapid infusion of 100 ml of hydroxyethyl starch solution (succinyl gelatin) are recommended ^[23-24,28]	3a
	22.Human albumin transfusion is recommended for those whose blood remains unrecovered ^[23-24,28]	3c
	23.Oxygen therapy is recommended ^[17,28]	2a
	24.Cardiac monitoring is recommended, and blood pressure should be rechecked every 5 min. ^[28]	1a
	25.Use of antihypertensive drugs (intravenous pumping of vasoactive drugs or orthostatic inotropic drugs) for those with hypotension despite adequate fluid intake ^[24,28]	2a
	26.Early termination of dialysis if treatment for severe hypotension is ineffective ^[24,28]	2a
Drug use	27.It is recommended that antihypertensive drugs should be discontinued/reduced prior to dialysis in patients with a tendency to develop hypotension on dialysis ^[17,19,24,28]	2a
	28.It is recommended that patients with residual urine output be given an oral diuretic to increase urine output, preferably a tab diuretic ^[17,27]	1a
	29.It is recommended to give 2.5~5.0mg of midodrine hydrochloride 15~30min before dialysis ^[17-18,28]	2a
	30.L-carnitine supplementation is recommended ^[17,19,24,28]	2a
	31.In elderly or comorbid diabetic patients, 20-40 ml of 50% dextrose can be given after 2 hours of dialysis to stabilize hemodynamics ^[19,23]	3a

Table 2 (Continued)

Category of evidence	Content of evidence	Level of evidence
Patient self-management	32.Improve nutritional status, correct hypoproteinemia, recommend serum Alb ≥ 35 g/L, serum Alb ≥ 40 g/L if available ^[23-25,28]	2a
	33.Correct anemia and recommend maintaining Hb levels at 110g/L~130g/L ^[19-20,23-25]	2a
	34.Control of weight gain during the interdialytic period should be prioritized by controlling sodium intake, with a recommended daily salt intake of <3 to 6 g (less than 3 g is preferred) ^[17,19-20,24-25,28]	1a
	35.Recommended weight gain between dialysis <5% of target weight (3% or less preferred) ^[25,28]	1a
	36. Water intake should include not only liquids but also water in food ^[20,25]	2b
	37.Recommended pre-dialysis systolic blood pressure <160 mmHg (with medication) ^[25]	5a
	38.In hypotensive dialysis patients and those with a tendency to hypotension on dialysis, fasting should be done during dialysis ^[17,19-21,24-25,28]	2a

4. Discussion

4.1. Regular assessment of target weight and cardiac function

Target weight is the weight a dialysis patient wishes to achieve at the end of dialysis under normal equilibrium conditions^[29]. Studies have shown that patients with MHD have lower all-cause mortality using target weight assessment compared to assessment through clinical performance^[30]. Pre-existing cardiovascular disease in the end-stage renal disease population as well as dialysis complications lead to systolic or diastolic dysfunction of the heart, increasing the risk of IDH^[19, 28]. Evidence 1–2 gives clear guidance on the frequency and manner of assessment of target body weight, recommending that it should be assessed using objective measures such as bioimpedance techniques, blood volume monitoring, and inferior vena cava or lung ultrasound. Evidence 3–4 states that patients' cardiac functional status should be assessed regularly and that primary causes of hypotension should be treated aggressively. Therefore, it is recommended that healthcare professionals enhance the comprehensive assessment of dialysis patients' volume status through multidisciplinary cooperation and the combined application of multiple methods.

4.2. Setting the appropriate ultrafiltration mode and rate

The application of ultrafiltration mode and rate is described in Evidence 5–7. The main mechanism of IDH occurrence is the reduction of effective circulating blood volume caused by ultrafiltration, and in order to alleviate the loss of blood volume, pure ultrafiltration is used to remove water from the body in order to minimize the change of plasma osmolality. Ultrafiltration modes can adjust the rate of ultrafiltration to influence blood volume changes. The most commonly used ultrafiltration curves are characterized by an initial high ultrafiltration rate, an intermediate linear decrease in ultrafiltration rate or intermittent ultrafiltration pulses, and finally a minimal ultrafiltration cycle. Guidelines state that controlling the ultrafiltration rate in dialysis to 13 ml/kg-h or less is effective in reducing the incidence of IDH in patients^[28]. Taken together, these recommendations suggest that the pattern and goals of individualized ultrafiltration should be carefully observed and set in dialysis.

4.3. Reasonable Dialysate Concentration and Temperature

Evidence 8–11 gives guidance on the concentration, type, and temperature of dialysate. Changes in the concentration of ionized calcium can affect myocardial contractility during dialysis. Therefore, enhancing cardiac

contractile function by elevating dialysate calcium concentration is also an effective means of preventing IDH; however, high-calcium dialysate may have short-term adverse effects on atherosclerosis and cardiac diastolic properties, and should be used with caution^[19]. It has been noted that elevating the sodium concentration of dialysate can maintain plasma osmolality^[17, 28]. However, the use of higher sodium concentrations for dialysis can affect sodium balance, leading to patient thirst and weight gain between dialysis sessions. Therefore, several guidelines do not recommend increasing sodium concentration to reduce the incidence of IDH, and national studies supporting the attitude are applying adjustable sodium in combination with other means, such as temperature or ultrafiltration mode to prevent IDH^[17–19, 28]. Studies have shown that dialysis with dialysate below body temperature can help prevent the development of IDH^[26–28]. A Cochrane systematic evaluation concluded that lowering the temperature of the dialysate, while reducing IDH, also increases patient discomfort^[31]. Several guidelines recommend that dialysate temperature should be $\leq 36^{\circ}\text{C}$ and $\geq 35^{\circ}\text{C}$ ^[19–21]. Therefore, dialysate temperature settings should be individualized.

4.4 Changing dialysis modality

Evidence 12–13 comes from expert panel opinions, which are not yet supported by high-quality studies, and therefore are not considered as the preferred measure to prevent IDH^[32]. Evidence 14–15 recommends the use of biofeedback to predict the occurrence of IDH. Hemodialysis is a treatment based on blood purification equipment, and modern dialysis equipment with biofeedback technology correlates with treatment through continuous monitoring of blood pressure and blood volume to improve hemodynamic stability in hemodialysis and achieve prevention of IDH, with some efficacy in clinical trials.

4.5 Timely and effective treatment

Evidence 16 states that enhanced blood pressure and heart rate monitoring during dialysis can predict the occurrence of IDH^[20]. Evidence 17–26 gives a step-by-step management plan for IDH based on the degree of hypotension and clinical symptoms. The occurrence of hypotension is often accompanied by reduced blood perfusion to tissues and organs and decreased oxygen delivery. Therefore, it is recommended that the hypoxic state of tissues and organs can be appropriately improved by timely oxygenation and cardiac monitoring. Clinical staff should be proficient in the management process of IDH to avoid more serious complications in patients caused by IDH, such as endocardial thrombosis^[33].

4.6. Standardizing the use of medications

Evidence 27–31 summarizes the management of medications in IDH-prone populations, including the use of antihypertensives, diuretics, and midodrine hydrochloride. Evidence 30–31 give references to the dosage of midodrine hydrochloride and 50% dextrose, and medical staff adjust the dosage of related medications in a timely manner according to the patient's blood pressure changes in the clinic, as well as monitor the effects of the medications and the adverse effects of long-term use.

4.7. Improving patient self-management

Evidence 32–38 places demands on patients, but requires healthcare professionals to provide guidance on nutrition, anemia and blood pressure management, control of fluid growth, and eating during dialysis^[34]. Improving the nutritional status of patients and actively correcting anemia may reduce the incidence of IDH by improving cardiac function. Blood glucose and blood pressure should be monitored during dialysis, individualized dietary guidance

should be implemented, fasting should be done for patients at risk of hypotension during dialysis, and eating should be encouraged for patients at risk of hypoglycemia^[35].

5. Conclusion

This study summarizes the current best evidence on the prevention and management of hypotension in maintenance hemodialysis patients on dialysis for healthcare professionals. The evidence mostly comes from the more authoritative guidelines and clinical decision-making at home and abroad in the past 5 years, and the overall quality is high, so it is recommended that clinical workers still need to combine the specific clinical situation and patients' wishes to apply the evidence judiciously in the process of selecting and applying the evidence.

Disclosure statement

The authors declare no conflict of interest.

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Systematic Evaluation and Meta-analysis of the Effects of Phase I Cardiac Rehabilitation on Heart Function of Patients after Percutaneous Coronary Intervention

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Abstract: *Objective:* To systematically evaluate the impact of phase I cardiac rehabilitation exercise prescriptions on cardiac function levels in patients after coronary intervention. *Methods:* Seven Chinese and English databases, including Cochrane Library, PubMed, Web of Science, ESC (European Society of Cardiology), and CNKI, as well as professional association websites, were searched using computers, with manual searching as a complement. Relevant literature published from the establishment of the database to February 2025 was retrieved. Two researchers independently screened the literature, extracted data, and evaluated the quality of the literature. Meta-analysis was performed using RevMan 5.3 software. *Results:* A total of 8 articles were included, involving 843 patients. Meta-analysis results showed that compared with routine nursing, phase I cardiac rehabilitation exercise prescriptions helped increase the 6-minute walking distance in patients after coronary intervention [$MD = 0.84$, 95% CI (0.57, 1.10), $P < 0.001$], increase the level of left ventricular ejection fraction in patients after coronary intervention [$MD = 0.67$, 95% CI (0.33, 1.00), $P < 0.001$], and cardiac rehabilitation combined with respiratory rehabilitation exercise could improve the level of left ventricular ejection fraction in patients after coronary intervention [$MD = 0.58$, 95% CI (0.40, 0.76), $P < 0.001$]. *Conclusion:* The implementation of phase I cardiac rehabilitation exercise prescriptions can help improve cardiac function levels in patients after coronary intervention. However, the standardization of outcome evaluation indicators needs to be improved, and the long-term effects of rehabilitation still require verification through a large number of high-quality studies.

Keywords: Cardiac rehabilitation; PCI; Exercise; Cardiac function; Systematic evaluation

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1. Introduction

Cardiovascular disease (CVD) is one of the leading causes of death and disability worldwide, and the prevalence and mortality rates of CVD in China have been increasing year by year^[1]. The “Report on Cardiovascular Health and Diseases in China 2023” estimates that there are 330 million people currently suffering from CVD, including 11.39 million with coronary heart disease (CHD). According to data from the Global Burden of Disease Study (GBD), the age-standardized incidence rate of CVD among people aged 1–79 in China increased from 646.2 per 100,000 person-years in 1990 to 652.2 per 100,000 person-years in 2019^[2]. Globally, it is estimated that the total cost of CVD will rise to an astonishing \$1,044 billion by 2030^[3]. The “China Health Statistics Yearbook 2022” indicates that cardiovascular disease (CVD) accounts for the highest proportion of deaths from diseases among urban and rural residents, with 48.98% and 47.35% of deaths in rural and urban areas, respectively, in 2021^[4]. Acute coronary syndrome (ACS) is an important component of CVD, and percutaneous coronary intervention (PCI) is a crucial treatment method for ACS that has been widely used in China in recent years^[5]. PCI can quickly restore coronary blood flow, improve symptoms of myocardial ischemia, and reduce the risk of cardiovascular events^[6]. However, despite successful PCI, patients still face high cardiovascular risks such as restenosis, arrhythmia, and heart failure^[7]. Additionally, there are various issues such as the impact of bed rest, decreased exercise capacity, and large individual differences. Therefore, postoperative rehabilitation treatment is crucial^[8].

Cardiac rehabilitation is a comprehensive medical measure designed to help patients with CVD restore heart function and improve quality of life through various means such as exercise training, nutritional support, psychological intervention, and drug treatment^[9]. As an essential component of secondary prevention of CVD, a reasonable exercise prescription can enhance myocardial contractility, improve blood circulation to the heart, and increase the heart’s reserve function^[10, 11]. Cardiac rehabilitation can effectively reduce the recurrence rate and mortality of CVD^[12]. Many countries have developed guidelines and standards for cardiac rehabilitation, emphasizing its importance in the prevention and treatment of CVD^[13, 14]. China’s cardiac rehabilitation industry has also made significant progress in recent years^[15]. China has released the “Chinese Expert Consensus on Coronary Heart Disease Rehabilitation and Secondary Prevention” and the “Guidelines for Cardiovascular Disease Rehabilitation/Secondary Prevention in China (2015 Edition)”, further standardizing the process and methods of cardiac rehabilitation^[16, 17].

Phase I cardiac rehabilitation refers to early cardiac rehabilitation treatment that patients undergo during hospitalization, typically beginning 2–3 days after PCI^[18]. It mainly promotes patients’ physical recovery, prevents the occurrence of complications, and improves patients’ self-confidence and ability to live independently^[19]. Phase I cardiac rehabilitation effectively improves heart function, increases left ventricular ejection fraction (LVEF), and reduces left ventricular end-diastolic diameter (LVEDD) in patients after PCI^[20, 21]. Additionally, it can improve myocardial metabolism and remodeling, reduce myocardial cell apoptosis and necrosis, and enhance myocardial endurance and anti-ischemic ability^[22, 23]. By developing personalized exercise prescriptions, patients’ exercise intensity and volume are gradually increased, improving their cardiopulmonary function and exercise endurance^[24–26].

The burden of CVD in China is heavy. Acute coronary syndrome (ACS) is a significant component of CVD, and percutaneous coronary intervention (PCI) is a crucial treatment method for ACS^[27]. Despite advancements in PCI technology, the rehabilitation outcomes for postoperative patients remain unsatisfactory, with high recurrence rates and mortality rates of cardiovascular events^[28–30]. Therefore, postoperative cardiac rehabilitation based on exercise is particularly important for patients after PCI. Currently, there are still some issues in cardiac rehabilitation treatment for patients after PCI, such as non-standardized cardiac rehabilitation programs and

unscientific rehabilitation training^[31, 32]. Specifically, further evidence-based medical evidence is needed to support the specific effects and measures for improving patients' heart function levels. Therefore, this study systematically and comprehensively evaluates the impact of Phase I cardiac rehabilitation exercise prescriptions on the heart function levels of patients after coronary intervention through a systematic review method, providing a reference for continuous improvement in early rehabilitation nursing for patients after coronary intervention.

2. Materials and methods

2.1. Inclusion and exclusion criteria

Inclusion and exclusion criteria are determined based on the PICOS principle.

Inclusion criteria are as follows: (1) Study population (P) consisted of patients aged ≥ 18 years who underwent coronary intervention; (2) Intervention (I) involved the implementation of a phase I cardiac rehabilitation exercise prescription; (3) Control intervention (C) included patients receiving routine care or no cardiac rehabilitation measures; (4) Outcome measures (O) included left ventricular ejection fraction, 6-minute walk test distance, and left ventricular end-diastolic diameter; (5) Study design (S) was randomized controlled trials to enhance the reliability of the research findings.

Exclusion criteria are: (1) Non-Chinese and non-English literature; (2) Duplicate publications or literature with incomplete data; (3) Literature where the full text was unavailable.

2.2. Literature search strategy

Computer searches are conducted in Chinese databases, including CNKI, WanFang Database, and VIP Database, as well as English databases such as Cochrane Library, PubMed, Web of Science, and the European Society of Cardiology (ESC). The search period is from the establishment of the databases until February 2025. Manual searches are also performed to trace the references of included literature. A combination of subject headings and free-text terms is used. For example, in PubMed, the search strategy is: ("Percutaneous Coronary Intervention"[Mesh]) AND [(("Exercise"[Mesh]) OR ("Cardiac Rehabilitation"[Mesh])) AND ((("Heart Function Tests"[Mesh]) OR ("Walk Test"[Mesh]) OR (Left ventricular end-diastolic diameter) OR (left ventricular ejection fraction))].

2.3. Literature screening and data extraction

After removing duplicates using Zotero 7.0 software, two graduate students trained in evidence-based nursing independently screened the literature by reading titles and abstracts, excluding clearly irrelevant articles. They then read the full texts for further screening and data extraction. A third researcher intervened in case of disagreement. Extracted information included: author, publication year, country, basic characteristics of the study population, intervention measures (experimental and control groups), intervention duration, and outcome measures.

2.4. Literature quality evaluation

The two researchers who extracted data independently evaluated the quality of the literature using the Cochrane Collaboration's risk of bias tool for randomized controlled trials. The tool consists of seven items, each rated as "low risk," "uncertain," or "high risk." Studies that fully met the criteria are considered to have the lowest risk of bias (quality grade A). Those that partially met the criteria are considered to have a moderate risk of bias (grade B).

Studies that did not meet the criteria are considered to have a high risk of bias (grade C) and are excluded.

2.5. Statistical methods

Statistical analysis is performed using RevMan 5.3 software. Continuous data are expressed as mean differences (*MD*) with 95% confidence intervals (*CI*). The chi-square test is used to determine the presence of heterogeneity among studies, with $P > 0.05$ and $I^2 < 50\%$ as the criteria for homogeneity. If both statistical conditions are met, a fixed-effects model is used for analysis. If one of the conditions is not met, indicating heterogeneity among studies, a random-effects model is applied. A $P < 0.05$ is considered statistically significant.

3. Results

3.1. Literature screening results

Initially, 1352 articles were retrieved. After screening, 8 articles were finally included, including 3 in English and 5 in Chinese^[33–40]. The literature screening process and results are shown in **Figure 1**.

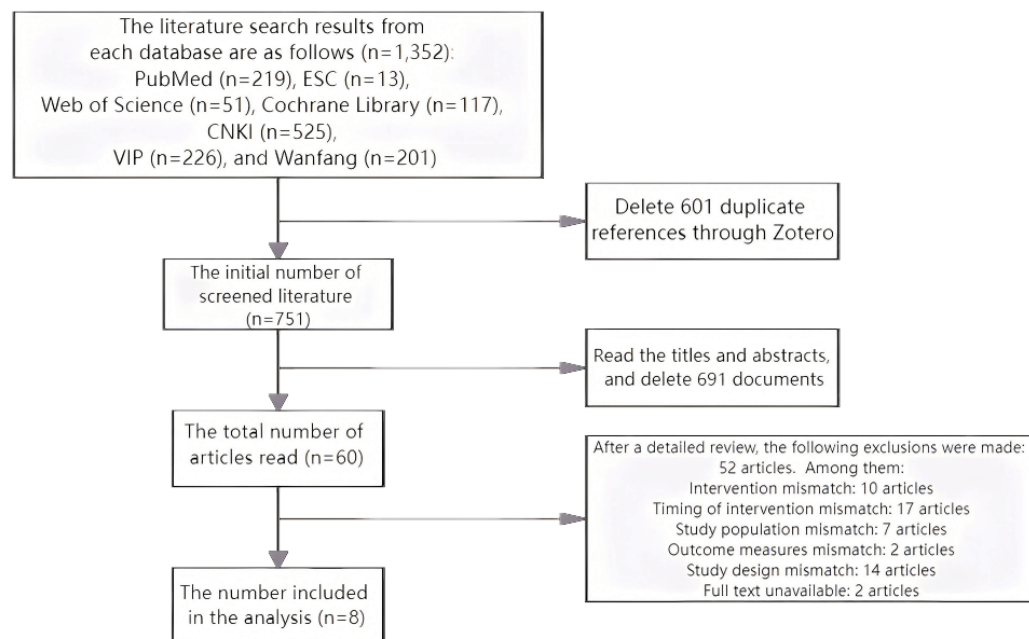


Figure 1. Flowchart of literature screening

3.2. Basic characteristics of included literature

The publication dates of the included literature ranged from 2017 to 2023, involving a total of 843 patients who underwent coronary intervention, with 422 in the experimental group and 421 in the control group. The basic characteristics of the included literature are shown in **Table 1**.

Table 1. Basic characteristics of included literature (*n*=8)

Included literature	Year	Country	Intervention group			Control group intervention	Outcome measures
			Sample size (E/C)	Intervention measures	Intervention method	Intervention duration	
Firoozeh Abtahi <i>et al.</i> ^[33]	2017	Iran	25/25	Comprehensive Cardiac Rehabilitation Program	Exercise training	Starting post-PCI, lasting 8 weeks	Risk factor management guidance only LVEF, LVESD, LVM
Ming-Gui Chen <i>et al.</i> ^[34]	2020	China	48/48	Baduanjin Exercise Training	Inpatient: Seated Baduanjin; Post-discharge: Standing Baduanjin	Starting the second day post-PCI, lasting 24 weeks	Routine care Quality of life, LVEF, BNP, BMI, Waist circumference
Liao Y ^[35]	2020	China	43/43	Individualized Cardiac Rehabilitation Training	Including respiratory training, rehabilitation exercises	Starting the second day post-PCI, lasting 24 weeks	Routine care Exercise compliance, Cardiac function, Cardiovascular adverse events
Bai FF <i>et al.</i> ^[36]	2020	China	125/125	Cardiac Rehabilitation Content	Health education, exercise rehabilitation & daily activity guidance, psychological intervention, smoking cessation management, nutritional management	Starting post-PCI, lasting 12 months	Routine drug therapy Cardiopulmonary assessment, Psychological assessment, Quality of life, Smoking cessation rate, Cardiovascular event rate
Chen Q <i>et al.</i> ^[37]	2020	China	54/ 53	Cardiac Rehabilitation Therapy	Phase I (in-hospital), Phase II (1st month post-discharge), Phase III (1-6 months post-discharge)	Starting post-PCI, lasting 6 months	Routine rehabilitation therapy Vascular endothelial indicators, Cardiac function indicators, Psychological cognitive status
Minghui Jiang <i>et al.</i> ^[38]	2021	China	49/49	Progressive Kinetic Exercise	Including bed mobility assistance, respiratory training, stretching exercises, etc.	Starting post-PCI, lasting 6 months	Routine intervention Cardiac function and Quality of life, Adverse event rate and Motor function
Zhou Y <i>et al.</i> ^[39]	2023	China	30/30	Early Cardiac Rehabilitation Training	Exercise Training	Starting post-PCI	Routine drug therapy LVEF, 6MWD, Quality of life score, Major adverse cardiovascular event (MACE) rate
Xu Y <i>et al.</i> ^[40]	2023	China	48/48	Phase I Cardiac Rehabilitation Exercise	Respiratory training, Exercise training		Routine care Cardiac function, Adverse reaction rate, Activities of daily living (ADL)

3.3. Methodological quality evaluation results of included literature

All 8 articles included were graded as B in quality, indicating a relatively high overall quality of the included literature. The methodological quality evaluation results of the included literature are shown in **Figure 2**.



Figure 2. Methodological quality evaluation results of included literature ($n=8$)

3.4. Meta-analysis and descriptive analysis results

3.4.1. Left ventricular end-diastolic diameter

Data from 5 articles^[33,36–38,40] were included in the analysis. A random effects model was used for analysis ($P < 0.01$, $I^2 = 94\%$). The results showed no statistically significant difference in left ventricular end-diastolic diameter between the two groups [$MD = 0.13$, 95% $CI (-0.61, 0.87)$, $P = 0.73$], as shown in **Figure 3**.

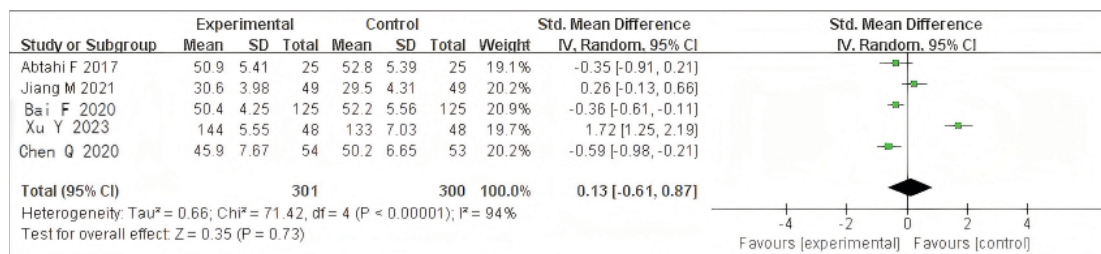


Figure 3. Forest plot of left ventricular end-diastolic diameter

3.4.2. 6-minute walk test distance

Data from 3 articles were included in the analysis^[35,39, 40]. A fixed effects model was used for analysis ($P = 0.44$, $I^2 = 0\%$). The results showed that the 6-minute walk distance in the experimental group was higher than that in the control group, and the difference was statistically significant [$MD = 0.84$, 95% $CI (0.57, 1.10)$, $P < 0.01$], as shown in **Figure 4**.

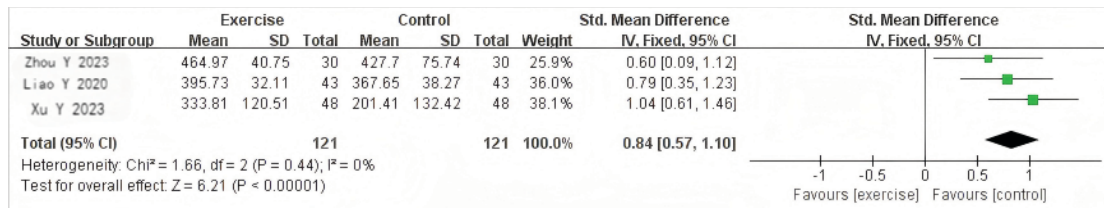


Figure 4. Forest plot of 6-minute walk test distance

3.4.3. Left ventricular ejection fraction

Data from 8 articles were included in the analysis^[33–40]. A random effects model was used for analysis ($P < 0.01$, $I^2 = 81\%$). The results showed that the left ventricular ejection fraction in the experimental group was higher than that in the control group, and the difference was statistically significant [$MD = 0.67$, 95% CI (0.33, 1.00), $P < 0.01$], as shown in **Figure 5**. Among them, 4 articles adopted cardiac rehabilitation combined with respiratory rehabilitation training and could be combined for analysis^[35–37, 39]. The heterogeneity among subgroups was moderate ($P = 0.18$, $I^2 = 39\%$). A random effects model was used for analysis. The subgroup analysis results showed that the left ventricular ejection fraction in the experimental group was higher than that in the control group, and the difference was statistically significant [$MD = 0.58$, 95% CI (0.40, 0.76), $P < 0.01$], as shown in **Figure 6**.

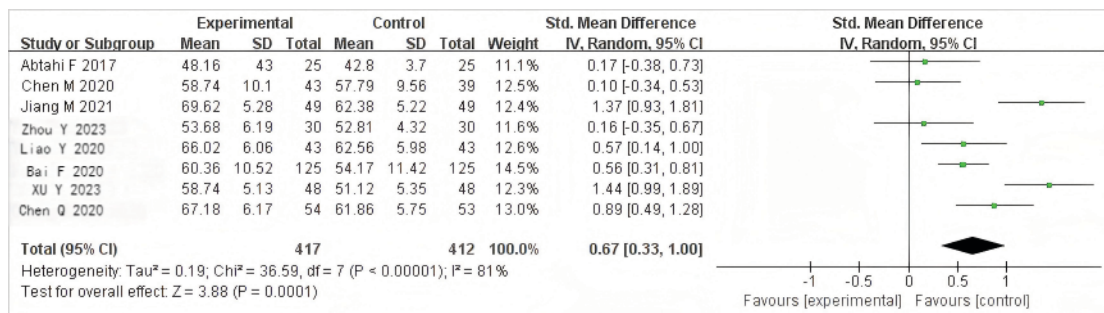


Figure 5. Forest plot of left ventricular ejection fraction

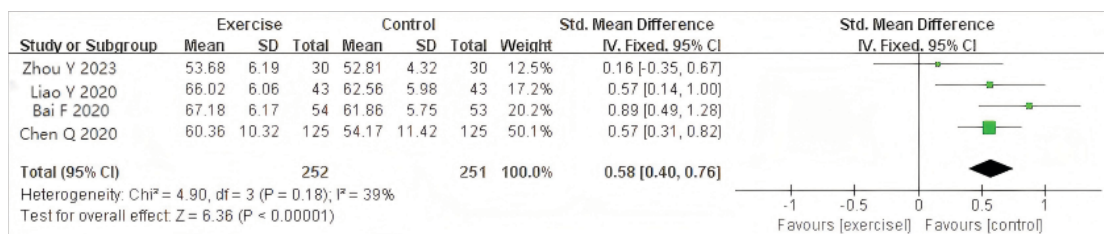


Figure 6. Subgroup analysis forest plot of left ventricular ejection fraction

3.5. Publication bias

In this study, less than 10 articles were included, so a funnel plot was not drawn.

4. Discussion

4.1. Phase I cardiac rehabilitation exercise prescription helps improve 6-minute walk test distance for patients after coronary intervention

The 6-minute walk distance (6MWD) is not only a commonly used indicator reflecting the cardiopulmonary

function of patients after coronary intervention, but also an objective evaluation index of patients' rehabilitation progress and treatment effect. Research has shown that Phase I cardiac rehabilitation focuses on evaluating and training patients' exercise capacity^[24]. By developing personalized exercise prescriptions, patients' exercise intensity and volume are gradually increased, improving their cardiopulmonary function and exercise endurance. Study indicates that Phase I cardiac rehabilitation can significantly improve the 6-minute walk distance (6MWD) and cardiopulmonary exercise test indicators, such as maximal oxygen uptake and anaerobic threshold, for patients after PCI^[25]. This study found that in improving the 6-minute walk test distance after coronary intervention, the Phase I cardiac rehabilitation exercise prescription is superior to traditional care. However, due to the limited number of studies that can be combined and analyzed under this outcome indicator, high-quality research is still needed for further verification.

4.2. Phase I cardiac rehabilitation exercise prescription contributes to improving left ventricular ejection fraction levels for patients after coronary intervention

According to research, early cardiac rehabilitation can alleviate myocardial ischemia, increase exercise tolerance, inhibit myocardial necrosis and apoptosis, reverse ventricular remodeling and myocardial remodeling, and enhance patients' heart function^[22]. The results of this study suggest that the Phase I cardiac rehabilitation exercise prescription is beneficial for improving the left ventricular ejection fraction level of patients after coronary intervention. Based on the subgroup analysis results, it is hinted that combining cardiac rehabilitation exercise prescriptions with respiratory rehabilitation has a better effect on enhancing the left ventricular ejection fraction level for patients after coronary intervention. Future research can explore the integration of cardiopulmonary rehabilitation training and develop more personalized rehabilitation strategies to enhance the rehabilitation outcomes for patients after coronary intervention.

4.3. Limitations and prospects of this study

This study has certain limitations. For instance, the searched databases are limited, and the existing Chinese and English databases and professional association websites are not fully covered. The sample sizes in the included literature are all limited, and the subjects come from different countries and regions with age variations. The specific implementation process of the cardiac rehabilitation exercise prescription is difficult to ensure homogeneity. Based on the results of this study, it is suggested to optimize the exercise prescription of the cardiac rehabilitation program, improve the quality of cardiac rehabilitation, and promote the clinical application of Phase I cardiac rehabilitation for patients after PCI.

5. Conclusion

This study comprehensively evaluated the impact of the Phase I cardiac rehabilitation exercise prescription on the cardiac function levels of patients after coronary intervention. It initially confirmed that the Phase I cardiac rehabilitation exercise prescription can promote the improvement of the 6-minute walk distance and left ventricular ejection fraction. Combining it with respiratory rehabilitation training can be more effective than conventional nursing care, which can promote the clinical application of the Phase I cardiac rehabilitation exercise prescription to a certain extent.

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Disclosure statement

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Emergency Nursing Care for a Pediatric Patient with Severe Scrub Typhus Complicated by Hemophagocytic Syndrome and Septic Shock

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Abstract: This article summarizes the nursing management of a pediatric patient with severe scrub typhus complicated by hemophagocytic syndrome (HPS) and septic shock. Key nursing interventions included early recognition and management of septic shock, rational oxygen therapy, fluid resuscitation, administration of vasoactive agents, early and targeted anti-infective therapy, management of hyperpyrexia, care of eschar and edematous skin, strict infection prevention and isolation protocols, and family health education. After 11 days of intensive treatment and nursing care, the patient recovered and was discharged.

Keywords: Scrub typhus; Hemophagocytic syndrome; Septic shock; Pediatric nursing; Critical care

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1. Introduction

Scrub typhus, also known as jungle typhus, is an acute zoonotic infectious disease caused by *Orientia tsutsugamushi* infection. It is transmitted through the bites of larval mites (chiggers) and can lead to various severe complications that threaten human health ^[1, 2]. Currently, there are few reports on severe scrub typhus complicated with hemophagocytic syndrome leading to septic shock. On September 30th, 2024, a child with severe scrub typhus complicated by hemophagocytic lymphohistiocytosis (HLH) is admitted, who subsequently developed septic shock. After active treatment and comprehensive nursing care, the child improved and was discharged after 11 days. The case is reported as follows.

2. Case presentation

2.1. Clinical data

The patient was a 3-year-and-1-month-old male child, admitted to the hospital's department due to "fever for 6

days, accompanied by rash and swelling of the left upper eyelid for 3 days” and was suspected to have “fever and reduced incidence of the three systems” on September 30th, 2024.

2.2. Course of treatment and clinical outcome

Upon admission, the child presented with recurrent high fever and generalized rash. Laboratory results indicated elevated inflammatory markers and pancytopenia. Further relevant tests and bone marrow smear examinations were conducted, and empirical antibiotic therapy with ceftriaxone was initiated. On the third day of hospitalization, the interval between fever peaks shortened, prompting a switch to meropenem for broader antimicrobial coverage.

On the morning of the fourth hospital day, the child exhibited signs of shock, including irritability, tachypnea, pallor, and hypotension during a febrile episode. Immediate interventions included intravenous fluid resuscitation with normal saline, electrocardiographic and oxygen saturation monitoring, low-flow nasal cannula oxygen administration, and addition of vancomycin for combination antimicrobial therapy. Initial resuscitation was successful.

Later that night, the child experienced another episode of shock. Aggressive anti-shock measures were implemented, including additional fluid resuscitation with normal saline, albumin infusion to enhance colloid osmotic pressure, norepinephrine for blood pressure support, and initiation of caspofungin for possible fungal infection. Resuscitation was successful.

On the fifth hospital day, metagenomic next-generation sequencing (mNGS) of pathogen DNA confirmed *Orientia tsutsugamushi* infection. Chest CT revealed pulmonary edema and pleural effusion. Albumin transfusions were administered, and azithromycin was added to the antimicrobial regimen. Following six days of intensive treatment and meticulous nursing care, the child’s condition improved significantly. Follow-up tests showed normalization of inflammatory markers, and the patient was discharged. Discharge diagnoses included: severe scrub typhus, hemophagocytic lymphohistiocytosis, septic shock, capillary leak syndrome, hypoalbuminemia, hepatic dysfunction, cholestasis, and hypokalemia.

3. Nursing care

3.1. Early recognition and management of septic shock

The Pediatric Early Warning Score (PEWS) was used to identify the child’s condition at an early stage. Pediatric patients often have limited verbal communication skills and poor cooperation during nursing procedures, and the normal ranges for vital signs vary significantly across age groups. This poses a significant challenge for clinical nurses in the early recognition of critically ill children.

PEWS is a simple pediatric scoring system that is intuitive, easy to use, and requires minimal technical expertise. It includes three domains—consciousness, cardiovascular status, and respiratory status—with a total of 11 indicators. Each domain is scored from 0 to 3 points, and the total score reflects the severity of illness; higher scores indicate more severe illness and a higher mortality risk.³ A score of 1–2 suggests relatively stable condition, 3 indicates a potential deterioration, and ≥ 4 indicates a critical condition requiring multidisciplinary intervention and resuscitation.

On the fourth day of hospitalization, this patient had a body temperature of 39°C, presented with irritability, pale lips, tachypnea (45 breaths/min), chills, cold extremities, capillary refill time (CRT) >3 seconds, no palpable dorsalis pedis artery pulses bilaterally, and blood pressure dropped to 76/30 mmHg. The PEWS score was 4.

Immediately, the primary physician and senior nurse were notified for assistance. The primary nurse promptly established two intravenous lines, initiated fluid resuscitation with normal saline, and applied electrocardiographic monitoring and low-flow nasal oxygen therapy.

Following these interventions, the child became less lethargic, skin color improved, respiratory rate decreased to 36 breaths/min, extremities warmed, CRT shortened to 1 second, dorsalis pedis pulses remained slightly weak, and blood pressure increased to 88/55 mmHg. The child also spontaneously voided 100 mL of urine. The PEWS score was reassessed as 1.

Arterial blood gas analysis showed lactate (Lac) level of 1.2 mmol/L, C-reactive protein (CRP) of 48.43 mg/L, serum amyloid A (SAA) >350.00 mg/L, and procalcitonin (PCT) of 3.83 ng/mL. These findings supported the diagnosis of septic shock and sepsis.

3.2. Rational oxygen therapy

After identifying insufficient systemic effective circulating volume and tissue hypoperfusion in pediatric shock, appropriate oxygen therapy should be administered immediately. Priority is given to nasal cannula or mask oxygenation, with non-invasive positive pressure ventilation (NIPPV) initiated if the initial methods are ineffective. Invasive mechanical ventilation may be necessary in severe cases ^[4]. Upon recognizing shock symptoms in this patient, low-flow oxygen was immediately provided via a dual-lumen nasal cannula. Airway secretions were promptly cleared to maintain airway patency. During oxygen administration, continuous monitoring of the child's lip, mucous membrane, and nail bed color, respiratory rate, and rhythm changes were conducted. The method of oxygen delivery, flow rate, and oxygen saturation were recorded hourly to ensure adequate tissue oxygen supply and organ function protection, thereby securing a critical time window for shock reversal. To prepare for potential deterioration, suction devices, endotracheal intubation kits, and emergency carts were kept bedside.

3.3. Fluid resuscitation

In the treatment of septic shock, fluid resuscitation is an effective intervention that can improve survival rates and outcomes when initiated early ^[4]. The principle of “crystalloids first, then colloids” and “rapid infusion initially followed by slower rates” is adhered to during fluid resuscitation, with timely assessment of tissue perfusion post-resuscitation ^[5]. On the fourth day of hospitalization, this patient presented with a temperature of 39°C, high fever, irritability, pale lips, tachypnea (45 breaths/min), chills, cold extremities, CRT > 3 seconds, no palpable dorsalis pedis artery pulses, and blood pressure of 76/30 mmHg. With a PEWS score of 4, two intravenous lines were established. A rapid infusion of 300 ml normal saline at 600 ml/h (20 ml/kg over 30 minutes) was initiated, resulting in a blood pressure of 96/33 mmHg upon recheck. Another 350 ml of normal saline was infused rapidly at 600 ml/h (23 ml/kg), then the blood pressure dropped to 82/31 mmHg. The infusion rate was then adjusted to 150 ml/h, and 50 ml of 20% albumin was administered intravenously, raising the blood pressure to 85/45 mmHg. During rapid fluid administration, close monitoring of heart rate, respiratory status, oxygen saturation, and blood pressure was essential. Regular blood pressure measurements were scheduled, and changes were promptly documented. The child's level of consciousness and pupil size were monitored, along with skin temperature and color at the extremities. Special attention was paid to signs of respiratory distress, coughing, sputum production, cyanosis, or pulmonary rales to prevent acute pulmonary edema. Families were instructed to accurately record 24-hour intake and output, particularly urine output.

3.4. Use of vasopressor agents

According to expert consensus on pediatric septic shock management, if a child still exhibits hypotension and tissue hypoperfusion after fluid resuscitation, vasopressor agents may be considered to increase and maintain perfusion pressure^[6]. Early, correct, and rational use of these drugs can significantly reduce mortality in septic shock cases^[7].

During the nighttime rescue attempt for this patient, when blood pressure dropped to 73/23 mmHg, a rapid infusion of 300 ml of normal saline at 900 ml/h was administered. Post-infusion, blood pressure ranged from 76–80/23–30 mmHg. Norepinephrine (2 mg + 5% dextrose solution 50 ml) was then infused intravenously at 2 ml/h using an infusion pump. Ten minutes later, blood pressure rose to 87/30 mmHg, and after another 10 minutes, it reached 86/37 mmHg. The norepinephrine infusion rate was adjusted to 4 ml/h, and 10 minutes post-adjustment, blood pressure measured 92/50 mmHg. Subsequently, blood pressure was beginning to stabilize blood pressure was stabilizing which fluctuated between 95–99/45–67 mmHg over time. Continuous electrocardiographic monitoring was set to measure blood pressure, heart rate, respiratory rate, and oxygen saturation every 60 minutes, while also observing peripheral circulation, urine output, and any adverse drug reactions.

Infusing vasopressors through peripheral veins can lead to complications such as extravasation and phlebitis. To minimize these risks, infusions should be administered via large, straight veins with good blood return, avoiding mixing with other medications and using precise micro-infusion pumps to control the flow rate. Nurses must regularly check the infusion speed and dose accuracy, patency of the vascular access, local skin condition at the infusion site, and observe the child's behavior for signs of discomfort or adverse reactions, promptly implementing protective measures and addressing any extravasation immediately.

3.5. Timing of blood culture collection and antibiotic administration

Blood cultures are crucial for guiding antibiotic selection and managing septic shock, adhering strictly to the “blood cultures first” principle by collecting samples before initiating antibiotics^[8]. Blood cultures help identify pathogens, enhancing diagnostic precision and treatment efficacy^[9]. After diagnosing septic shock, antibiotics should be administered within one hour to positively impact treatment outcomes. When the child presented with high fever, chills, and shock, immediate fluid resuscitation with normal saline was initiated alongside electrocardiographic monitoring and low-flow oxygen therapy to stabilize circulation. Simultaneously, blood cultures were collected according to standard protocols. Laboratory results showed CRP at 48.43 mg/L, SAA > 350.00 mg/L, IL-6 at 132.0 pg/mL, and PCT at 3.83 ng/mL. Broad-spectrum antimicrobial therapy with meropenem and vancomycin was started, followed by dynamic monitoring of procalcitonin levels. Based on subsequent metagenomic sequencing that identified *Orientia tsutsugamushi*, targeted therapy with adding azithromycin following consultation with the pharmacy department. This approach ensured a transition from empirical to precise antimicrobial treatment, optimizing therapeutic effectiveness while minimizing resistance risk.

3.6. Nursing care for high fever

Closely monitor the changes in the child's body temperature. When the body temperature is > 39°C, measure and record the temperature every hour. Recheck the temperature 30 minutes after using drug or physical cooling to evaluate the effect. Closely observe the child's mental state, circulatory condition, and manifestations of chills and shivering. If the body temperature is > 38.5°C, immediately report to the doctor, promptly give physical or drug cooling, and observe the curative effect in time.

3.7. Nursing care for eschar and edematous skin

In wound care, keep the wound clean and dry to reduce the risk of infection. Observe the distribution, appearance, size, shape, and changes of the child's eschar, keep the skin at the eschar site clean and dry, guide the child and family members to avoid forcibly peeling off the eschar or scratching the skin, standardize nail trimming, and strengthen hand hygiene management. Record the child's weight, the tension and color of the skin at the edematous site every day, and timely record the progression trend of the child's edema.

3.8. Disinfection isolation and infection prevention and control measures

Nursing measures such as disinfection and isolation help reduce the incidence of infection and bleeding, thereby improving the prognosis of children ^[10]. Due to the reduction of three blood cell lines indicated by the blood routine test, the child is at high risk of infection and bleeding, and strict disinfection, isolation, and protection measures are required. The child should be placed in a blood isolation ward for protective isolation to reduce the risk of cross-infection, limit the number of visitors, and prohibit contact with respiratory tract infected persons. The ward should be disinfected with ultraviolet air once a day. Medical staff and family members must strictly perform hand hygiene before and after contacting the child.

3.9. Psychological nursing

The child's condition is critical, and the family members are anxious. In the psychological nursing of the child's family members, a communication model with empathy as the core should be established, patiently listening to the family members' emotional venting, explaining the child's condition and treatment nursing measures in simple terms, guiding the family members to participate in the child's nursing by keeping a nursing diary, and using visual tools (such as temperature curve charts) to display the treatment progress to enhance confidence. By explaining the child's condition to the family members, they can better understand the relevant knowledge of the disease and the child's condition progress, thereby reducing anxiety and better cooperating with condition observation and related treatments.

4. Discussion

This nursing case study has limitations due to the single sample of a critically ill child with scrub typhus complicated by hemophagocytic syndrome leading to septic shock. The effectiveness of its intervention measures may be affected by differences in the child's age, the severity of underlying diseases, and treatment response. In the future, it is necessary to expand the sample size and carry out multicenter studies relying on a multi-hospital vertical management model to further improve the scientificity and universality of the research design.

5. Conclusion

Through comprehensive and meticulous nursing interventions, including early recognition and management of septic shock, targeted anti-infective therapy, meticulous skin care, strict infection control, and family education, the pediatric patient with severe scrub typhus complicated by hemophagocytic syndrome and septic shock achieved successful recovery and was discharged after 11 days of intensive care. This case highlights the critical role of systematic nursing management in improving outcomes for critically ill pediatric patients with complex infections.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

Conceptualization: Ruizhi Huang, Jialin Ye

Methodology: Ruizhi Huang, Jialin Ye

Formal analysis: Ruizhi Huang, Xiaoxiao He, Jialin Ye

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Writing – review & editing: Ruizhi Huang, Jialin Ye

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Visualization Analysis of Mental Health of Patients with Chronic Kidney Disease at Home and Abroad Based on CiteSpace

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Abstract: *Objective:* To analyze the current status, hotspot and trend of mental health research in patients with chronic kidney disease at home and abroad. *Methods:* China National Knowledge Infrastructure, WanFang, VIP, China Biology Medicine database, PubMed, and Web of Science core collection database were used as search sources from January 2004 to December 2024, and CiteSpace software was used for visual analysis and knowledge mapping. *Results:* A total of 2059 Chinese and 1678 foreign literatures were included. The number of publications showed a fluctuating upward trend, but the collaboration among authors was relatively loose. Negative psychology, such as depression and anxiety, as well as the quality of life of chronic kidney disease patients, were the main research hotspots. *Conclusion:* In the future, it is necessary to enhance cooperation and communication among researchers, continue to explore the mechanism of mental health, optimize research designs, innovate psychological nursing intervention measures, and focus on improving the psychological resilience and social support levels of patients.

Keywords: Chronic kidney disease; Mental health; Research hotspot; Visual analysis

Online publication: July 4, 2025

1. Introduction

Chronic Kidney Disease (CKD) refers to kidney damage or decreased kidney function caused by multiple factors, with a disease duration of ≥ 3 months^[1]. With the aging of the population and the increasing prevalence of chronic diseases year by year, the prevalence of CKD has also increased. Globally, the prevalence of CKD has reached 9.1%, with nearly 697.5 million people affected^[2]. In China, the number of patients has reached 118.4 million and is expected to continue to increase to 153 million by 2045^[3]. CKD is characterized by insidious onset, long duration, recurrent episodes, and difficulty in curing, and it may ultimately progress to end-stage renal disease, requiring long-term renal replacement therapy. During treatment, patients not only face physical pain caused by the disease

itself and its complications (such as anemia and bone disease) but also bear a huge economic burden. These factors can increase patients' mental health risks, inducing negative psychological states such as anxiety and depression. Moreover, negative psychology and poor health outcomes can form a vicious cycle, leading to a decline in quality of life and a higher risk of death ^[4, 5]. Modern medical concepts have gradually expanded from a purely biological perspective to a comprehensive model that takes into account psychological factors and social environmental impacts. This has led to increasing attention being paid to patients' psychological states by medical and nursing workers. The "Healthy China 2030" planning outline also emphasizes the need to strengthen early intervention for common psychological disorders such as depression and anxiety to achieve early detection, diagnosis, and treatment ^[6]. Researchers at home and abroad have conducted studies on the mental health of CKD patients from multiple perspectives, such as biology, psychology, and sociology. However, existing research mostly focuses on a single perspective and lacks comprehensive and systematic bibliometric analysis and visualization. Therefore, this study will use CiteSpace software to systematically review and analyze the current status, hotspots, and trends of research on the mental health of CKD patients, providing references for further exploration of new research directions.

2. Materials and methods

2.1. Search strategy and results

Chinese databases, including CNKI, Wanfang, VIP, and the Chinese Biomedical Literature Database, as well as international databases such as PubMed and the Web of Science Core Collection, are systematically searched. Advanced search techniques are employed, covering the period from January 2004 to December 2024. The Chinese search strategy is: [Subject: Chronic Kidney Disease OR Chronic Renal Failure OR Chronic Renal Insufficiency OR Hemodialysis OR Uremia OR End-Stage Renal Disease OR Peritoneal Dialysis OR Renal Transplantation (precise)] AND [Subject: Mental Health OR Psychological Status OR Psychological Resilience OR Rumination OR Anxiety OR Depression OR Demoralization Syndrome (precise)]. This yields a total of 2,059 Chinese articles.

The English search formula is: [TS = ("Chronic Kidney Disease*" OR "Chronic Kidney Insufficiency*" OR "Chronic Renal Disease*" OR "Chronic Renal Insufficiency*" OR "Kidney Insufficiency*" OR "Renal Insufficiency*" OR "Kidney Disease*" OR "Renal Disease*" OR hemodialysis OR "peritoneal dialysis" OR uremia OR "end-stage renal disease" OR "kidney transplant" OR "renal transplant")] AND [TS = ("mental health" OR "mental hygiene" OR "psychological status" OR "mental status" OR "psychological problem*" OR "mental problem*" OR "psychological situation*" OR "mental situation*" OR "psychological condition*" OR "mental condition*" OR anxiety OR depression OR "negative emotion" OR resilience OR rumination OR demoralization syndrome)]. A total of 1,678 foreign articles are included.

2.2. Inclusion and exclusion criteria

Articles that are relevant to the search topic, publicly published, and available in full-text are selected. Communications, discussions, conference papers, dissertations, news reports, and duplicate or incomplete articles are manually excluded.

2.3. Research methods and tools

The retrieved articles were exported in bibliographic format to NoteExpress. After duplicate checking, two researchers screened the articles by reviewing their titles, abstracts, and full texts, excluding those that did not

meet the criteria. A third person made decisions when there were disagreements. The selected articles were then exported in RefWorks-CiteSpace format and imported into CiteSpace 6.3.R1 software for analysis. The time slicing was set from January 2004 to December 2024, with a single time slice of 1 year. The G-index was set to 9 and TOP N=50 for Chinese articles, and the G-index was set to 11 and TOP N=50 for foreign articles. After setting the parameters, the publication volume, authors, and keywords are analyzed, and knowledge maps are generated.

3. Results

3.1. Analysis of publication volume in Chinese and foreign literature

Through screening relevant literature, 2059 Chinese articles and 1678 foreign articles were included. The overall publication volume has shown a fluctuating increase in the past 20 years. Except for 2022 and 2023, the annual publication volume of Chinese literature is higher than that of foreign literature; the publication volume of Chinese literature peaked in 2021, while foreign literature peaked in 2023. **Figure 1** shows the details.

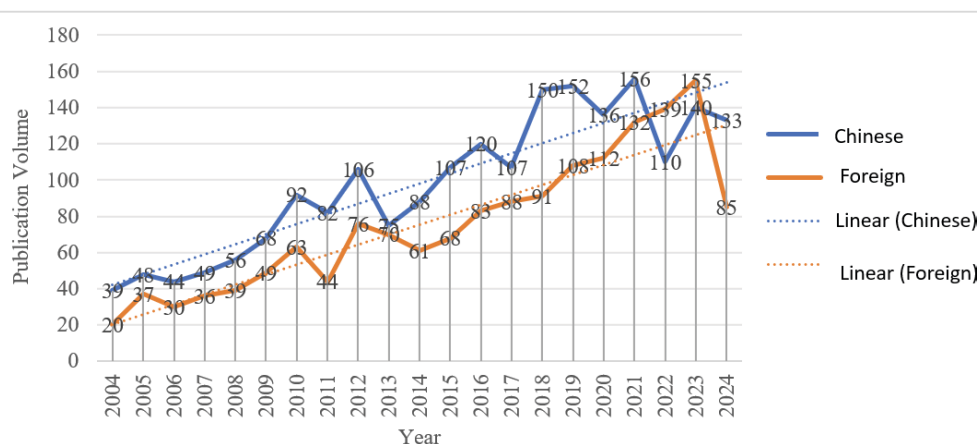


Figure 1. Publication volume of Chinese and foreign literature

3.2. Analysis of authors in Chinese and foreign literature

Among Chinese literature, the top 5 authors with the highest publication volume and their respective articles are: Diao Yongshu (9 articles), Huang Yanlin (7 articles), Dong Jie (7 articles), Shi Yaoxun (5 articles), and Wang Tao (4 articles). Among foreign literature, the top 5 authors with the highest publication volume and their respective articles are: L, Kimmel P (20 articles), Cukor, D (19 articles), Griva, K (12 articles), Chilcot, J (11 articles), and Honig, A (10 articles). Refer to **Table 1** for details.

The co-authorship network can show the core authors and their team collaborations in this field. The nodes in the graph represent each author, and the size of the nodes and names is proportional to the publication volume. The connections between nodes indicate the degree of collaboration between authors. The analysis results show that there are 295 nodes (N) and 229 edges (E) in Chinese literature, with a network density of 0.0053 (Density). Foreign literature has 284 nodes, 431 edges, and a network density of 0.0107. Refer to **Figure 2** and **Figure 3** for details.

Table 1. Publication volume of Chinese and foreign authors (Top 15)

Chinese publications			Foreign publications		
Publication volume	Year of first publication (Chinese)	Name	Publication volume	Year of first publication (Chinese)	Name
9	2011	Yongshu Diao	20	2006	L, Kimmel P
7	2009	Yanlin Huang	19	2006	Cukor, D
7	2007	Jie Dong	12	2014	Griva, K
5	2015	Yaoxun Shi	11	2011	Chilcot, J
4	2004	Tao Wang	10	2010	Honig, A
4	2018	Juan Zhang	10	2005	A, Peterson R
4	2016	Jing Shangguan	9	2012	W, Dekker F
3	2009	Yanjuan Teng	7	2023	Zhang, L
3	2021	Min Liu	7	2014	L, Yu Z
3	2016	Pingping Liang	7	2021	C, Abrahams A
3	2016	Zhenyun Li	6	2018	Gerogianni, G
3	2009	Juanfeng Long	6	2012	S, van Dijk
3	2009	Haoyu Li	6	2007	A, Tavallaii S
3	2016	Ting Li	6	2022	Chen, Y
3	2009	Jianshan Lin	6	2019	J, Vleming L

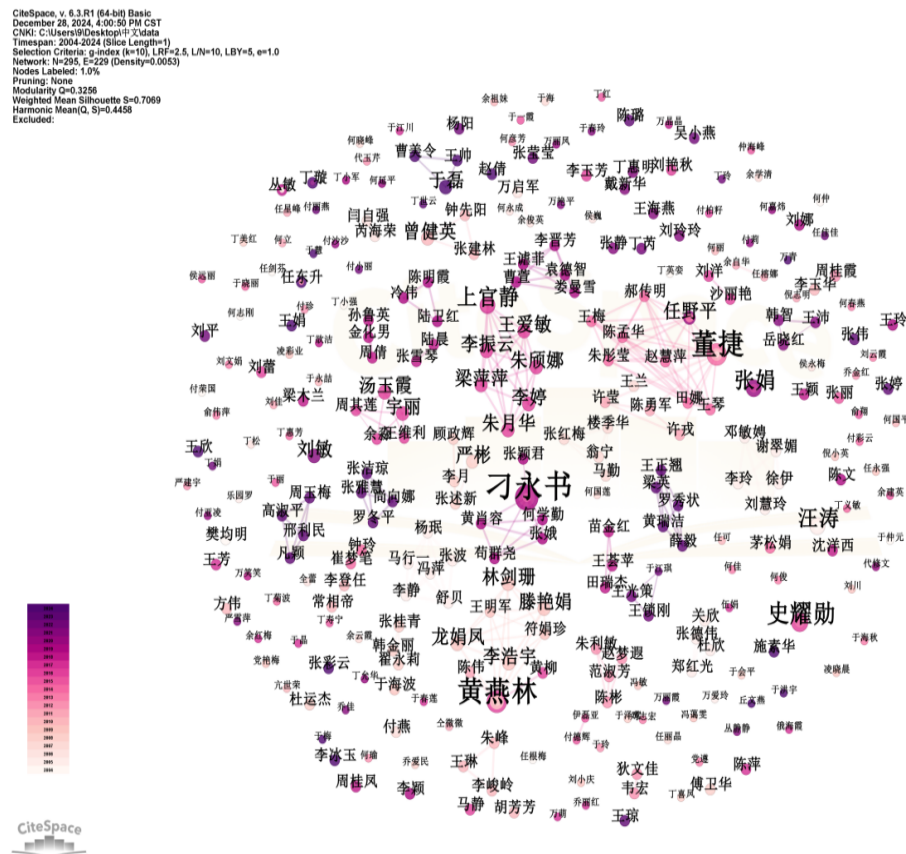


Figure 2. Co-authorship network of Chinese authors

Table 2. High-frequency keywords in Chinese and foreign literature (Top 15)

High-frequency keywords		Frequency		Centrality	
Chinese	Foreign	Chinese	Foreign	Chinese	Foreign
血液透析	Chronic kidney disease	631	287	0.26	0.28
抑郁	Quality of life	364	214	0.15	0.36
焦虑	End stage renal disease	326	134	0.11	0.23
尿毒症	End-stage renal disease	316	112	0.14	0.09
心理护理	Peritoneal dialysis	299	85	0.19	0.07
生活质量	Kidney transplantation	281	72	0.1	0.06
慢性肾衰竭	Mental health	189	69	0.11	0.08
腹膜透析	Psychosocial factors	161	63	0.17	0.06
慢性肾脏病	Depressive symptoms	134	61	0.08	0.03
心理状态	Major depression	121	59	0.06	0.04
终末期肾病	Dialysis patients	119	36	0.14	0.02
心理干预	Chronic kidney-disease	116	31	0.07	0.02
护理干预	Social support	116	29	0.05	0.02
护理	Hemodialysis patients	115	27	0.1	0.04
心理弹性	Psychological distress	103	26	0.05	0.03

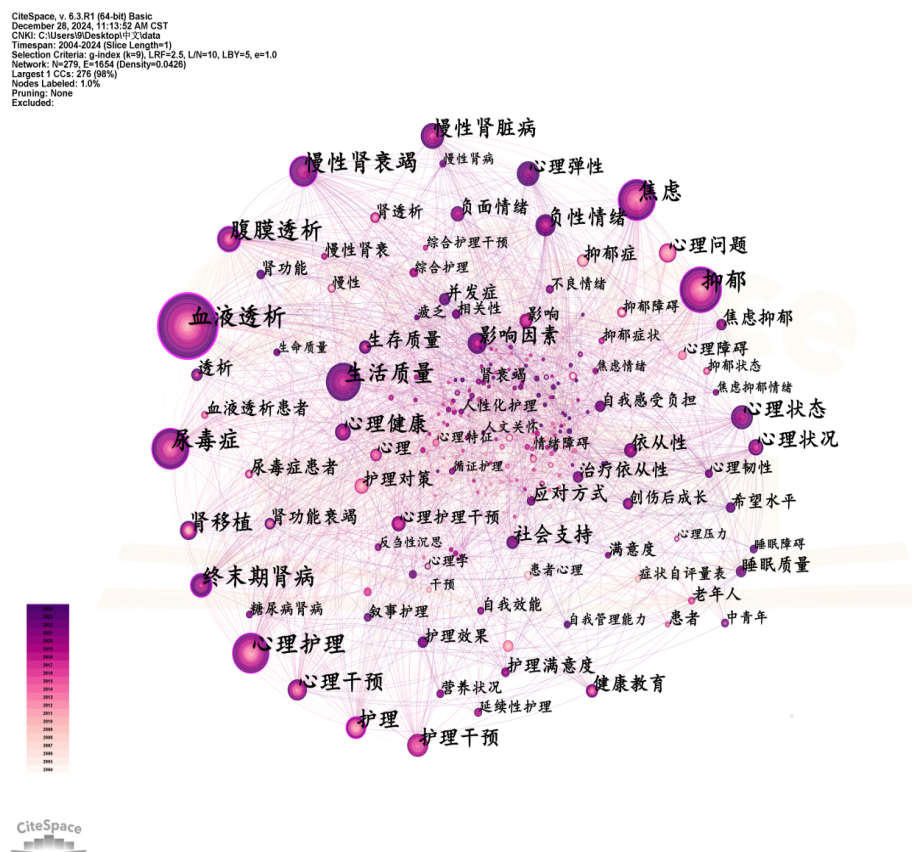


Figure 4. Co-occurrence network of Chinese keywords

Nodes Labeled: 5
Pruning: None
Excluded:

CiteSpace



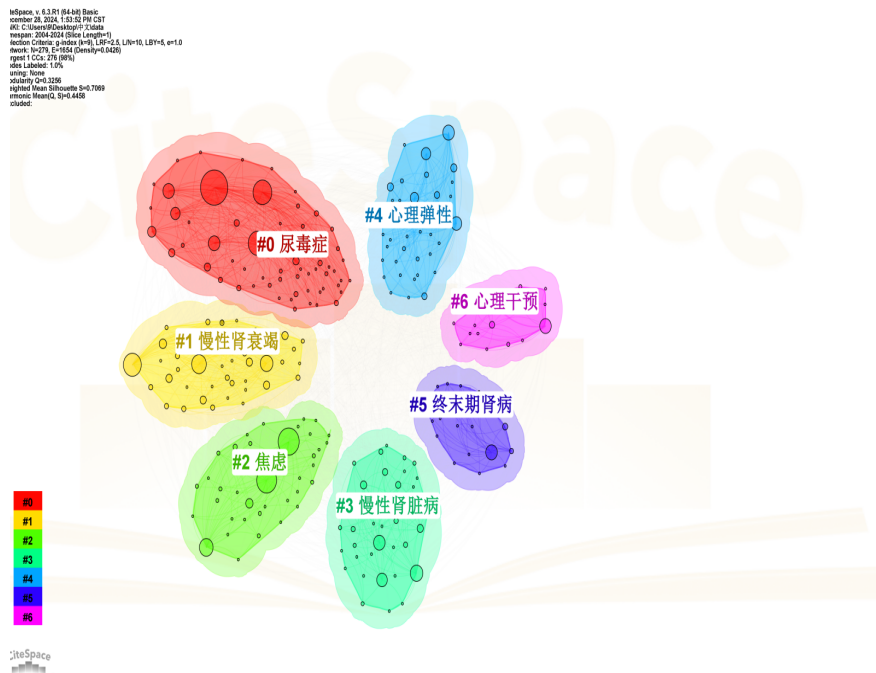


Figure 6. Chinese keyword cluster map

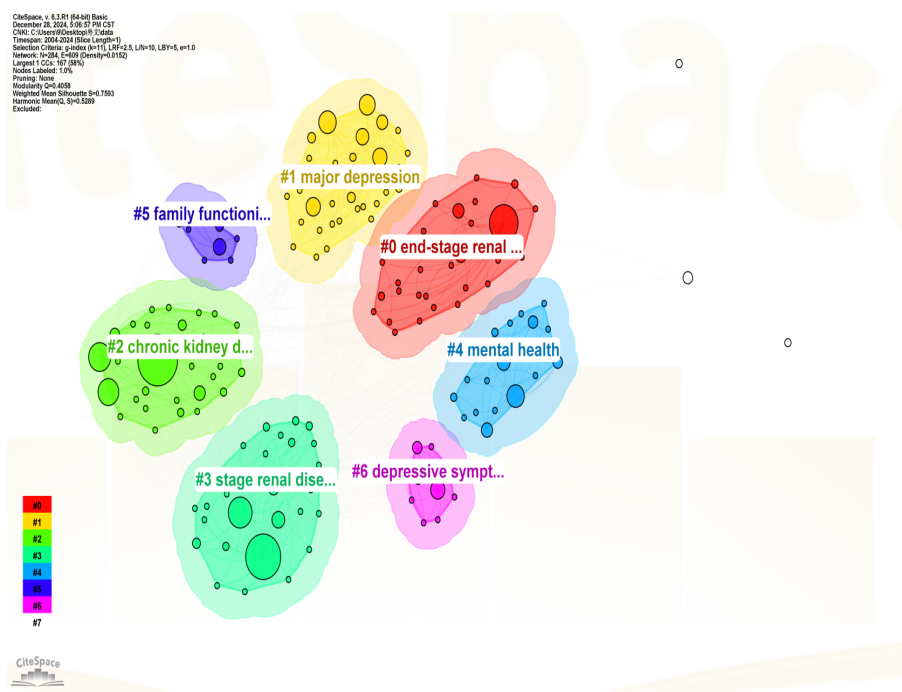


Figure 7. Foreign keyword cluster map

3.3.3. Keyword timeline analysis

Based on the keyword clustering results, a keyword timeline map was created to reflect the evolution of keywords within a cluster over time. A longer horizontal line segment indicates a longer duration of the cluster. Excluding clustering words related to the theme, the clusters in the domestic (**Figure 8**) keyword clustering analysis that

extended to the past two years were #0 Uremia, #2 Anxiety, #4 Psychological resilience, and #5 End-stage renal disease. In the foreign (Figure 9) keyword clustering analysis, the clusters that extended to the past two years were #0 End-stage renal disease, #3 Stage renal disease, #4 Mental health, #5 Family functioning, and #6 Depressive symptoms.

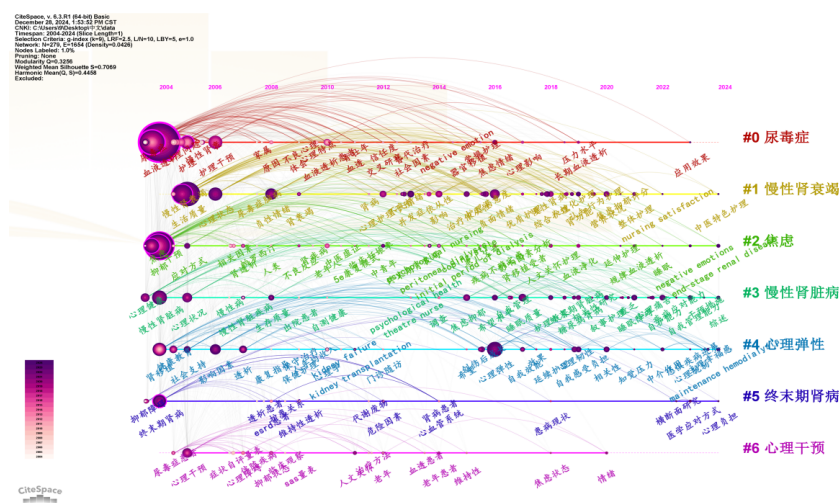


Figure 8. Chinese timeline map

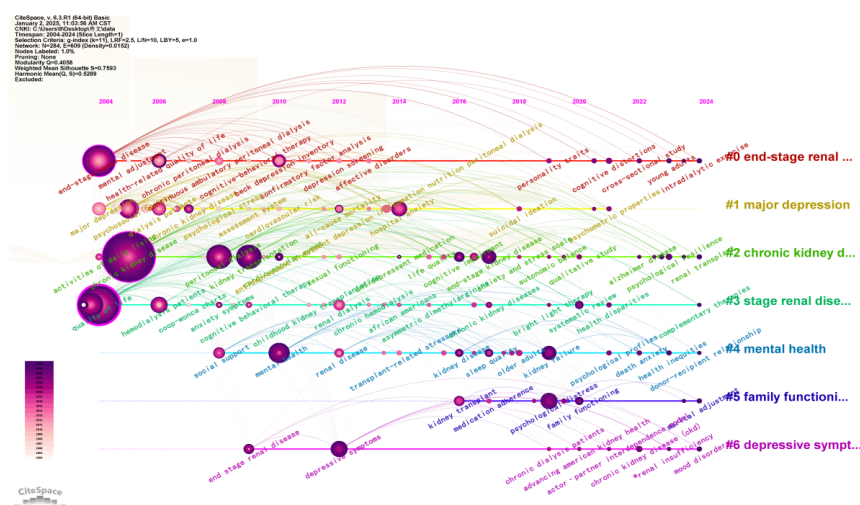


Figure 9. Foreign timeline map

3.3.4. Analysis of keyword emergence

Emerging keywords refer to those that appear frequently in a short period, reflecting changes in research hotspots and helping to predict trends in the field. The red lines indicate the years when a keyword is emerging, and their length represents the duration of the keyword's popularity. "Strength" denotes the intensity of emergence, with a higher value indicating greater influence of the keyword. By selecting "Burstness" in the control panel, the γ value is set to 1.0, while all other parameters remain at their default settings.

In Chinese literature (Figure 10), there are 25 emerging keywords, presenting three stages based on their

changes: From 2004 to 2014, emerging keywords included “psychological problems,” “nursing countermeasures,” “psychological analysis,” “psychological obstacles,” “psychological nursing,” and “psychological intervention,” focusing on analyzing patients’ psychological issues and providing psychological care. From 2014 to 2020, emerging keywords shifted to “compliance behavior,” “negative emotions,” “psychological state,” “sleep quality,” “treatment adherence,” and “nutritional status,” examining the impact of psychological states on patients’ sleep, nutrition, and treatment adherence.

From 2021 to 2024, emerging keywords included “psychological resilience,” “complications,” and “nursing effect,” focusing on patients’ nursing outcomes and psychological coping abilities in the face of adverse stress events. Depression, psychological problems, nursing countermeasures, psychological analysis, and psychological obstacles are among the longer-lasting emerging keywords, while psychological resilience, psychological problems, nursing, nursing intervention, and kidney transplantation have greater influence. Recent research hotspots center on psychological resilience, psychological state, treatment adherence, complications, and nursing effect.

Top 25 Keywords with the Strongest Citation Bursts

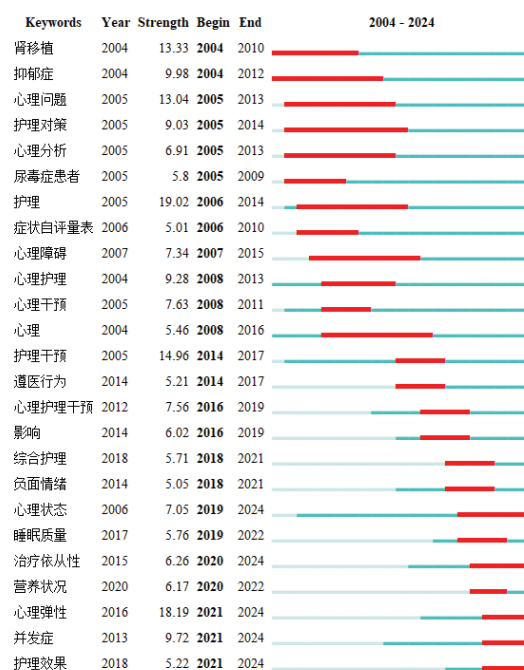


Figure 10. Emergence map of Chinese keywords

In foreign literature (**Figure 11**), there are 15 emerging keywords, also presenting three stages: From 2004 to 2005, emerging keywords were “major depression,” “psychosocial factors,” and “behavioral compliance,” analyzing the impact of psychological states on patients’ treatment adherence. From 2006 to 2012, emerging keywords included “dialysis patients,” “end-stage renal disease,” “renal transplantation,” and “renal dialysis,” exploring research related to different renal replacement therapies. From 2014 to 2024, the focus shifted to patients’ psychosocial issues, with emerging keywords such as “hospital anxiety,” “psychological distress,” and “mental health.” Major depression, psychosocial factors, and dialysis patients are among the longer-lasting emerging keywords, while recent research hotspots concentrate on psychosocial distress, mental health, and end-stage kidney disease.

Top 15 Keywords with the Strongest Citation Bursts

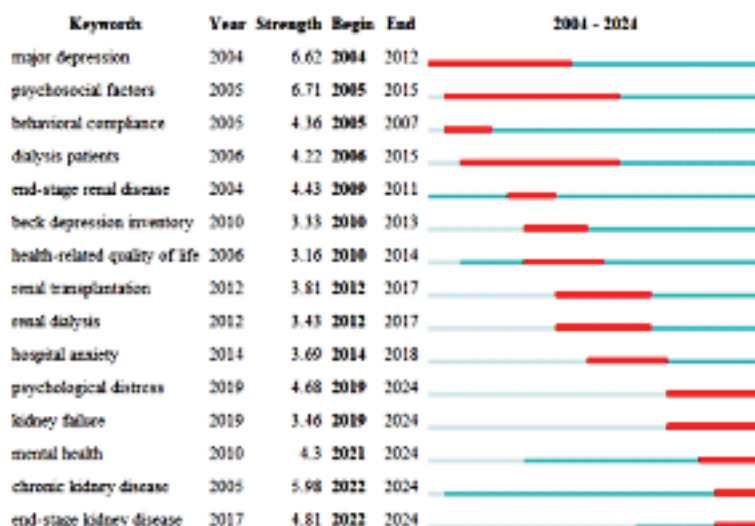


Figure 11. Emergence map of foreign language keywords

4. Discussion

4.1. Current research status

The number of publications in a research field can reflect the level of attention given to that field. From 2004 to 2024, there has been an overall upward trend in the number of research articles on the mental health of patients with CKD both domestically and internationally, indicating that mental health issues are receiving increasing attention in the management of this disease. Specifically, in Chinese literature, the peak number of publications was reached in 2021, while foreign literature peaked in 2023. This difference may be related to varying levels of investment and interest in chronic kidney disease research across different regions. The network of collaboration among authors facilitates interdisciplinary and cross-regional research exchanges. However, as can be seen from the figures, current collaborations among researchers both domestically and internationally are relatively fragmented, with most operating in independent research states and small team radiation ranges. Therefore, it is suggested that researchers strengthen cooperative exchanges, realize resource sharing, and carry out interdisciplinary and multi-professional collaborations to broaden research ideas and further promote the development of mental health research for patients with CKD.

Based on keyword co-occurrence and clustering maps, it can be seen that research on the mental health of patients with CKD, both domestically and internationally, is mainly focused on patients undergoing dialysis and those with end-stage renal disease. This may be because dialysis is the main replacement therapy for patients with end-stage renal disease, and these patients, who endure long-term dialysis treatment, are more prone to mental health issues. According to research, by the end of 2020, the number of hemodialysis patients in China had reached 690,000, an increase of 3.1 times compared to 2011, making China the country with the largest number of hemodialysis patients in the world ^[7]. Among adult patients with CKD, the proportions in CKD stages 1–2, 3, and 4–5 are 73.3%, 25.0%, and 1.8%, respectively. From this, it can be inferred that the prevalence rate for stages 1–3 is as high as 98.3%, indicating a large number of early-stage patients ^[8]. Therefore, while focusing on dialysis patients in the future, attention should also be paid to the psychological state of early-stage CKD patients,

and appropriate nursing interventions should be implemented to reduce the impact of psychological issues on the disease and effectively delay its progression.

4.2. Research hotspots

4.2.1. Anxiety and depression

Anxiety and depression are common among patients with CKD, with depression identified as the most prominent negative psychological issue faced by these patients^[9, 10]. A systematic evaluation revealed that the overall incidence of depression among patients with CKD is 26.5%, and epidemiological data shows a continuous upward trend in its incidence^[11]. The detection rates of anxiety and depression among patients undergoing maintenance hemodialysis are 16.38% and 34.48%, respectively^[12]. An international multicenter study found that depressive symptoms are also widespread among CKD patients in various countries, but there are significant differences in their incidence rates, such as 2% in Japan and 21.7% in the United States^[13]. These differences may be attributed to factors such as regional cultural variations, CKD staging, age, renal replacement therapy modalities (hemodialysis and peritoneal dialysis), research methods, and heterogeneity in assessment tools.

Anxiety and depression can not only cause neurological dysfunction and neuropathy but also reduce immune function, accelerate disease progression, lead to a decline in quality of life, and increase mortality^[14]. Research has shown that depression is an important risk factor for increasing hospitalization rates and mortality among dialysis patients, even when dialysis is adequate^[15]. For CKD patients not receiving dialysis treatment, moderate to severe depressive symptoms can accelerate the progression of renal function deterioration^[16]. Many patients often experience anxiety and depression due to concerns about disease progression, poor treatment outcomes, and a significant decline in quality of life. Long-term treatment brings pain, social isolation, changes in social roles, loss of life goals, economic pressure, and other factors that can cause patients to lose the courage to live. Focusing on patients' psychological states and providing timely diagnosis and care for anxiety and depression can mitigate adverse consequences and improve outcomes. Wang *et al.* have found that strengthening sleep management for patients can promote the prevention and treatment of anxiety and depression in patients with CKD^[17]. Shen *et al.* have proposed that mindfulness therapy can effectively improve the negative psychology of patients with CKD^[18].

4.2.2. Resilience

The concept of resilience, also known as psychological resilience or toughness, was first established by American scholar Anthony *et al.* in the 1970s^[19]. It specifically refers to an individual's ability to maintain or restore a normal psychological state when facing stress or trauma. Research has shown that good resilience not only effectively alleviates the impact of psychological obstacles but also enhances the body's resistance to diseases^[20, 21]. Under the framework of contemporary positive psychology research, resilience is recognized as an important protective factor that promotes individual health development and has become a research hotspot in the field of psychology. Regarding the mechanism and influencing factors of resilience, existing research presents diversified theoretical perspectives. In the field of clinical medicine, Hou *et al.* found through analysis that resilience has a mediating effect between the level of hope and fatigue symptoms among hemodialysis patients, meaning that patients with high resilience can effectively regulate the negative impact of disease stress^[22]. Similarly, Hou *et al.* research points out that resilience plays a key intermediary role between the social support system and various dimensions of patients' quality of life^[23]. These findings provide empirical evidence for understanding the mechanism of resilience. From the perspective of developmental psychology, Felicity *et al.* combining longitudinal

and qualitative research, found that improving interpersonal relationships and cultivating personal strength traits (such as optimism and self-efficacy) can significantly enhance patients' resilience levels ^[24]. Shafiei *et al.* research further confirms that a well-established social support network can not only improve the resilience of terminal patients but also effectively alleviate their death anxiety ^[25]. As research progresses, intervention studies to promote resilience have gradually increased. Currently, intervention programs in clinical practice include cognitive nursing intervention, mindfulness therapy intervention, personalized psychological intervention, social support, and sandplay therapy. These interventions help alleviate patients' psychological obstacles and significantly improve their resilience levels through different pathways.

4.3. Research trends

4.3.1. Improving social support levels to promote physical and mental health of CKD patients

Social support refers to the emotional care, sense of self-worth, and material support that individuals obtain from others and society ^[26]. It includes three aspects: individual subjective experience, objective social support, and the utilization of social support ^[27]. Subjective experience refers to an individual's emotional experience of being understood, respected, and cared for; objective social support includes material aid and social relationship networks ^[28]. Among them, social relationship networks can be further divided into formal and informal support. Governments, institutions, businesses, and communities are considered formal support, while support from family, neighbors, friends, and colleagues is informal support ^[29, 30]. The utilization of social support reflects an individual's tendency to actively seek and accept help, and patients with high utilization are more likely to actively participate in social interactions ^[31]. It's worth noting that different individuals have varying degrees of social support utilization ^[32]. For example, some people may avoid or refuse support despite having a social support network, which can directly affect the actual effectiveness of the support system.

For CKD patients, the integrity of the social support system can directly affect disease prognosis. Issues such as dysfunction, economic pressure, and care dependency caused by the disease often lead to significant psychosocial distress. Research has shown that patients who lack effective social support are more prone to treatment resistance or even abandonment of treatment ^[33]. In addition, when encountering social isolation or discrimination, patients are prone to depression and social difficulties, which may accelerate the deterioration of renal function through neuroendocrine mechanisms ^[34]. On the contrary, a good family and social support system can effectively alleviate patients' psychological distress, improve their psychological endurance, and help them adjust to feelings of social isolation. For example, family and friends can provide emotional venting channels, helping patients express emotions, reduce stress responses, build treatment confidence, and positively impact treatment adherence and quality of life.

Governments and medical companies can use community hospitals and health service stations to improve the social support system, and also provide professional rehabilitation guidance and employment support to promote patients' return to society. Based on existing research, future clinical practice should focus on evaluating patients' social support levels, exploring the mechanisms of different forms of support, developing personalized support programs with a focus on strengthening informal support systems, and integrating medical, community, and family resources to form a comprehensive support system. This will promote the physical and mental health development of CKD patients and provide new practical ideas for psychosocial intervention.

4.3.2. Innovative nursing interventions to alleviate psychological barriers for patients with chronic kidney disease

Psychological nursing, based on the patient's psychological state, involves targeted nursing interventions that can improve patients' psychological barriers and create an optimal psychological state conducive to treatment and recovery. As understanding of the mental health issues facing CKD patients deepens, researchers have begun to explore diverse psychological nursing interventions, such as traditional Chinese medicine nursing, continuous nursing, cognitive behavioral nursing, high-quality nursing, individualized nursing, holistic nursing, and treatment adherence. Among these, traditional Chinese medicine nursing shows significant potential and advantages in improving the mental health of CKD patients. For instance, Shi pointed out in his research that high-quality nursing in traditional Chinese medicine can effectively alleviate generalized anxiety and depression in CKD patients, thereby improving their quality of life ^[35–37]. Tang *et al.* have expanded upon various traditional Chinese medicine intervention methods, offering multiple treatment options for hemodialysis patients with emotional disorders ^[38].

Meanwhile, the “Healthy China 2030” planning outline also clearly proposes to fully leverage the unique role of traditional Chinese medicine in the prevention and treatment of chronic diseases, innovate and develop traditional Chinese medicine's preventive healthcare services, and promote the inheritance and innovation of traditional Chinese medicine. Combining the unique advantages of traditional Chinese medicine with innovative approaches from modern medicine enhances the promotion of both physical and mental health in patients with chronic kidney disease (CKD). Continuous nursing, which extends medical and nursing services from hospitals to families and communities, has developed gradually in China since 2003 ^[39]. It includes various forms such as telephone consultations, home visits, online consultations, community health lectures, and patient support groups. With the rapid development of mobile medical information technology, intelligent continuous nursing models can achieve more precise psychological state monitoring and intervention, significantly improving the accessibility and effectiveness of nursing care ^[40].

Furthermore, multiple studies have verified the positive effects of compound psychological nursing. Wang *et al.* have confirmed that health education combined with focused psychological nursing can effectively enhance medication adherence among CKD patients, improve disease awareness, and reduce negative emotions ^[41]. Similar research conclusions have been reached by Tan *et al.* and Zhang *et al.*, further confirming the positive effects of this nursing model ^[42, 43]. Xu pointed out that cognitive behavioral group psychological intervention has a significant effect on hemodialysis patients, which can not only effectively alleviate anxiety and depression but also improve patients' psychological resilience and subjective well-being ^[44]. These innovative interventions provide important references for promoting the mental health of CKD patients. Future research should focus on exploring optimal combinations of different intervention programs and longitudinally tracking long-term intervention effects to provide a more reliable evidence-based basis for clinical practice.

4.4. Limitations

This article only searched for literature from January 2004 to December 2024, potentially missing some important literature and causing deviations in the results. Additionally, the CiteSpace software analysis only selected authors and keywords as node types, without analyzing co-citation or author contribution. Future research could expand the scope of the study and explore the publishing institutions, co-citations, author nationality, and author contribution to improve the comprehensiveness and accuracy of the research results.

5. Conclusion

In summary, this study utilized CiteSpace software to review research on the mental health of patients with chronic kidney disease over the past 20 years, objectively presenting the current research status, hotspots, and trends in this field, and providing references for future research. Through keyword analysis, it was found that negative psychological states such as depression and anxiety, as well as quality of life, are the main research hotspots in patients with chronic kidney disease. Hemodialysis, peritoneal dialysis, and end-stage renal disease patients are the main research subjects. Additionally, foreign studies tend to focus more on psychosocial distress and social support systems, while domestic scholars are more focused on exploring psychological resilience training and nursing intervention measures. From a methodological perspective, most of the current literature at home and abroad consists of cross-sectional studies, and there is a lack of high-quality longitudinal follow-up studies. The research methods are relatively homogenous, with insufficient application of qualitative and mixed research methods. Intervention studies often suffer from small sample sizes and short intervention and follow-up periods, making it difficult to observe the continued effects of interventions. In the future, research design should be gradually optimized. Drawing on effective intervention programs from abroad, it is possible to develop targeted measures that align with China's medical and cultural context. This approach continuously promotes the translation of basic research findings into clinical practice, thereby rapidly and efficiently advancing the research level in this field within China.

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Disclosure statement

The authors declare no conflict of interest.

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A Study of the Correlation between Psychological Status and Disease Perception in Adolescent Inflammatory Bowel Disease Patients

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Abstract: *Objective:* To investigate and explore the current status and correlation between psychological status and disease perception of adolescent patients with inflammatory bowel disease. *Methods:* Adolescent patients hospitalized in a tertiary hospital in Zhejiang Province and some adolescent patients attending the summer camp of Zhejiang Province Aizaiyanchang Foundation for Inflammatory Bowel Disease were selected as the study subjects, and a questionnaire survey was carried out on 148 adolescent patients with inflammatory bowel disease by using the Generalized Anxiety Disorder Scale (GAD-7), Patient Health Questionnaire (PHQ-9), and the Simplified Version of the Disease Perception Questionnaire (BIPQ). *Results:* The depression score of adolescent inflammatory bowel disease patients was (16.40 ± 8.30) , the anxiety score was (12.55 ± 5.34) , and the total illness perception score was (43.75 ± 10.41) . Disease perception of adolescent inflammatory bowel disease patients was at moderate to high level, in which adolescent inflammatory bowel disease patients had the strongest perception of disease control in cognitive dimension as (7.20 ± 0.98) score, followed by strong perception of treatment effect in cognitive dimension as (6.95 ± 2.23) score. According to Pearson correlation analysis it was concluded that their disease perception was positively correlated with anxiety and depression. *Conclusion:* The psychological condition of adolescent patients with inflammatory bowel disease is poor, and there are significant individual differences in the level of disease perception. Healthcare professionals should provide appropriate knowledge support and psychological interventions according to the different needs of adolescent patients. In addition, an online and offline communication platform should be established to better help adolescent patients with inflammatory bowel disease.

Keywords: Adolescents; Inflammatory bowel disease; Psychological profile; Disease perception

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1. Introduction

Inflammatory bowel disease (IBD) is an immune-mediated chronic inflammatory disorder affecting the gastrointestinal

tract, including Crohn's disease (CD), ulcerative colitis (UC), and indeterminate type IBD (IBD-U) ^[1]. It is a long-term and incurable chronic condition, characterized by atypical symptoms and a complex and challenging diagnostic and differential diagnosis process. Additionally, the lack of specialized IBD clinical and pathological physicians in China often leads to misdiagnosis and mistreatment, causing irreversible damage ^[2].

The adolescent group is a high incidence of inflammatory bowel disease, the incidence of inflammatory bowel disease in children and adolescents continues to rise globally, according to relevant data, the incidence of inflammatory bowel disease in children aged 0 to 14 years old in China rose from 0.5/1 million in 2001–2010 to 6/100,000 in 2011, an increase of up to 12 times ^[3]. Inflammatory bowel disease is prolonged and characterized by a certain degree of disability, which puts adolescent patients in a state of exacerbation and consultation, affecting their physical and mental health and quality of life, and bringing suffering to adolescent patients with inflammatory bowel disease.

Due to multiple factors such as the recurrence of the disease and the complexity of the drug treatment program, adolescent patients often experience huge psychological pressure and burden when dealing with this situation. In addition, people with IBD often face health problems related to extra-intestinal stress. Studies have shown that the prevalence of mental illness in IBD patients is as high as 50% ^[4]. Other studies have confirmed that mental health disorders in childhood and adolescence can lead to long-term mental health problems ^[5, 6].

The common sense model of disease proposes that when individuals experience a health threat (i.e., illness), they form cognitive and emotional representations of that threat, a process collectively known as disease perception ^[7]. Disease perception is an individual's belief about their illness at various dimensions and determines their efforts to minimize and/or deal with health threats, which in turn is closely related to clinical and psychological outcomes ^[8–10]. The model and its ability to predict disease perception have been demonstrated in multiple chronic disease and health behavior studies, including non-adherence to medication, depression, and mortality ^[11–13]. Relevant foreign studies have confirmed that in adult IBD patients, disease perception is associated with the incidence of mental illness ^[14–17] coping, and adjustment. Adjustment was measured from the perspectives of psychological distress, quality of life, and functional independence. Illness perceptions (particularly perception of consequences of IBD).

At present, there is a relative lack of research on the correlation between psychological status and disease perception in adolescent IBD patients in China. Therefore, this study intends to investigate the current status of adolescent IBD patients in order to explore the psychological status of adolescent inflammatory bowel disease patients and their ability to perceive disease, and to provide a reference basis for clinical intervention.

2. Methodology

2.1. Object selection

Objective sampling method is used to select young patients with inflammatory bowel disease who are hospitalized in a grade-III hospital in Zhejiang Province and some young patients who participated in the inflammatory Bowel Disease Summer camp of Aizaiyanchang Foundation in Zhejiang Province from July 2021 to July 2024 as the study objects. Diagnostic criteria: The diagnostic criteria for IBD formulated by the Gastroenterology Branch of the Chinese Medical Association in 2018 were met. Inclusion criteria are: (1) age \leq 18 years old; (2) Primary school or above education level, able to understand and answer the questions in this questionnaire. Meanwhile, the exclusion criteria includes: (1) accompanied by malignant tumors, chronic diseases such as heart, liver,

kidney and lung; (2) suffering from mental illness or cognitive impairment; (3) With other intestinal diseases. The sample size was calculated according to the sample size calculation formula, and the maximum number of items in the questionnaire was 9^[18]. Considering that (10%–15%) is the expected non-recovery rate and inefficiency of the questionnaire, the calculation calculated that at least 99 questionnaires were collected. A total of 148 questionnaires are collected in this study, and 8 invalid questionnaires are excluded (the answers were regular), and 140 valid questionnaires are finally collected. The effective rate is 94.59%. Patients and their families agreed to participate in the study voluntarily. This study is approved by the Ethics Committee of Hangzhou Normal University (2022062) Ethics.

The sample size is calculated according to the sample size calculation formula, and the maximum number of items in the questionnaire was 9^[18]. Considering that (10–15%) is the expected non-recovery rate and inefficiency of the questionnaire, the calculation calculated that at least 99 questionnaires are collected. A total of 148 questionnaires are collected in this study, and 8 invalid questionnaires are excluded (the answers were regular), and 140 valid questionnaires are finally collected. The effective rate is 94.59%. Patients and their families agreed to participate in the study voluntarily.

2.2. Research tools

2.2.1. The general data scale

The general data scale is designed by ourselves, including the demographic characteristics of adolescents (gender, age, place of residence and schooling).

2.2.2. Generalized Anxiety Disorder Scale (GAD-7)

The Generalized Anxiety Scale (GAD-7) is a tool developed by Spitzer *et al.* to screen for generalized anxiety and assess the severity of its symptoms. Foreign research results have shown that the GAD-7 scale has good reliability and validity^[19, 20]. The Chinese version of GAD-7 scale was translated and adapted by Chinese scholar He *et al.*, and has been proved to have reliable screening value in primary medical and clinical application in China. The seven items in the scale are based on the seven Diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders Fourth edition (DSM-IV)^[21]. Survey patients or patients self-reported the time (days) that they are troubled by each item in the past 2 weeks, with a total score of 21 points and GAD-7 score ≥ 10 points, patients are judged to be anxious^[22–25]. In this study, the Cronbach's α coefficient of this scale is 0.945.

2.2.3. Patient Health Questionnaire Scale (PHQ-9)

The patient Health Questionnaire Scale (PHQ-9) is compiled by Spitzer *et al.* in 1999 according to the diagnostic criteria of DSM-IV, and then translated and translated into Chinese by Chinese scholar Cui *et al.*^[26, 27]. This scale is a self-rating questionnaire for depression containing 9 items, 9 items reflect MDD in DSM-IV standards, and the score range of each item is 0 to 3 points, with a 4-level score^[28]. The questionnaire is designed to assess the subjects' emotional state over the past two weeks. The total score of the questionnaire is the cumulative score of 9 items, and the total score ranges from 0 to 27 points. The higher the score, the more serious the depressive symptoms are. The reliability and validity of PHQ-9 in Chinese adolescents have been confirmed^[29]. In this study, the Cronbach's α coefficient of this scale is 0.960.

2.2.4. Brief illness perception questionnaire (BIPQ)

The brief illness perception questionnaire (BIPQ), developed by Broadbent *et al.*, has been used to assess an individual's cognitive and emotional responses to their illness^[23]. The questionnaire consists of nine items, ranging from disease impact ("how much does inflammatory bowel disease (IBD) affect your life?"), disease duration ("how long do you think IBD will last?"), personal control ("how much control do you feel you have over your illness?"), treatment control ("how much do you think your treatment is helping IBD?"), symptom recognition ("how many symptoms of IBD do you feel?"), illness concern ("how much do you worry about IBD?"), illness comprehensibility ("how much do you know about IBD?"), illness mood ("how much is IBD affecting your mood?", e.g., "does it make you angry, scared, sad, depressed?") surveys are conducted. Three entries, personal control, treatment control, and illness comprehensibility, are reverse scored on a 10 to 0 scale. The sum of the scores of each entry is the total score of the scale, and a higher total score means that the patient may have more serious negative perceptions and feelings about the threat of the disease. The internal consistency coefficient of this questionnaire is 0.66 to 0.92. This questionnaire has been translated into several languages and is widely used in studies of patients with COPD, cancer, and other diseases^[31–33]. The Cronbach's alpha coefficient for this scale in this study is 0.616.

2.5. Data collection

This study conducted data collection by combining the questionnaire star platform with paper questionnaires. For the electronic questionnaire, IP restrictions are set to ensure that each IP address could only be filled out once. Prior to the implementation of the survey, the investigators are uniformly trained to explain the survey steps and matters to be noted, and are especially taught how to instruct adolescents to fill out the questionnaire correctly. The purpose of the study and its importance are explained to the patients in detail and standardized guides are used. After the patients gave their consent, they are instructed to fill out the questionnaire. The investigator is present throughout the completion of the questionnaire and is always available to answer the questions of the adolescents, seeking the assistance of their guardians if necessary. All entries had to be filled in completely before submission. The paper version of the questionnaire is collected on-site, and after the electronic version of the questionnaire is recovered, the questionnaires whose responses are regular or whose response time is too short are excluded, and the rest of the qualified questionnaires are double-checked to ensure the accuracy of the data, and the information is finally entered into the system.

2.6. Statistical methods

Statistical analyses are processed by using the SPSS 27.0 software. Normal measurement data are described by applying ($M \pm SD$) deviation. Count data are expressed as frequency and percentage, and comparisons between groups are made by χ^2 test. Pearson correlation analysis is used for analysis, with a test level of $\alpha = 0.05$, and $P < .05$ as the difference is statistically significant.

2.7. Ethics

This study is approved by the Ethics Committee of Hangzhou Normal University (2022062) Ethics.

3. Results

3.1. General information of adolescents with inflammatory bowel disease

A total of 140 respondents aged 9 to 18 years, with a mean age of (13.75 ± 2.33) years, of whom 61 (43.6%) were female and 79 (56.4%) were male; 129 (92.1%) lived in urban areas and 11 (7.9%) lived in rural areas; 41 (29.3%) attended elementary schools, 84 (60.0%) attended junior high schools and 15 (10.7%) attended senior high schools.), 84 (60.0%) in middle school, and 15 (10.7%) in high school. There were statistically significant differences in adolescent anxiety symptom scores by age and attendance ($P < 0.05$); adolescent depression symptom scores by age, gender, and attendance ($P < 0.05$); and adolescent illness perception scores by age and attendance ($P < 0.05$), as shown in **Table 1**.

Table 1. General data of adolescents with inflammatory bowel disease

Characteristic	Number of cases	Constituent ratio (%)	Anxiety score	χ^2	P	Depression score	χ^2	P	Disease perception score	χ^2	P
Gender				2.59	0.995		39.58	<0.01		31.85	0.573
Male	79	56.4	12.67 ± 5.51			15.66 ± 8.41			43.67 ± 11.14		
Female	61	43.6	12.39 ± 5.16			17.36 ± 8.12			44.25 ± 9.44		
Age				59.76	<0.01		86.28	<0.01		142.56	<0.01
<12	28	20.0	11.36 ± 4.92			16.39 ± 8.10			40.71 ± 9.87		
$12 \leq 15$	74	52.9	12.53 ± 5.31			14.53 ± 7.96			42.26 ± 10.80		
$16 \leq 18$	38	27.1	13.47 ± 5.67			20.05 ± 8.06			48.89 ± 8.20		
Residence				10.36	0.498		13.71	0.249		32.19	0.557
City	129	92.1	12.53 ± 5.37			16.24 ± 8.19			44.06 ± 10.44		
Country	11	7.9	12.72 ± 5.24			18.27 ± 9.64			40.09 ± 9.74		
Attendance				75.54	<0.01		85.21	<0.01		121.15	<0.01
Primary School	41	29.3	10.63 ± 4.58			14.71 ± 7.35			41.29 ± 10.26		
Junior High School	84	60.0	13.21 ± 5.35			16.19 ± 8.52			44.14 ± 10.57		
Senior High school	15	10.7	14.07 ± 6.19			22.2 ± 7.36			48.27 ± 8.50		

3.2. Mental health status of adolescent inflammatory bowel disease (IBD) patients

The total anxiety symptom score of 140 adolescent IBD patients was (12.55 ± 5.34), of which 35 (25%) showed severe anxiety. The total score of depressive symptoms was (16.40 ± 8.30), of which 63 (45%) showed severe depression, as shown in **Table 2**.

Table 2. Psychological status score table of adolescent inflammatory bowel patients

	N	Minimum	Maximum	Average	Standard deviation
Anxiety score	140	7.00	26.00	12.5500	5.34335
Depression score	140	9.00	33.00	16.4000	8.29648

3.3. Status of disease perception

Among 140 IBD patients, the total score of disease perception was (43.75 ± 10.41), and the score of cognitive dimension was (29.50 ± 5.82). The score of emotion dimension was (8.25 ± 5.52); The score of disease understanding ability was (6.00 ± 2.29). The top three scores were (7.20 ± 0.98) for disease control in cognitive dimension, (6.95 ± 2.23) for treatment effect in cognitive dimension and (6.75 ± 2.89) for duration of disease in cognitive dimension, as shown in **Table 3**.

Table 3. Scores of BIPQ scales in adolescents with inflammatory bowel disease ($\bar{x} \pm s$)

Dimension	Entry	Score ($\bar{x} \pm s$)	Arrange in order
Cognitive	(1) How much inflammatory bowel disease (IBD) affects your life?	3.90 ± 2.13	8
	(2) How long do you think IBD will last?	6.75 ± 2.89	3
	(3) How much control you feel you have over your disease?	7.20 ± 0.98	1
	(4) How much you think your treatment has helped IBD?	6.95 ± 2.23	2
Emotional	(5) How many symptoms of IBD you feel?	4.70 ± 2.44	5
	(6) How worried are you about IBD?	4.05 ± 3.20	7
	(7) How much does IBD affect your mood? (e.g. does it make you angry, scared, sad, depressed?)	4.20 ± 3.12	6
Disease understanding	(8) How much do you know about IBD?	6.00 ± 2.29	4

3.4. Correlation analysis of disease perception with anxiety and depression

The results of Pearson correlation analysis showed that there was a positive correlation between the patients' anxiety and depression status scores and disease perception ($P < 0.05$), as shown in **Table 4**.

Table 4. Correlation analysis between BIPQ score and depression and anxiety

		Total BIPQ score	Anxiety	Depression
Total BIPQ score	<i>P</i>	1	0.679**	0.670**
	Significance (two-tailed)		0.000	0.000
Anxiety	<i>P</i>	0.679**	1	0.896**
	Significance (two-tailed)	0.000		0.000
Depression	<i>P</i>	0.670**	0.896**	1
	Significance (two-tailed)	0.000	0.000	

**. At the 0.01 level (two-tailed), the correlation was significant.

4. Discussion

4.1. Emphasize and improve the mental health of adolescent patients with inflammatory bowel disease

This study found that anxiety and depression were prevalent in our adolescent IBD patients. This is consistent with the results of a previous cohort study, in which the prevalence of depression and anxiety was higher in patients with IBD than in normal subjects ^[34]. A related longitudinal study showed that anxiety or depressive symptoms in adolescence significantly increased the risk of recurrent anxiety or depression in adulthood by two to three times ^[35]. Even subclinical symptoms of depression in adolescence may lead to severe depression in adulthood ^[36]. There are several reasons for the risk of psychiatric disorders in adolescents with inflammatory bowel disease. First, adolescence is a critical period of cognitive and emotional transition, and illness may lead to a decline in quality of life and social functioning ^[37]. Second, chronic illnesses can negatively affect the mental status of adolescents ^[38]. Furthermore, patients with inflammatory bowel disease (IBD) often experience uncomfortable symptoms that can cause greater psychological distress in the adolescent population. Additionally, frequent treatment with corticosteroids may have a direct impact on the patient's emotional state. All of these factors may affect the psychological status of adolescent patients with inflammatory bowel disease. Therefore, healthcare teams should pay great attention to the psychological status of adolescent IBD patients and take active and effective measures to alleviate these negative emotions. For example, measures such as helping adolescent patients through psychological interventions and providing them with family and social support should be taken to promptly identify and intervene in possible psychological problems of adolescent IBD patients in order to promote their full physical and psychological recovery.

4.2. Moderate adjustment of disease perception of adolescent inflammatory bowel disease patients

In this study, it was found that the disease perception of adolescent inflammatory bowel disease patients in China was in the middle-upper level, which was slightly lower compared to the results of the study conducted by Chia *et al.* (48.47 ± 5.80 points) ^[39]. The highest score for each entry was for disease control in the cognitive dimension, followed by treatment effectiveness in the cognitive dimension. Meanwhile, the results of this study revealed that the total BIPQ score was positively correlated with the level of anxiety and depression in adolescent inflammatory bowel disease patients, i.e., the higher the total score of disease perception, the more likely the presence of anxiety and depressive symptoms, which is consistent with the results of several similar studies abroad ^[40–42]. It has been shown that disease perception is a key link in determining patients' behavior, which has a great impact on patients' mental health and quality of life ^[43]. This is consistent with the findings of a recent cross-sectional survey of adult IBD patients, in which negative perceptions of the consequences of the disease were associated with lower levels of physical and mental health, as well as impaired activity and reduced work ^[17]. This can even have a negative impact on self-management behaviors such as low adherence, potential health risk behaviors, and subsequent loss of personal and societal costs due to delayed work, and the negative impact of the disease on adolescents is particularly pronounced in different populations ^[17, 44]. Therefore, adjustments in disease perception in adolescent inflammatory bowel disease patients should be emphasized to avoid or reduce physical and mental problems caused by disease perception problems in adolescent inflammatory bowel disease patients.

4.3. Providing multidimensional continuity of care support

Adolescent patients with inflammatory bowel disease (IBD) are at serious risk of chronic mental health disorders, an issue that requires urgent attention and comprehensive care support ^[42]. However, current mental health care for patients with IBD takes a largely reactive approach rather than preventive measures, with studies confirming the effectiveness of psychological interventions to alter disease perception, and previous reviews suggesting that psychological interventions may be particularly beneficial for adolescents with IBD ^[45–48]. Evidence on the impact of psychotherapy on patients with IBD suggests that current treatments (particularly cognitive behavioral therapy) may have a positive effect on depression scores in the short term ^[49]. In other chronic diseases, evidence based on common sense modeling through interventions targeting perceptions of illness has confirmed that these negative effects can be modified through psychological interventions, and if psychological interventions can be provided to adolescents with IBD in a timely manner, it will help to effectively improve their mental health ^[47]. At the same time, a communication platform combining online and offline can be set up for adolescent IBD patients, so that they can obtain more information related to the disease and exchange their emotional experiences with other adolescent patients, which is necessary to reduce the negative emotions of adolescent inflammatory bowel disease patients and improve their physical and mental health. When necessary, psychological interventions should be provided to these adolescent patients as early as possible to improve their mental health and encourage them to adopt positive health behaviors and lifestyles, so as to enhance the physical and mental health of adolescent IBD patients in an all-round way.

5. Conclusion

In summary, anxiety and depression are common in adolescent inflammatory bowel disease patients. Meanwhile, disease perception will have an impact on the psychological health of adolescent IBD patients. Therefore, the psychological condition and disease perception of adolescent IBD patients should be emphasized and an all-round psychological support platform should be built for them. Comprehensive education should be provided to adolescent inflammatory bowel disease patients from multiple dimensions, including the disease itself, treatment programs, nutritional support, and psychological status, covering their cognitive, emotional, and disease comprehension abilities, and comprehensive measures should be taken for intervention.

There are some limitations in this study, such as the limited sample size of the survey and the limited area in which the study was conducted. In future studies, it is proposed to use joint multicenter research to further expand the sample size and radiate the exploration of other relevant influencing factors in order to provide effective interventions for adolescent IBD patients in a more scientific and comprehensive way.

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Disclosure statement

The authors declare no conflict of interest.

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Current Status and Influencing Factors of Social Alienation Among Young and Middle-Aged Stroke Patients in Dali

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Abstract: *Objective:* To explore the current status of social alienation and its influencing factors among young and middle-aged stroke patients in Dali. *Methods:* A convenience sampling method was used to survey 385 young and middle-aged stroke patients in a tertiary hospital in Dali from December 2024 to July 2025. Questionnaires including general demographic information, the General Alienation Scale, the Athens insomnia scale, and others were administered. *Results:* The social alienation score of young and middle-aged stroke patients in Dali was (35.67 ± 3.46). Univariate analysis showed that general demographic factors [education level, monthly household income, whether it was the first onset, presence of sequelae, disease duration, activities of daily living (ADL, Barthel Index)], social support, stigma, self-perceived burden, anxiety and depression, and sleep status were influencing factors of social alienation ($P < 0.05$). Regression analysis indicated that social support, anxiety and depression, disease duration, stigma, presence of sequelae, and self-care ability were significant influencing factors of social alienation ($P < 0.01$), explaining 65.3% of the total variance. *Conclusion:* The level of social alienation among young and middle-aged stroke patients in Dali is relatively low. Special attention should be paid to patients with a disease duration of < 7 days, those with sequelae, moderate-to-severe dependence in self-care, low social support, high stigma, and high levels of anxiety and depression, to effectively reduce their social alienation.

Keywords: Young and middle-aged stroke; Influencing factors; Social alienation

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1. Introduction

Stroke, as a major public health issue in China, is characterized by its “four highs” (high incidence, mortality, disability, and recurrence rates), which not only threaten national health but also impose a heavy socioeconomic burden. According to the “China Stroke Report 2019,” the incidence of stroke in China has reached 1114.8 per

100,000, and the mortality rate has reached 149.49 per 100,000 in 2020, highlighting the urgency of disease prevention and control ^[1, 2]. In recent years, there has been a significant trend of younger onset, with young and middle-aged groups (aged 18–59) accounting for 31% of stroke patients ^[3]. Young and middle-aged stroke patients face a dual health crisis: on the one hand, 70%–80% of patients suffer from sequelae such as physical dysfunction, leading to a decreased ability to live independently and increased risk of recurrence ^[4, 5]. On the other hand, this group is in a critical period of career development and peak family responsibilities, and sudden health impairments not only affect physiological functions but also easily lead to psychosocial adaptation disorders. Studies have shown that approximately 40% of young and middle-aged stroke patients exhibit social alienation behaviors such as reduced social participation and interpersonal withdrawal ^[6]. This “physiological-psychological-social” multidimensional functional impairment forms a vicious cycle, further exacerbating the difficulty of rehabilitation. The occurrence of social alienation has significant regional differences. As a border prefecture-level city in Yunnan Province, Dali City has a relatively lagging economic development level, and socioeconomic status has been proven to have a significant negative correlation with social alienation. Currently, there are few reports on social alienation among young and middle-aged stroke patients in underdeveloped areas of southwest China. Therefore, this study explores the current situation and influencing factors of social alienation among young and middle-aged stroke patients in Dali City, aiming to construct an intervention model suitable for this region and provide a scientific basis for improving China’s stroke rehabilitation service system.

2. Research objects and methods

2.1. Research objects

Using convenience sampling, 385 young and middle-aged stroke patients are selected from a tertiary hospital in Dali City from December 2024 to July 2025. The inclusion criteria of the study are: (1) Diagnosed with various types of “stroke” according to the diagnostic criteria established by the Chinese Medical Association based on craniocerebral CT or MRI examination ^[7, 8]; (2) Age: 18–59 years old; (3) Informed consent, possessing a certain level of reading and comprehension skills, and willing to participate in the questionnaire survey; (4) Conscious, without mental illness or cognitive impairment; (5) Aware of their own condition and in a stable condition.

The exclusion criteria included: (1) Patients with mental illness; patients with unstable vital signs; (2) Patients with malignant tumors; (3) Patients with severe cardiac, liver, kidney, or pulmonary insufficiency; (4) Patients who refuse to participate in the study; (5) Patients who have experienced major family events in the past six months.

The elimination criteria are: (1) Missing data exceeding 10% of the total; (2) Selecting only one answer option; (3) Treating multiple-choice questions as single-choice questions or selecting all options.

2.2. Research tools

2.2.1. General information questionnaire

Developed based on literature review and group discussions, it mainly includes general patient information such as age, gender, disease information, and other relevant indicators.

2.2.2. Athens Insomnia Scale (AIS)

This scale, developed by Professor Dan Sedmark, the Vice Dean of the Ohio State University Medical School in 1985, is used to evaluate patients’ sleep status. It consists of 8 items rated on a 4-point scale from 0 (no problem) to

3 (severe impact). A score of < 4 indicates no sleep disturbance, 4–6 suggests possible insomnia, and > 6 indicates insomnia^[9, 10].

2.2.3. Self-perceived Burden Scale (SPBS)

Developed by Cousineau *et al.*, this scale assesses the self-perceived burden (SPB) of patients with chronic diseases^[11]. It contains 25 items across three dimensions, with a Cronbach's α coefficient of 0.85.

2.2.4. Hospital Anxiety and Depression Scale (HADS)

Adapted by Chinese scholars such as Ye, this scale includes 14 items divided into anxiety and depression subscales. Each subscale has 7 items rated on a Likert scale from 0 to 3. The scoring ranges for both subscales are as follows: 0–7 indicates no symptoms, 8–10 suggests possible symptoms, and 11–21 indicates significant symptoms. The Cronbach's α coefficient for the Chinese version is 0.879^[12].

2.2.5. Social Support Rating Scale (SSRS)

Revised by Xiao and first applied in clinical research in 1986, this scale has good reliability and validity (Cronbach's $\alpha = 0.78$, test-retest reliability = 0.81)^[13]. It consists of 10 items divided into three dimensions: objective support, subjective support, and utilization of social support. The total score ranges from 12 to 66. Scores ≤ 22 indicate a low level of social support, 23–44 indicate a moderate level, and 45–66 indicate a high level^[14].

2.2.6. Stroke stigma scale

Developed by Zhu *et al.*, this scale assesses stigma among stroke patients^[15]. It contains 16 items divided into four dimensions: “physical obstacles” (4 items), “experience of discrimination” (3 items), “social interaction” (4 items), and “self-perception” (5 items). It uses a Likert 5-point rating scale (1–5). The total score ranges from 16 to 80, with 16–32 indicating a low level of stigma, 33–48 indicating a moderate level, and ≥ 49 indicating a high level. The Cronbach's α is 0.916.

2.2.7. Generalized Social Alienation Scale (GSAS)

Developed by Jessor and Jessor in 1977 and later adapted into Chinese by domestic scholar Wu, this scale consists of 15 items divided into four dimensions: self-alienation, alienation from others, skepticism, and sense of meaninglessness^[16, 17]. It uses a Likert 4-point rating scale (1–4, ranging from “strongly disagree” to “strongly agree”). A social alienation score of ≥ 35 indicates the presence of social alienation. This scale is widely used to measure the level of social alienation among stroke patients, with a Cronbach's α coefficient of 0.77.

2.3. Sample size calculation

Using the Kendall sample size calculation method, the included sample size should be 5–10 times the number of independent variables. With a total of 35 variables and considering a 20% survey missing rate, the minimum sample size is 210 cases. The final sample size is determined to be 385 cases.

2.4. Data collection

This study has been approved by the hospital ethics committee (Review No.: DFY20241129005). Researchers are uniformly trained before the survey to avoid subjective and inductive language that could influence patients. The

completeness of the questionnaire is also checked. A total of 385 questionnaires are distributed and collected, with a valid recovery rate of 100%.

2.5. Statistical methods

Data is processed using SPSS 22.0 software. Normally distributed data is presented as mean \pm standard deviation (\pm s). Count data is expressed as the number of cases (n) and percentage (%). Quantitative data is analyzed using t-test or q-test for single-factor analysis. Qualitative data is analyzed using the chi-square test. Pearson correlation analysis and multiple linear regression analysis were performed. A p -value < 0.05 is considered statistically significant.

3. Results

3.1. Single-factor analysis of social alienation scores among young and middle-aged stroke patients with different demographic and disease characteristics

There were statistically significant differences in social alienation scores among young and middle-aged stroke patients with different levels of education, monthly income, residual sequelae, disease duration, self-care ability, and whether it was the first onset ($P < 0.05$), as shown in **Table 1**.

Table 1. Univariate analysis of scores of social alienation among young and middle-aged stroke patients with different demographics and disease profiles (\pm S, $n = 385$)

Item	Cases [n (%)]	Social alienation score (points)	$t/q/\chi^2$	P
Age			1.358	0.351
18–44 years	164 (43.6)	35.95 \pm 3.545		
45–59 years	221 (57.4)	35.46 \pm 3.389		
Gender			1.422	0.157
Male	264 (68.6)	35.84 \pm 3.472		
Female	121 (31.4)	35.30 \pm 3.420		
Education level			28.677	< 0.001
Illiterate	26 (6.8)	37.27 \pm 4.006		
Primary school	162 (42.0)	36.58 \pm 3.642		
Junior high/ Vocational	171 (44.4)	34.84 \pm 3.040		
High school	21 (5.5)	33.90 \pm 1.998		
College	5 (1.3)	33.60 \pm 0.894		
Bachelor's or above	0 (0)	0 [None]		
Marital status			0.632	0.73
Unmarried	1 (0.3)	34		
Married	381 (99.0)	35.66 \pm 3.462		
Divorced	3 (0.7)	37.33 \pm 4.041		

Table 1 (Continued)

Item	Cases [n (%)]	Social alienation score (points)	$t/q/\chi^2$	<i>P</i>
Widowed	0 (0)	0 [None]		
Residence			-3.339	0.414
Rural	256 (66.5)	35.63 ± 3.538		
Urban	129 (33.5)	35.75 ± 3.312		
Occupation			6.226	0.101
Farmer	319 (82.9)	35.84 ± 3.508		
Company employee	7 (1.8)	33.71 ± 2.138		
Public institution	7 (1.8)	33.86 ± 2.268		
Other	52 (13.5)	35.13 ± 3.290		
Monthly income (¥)			8.399	0.015
< 3000	17 (4.4)	35.18 ± 3.127		
3000–6000	312 (81.0)	35.89 ± 3.514		
> 6000	56 (14.6)	34.59 ± 3.062		
Sequelae			57.158	< 0.001
1 type	78 (20.3)	38.14 ± 3.758		
2 types	10 (2.6)	39.25 ± 2.150		
> 2 types	4 (1.0)	36.25 ± 3.775		
None	293 (76.1)	34.88 ± 3.007		
Disease course			90.813	< 0.001
< 7 days	122 (31.7)	38.11 ± 3.356		
7–14 days	257 (66.8)	34.49 ± 2.849		
15 days–1 month	6 (1.5)	36.17 ± 3.764		
>1 month to 6 months	0 (0)	0 [None]		
> 6 months	0 (0)	0 [None]		
Self-care ability			103.77	< 0.001
No dependency	108 (28.0)	34.28 ± 2.657		
Mild dependency	161 (41.8)	34.82 ± 3.263		
Moderate dependency	100 (26.0)	38.50 ± 2.983		
Severe dependency	16 (4.2)	35.88 ± 2.941		
First episode?			-2.249	< 0.001
Yes	282 (73.2)	35.43 ± 3.289		
No	103 (26.8)	36.32 ± 3.833		

3.2. Scores related to psychosocial and emotional factors in young and middle-aged stroke patients

In this study, the score for social support was (30.31 ± 5.243), indicating a moderate level. The score for stroke

stigma was (35.44 ± 11.815), also at a moderate level. The score for hospital anxiety and depression was (13.21 ± 8.194), suggesting significant symptoms. The score for Athens insomnia was (6.99 ± 4.716), indicating the presence of symptoms and the score for self-burden was (28.63 ± 7.343), which was at a mild level.

3.3. Relationship between social alienation and social support, stigma, psychological distress, insomnia, and self-burden in stroke patients

Correlation analysis showed a significant negative correlation between social support and total social alienation score ($P < 0.01$). Stroke stigma, hospital anxiety and depression, Athens insomnia, and self-burden were significantly positively correlated with total social alienation score ($P < 0.01$) as shown in **Table 2**.

Table 2. Correlation analysis between social alienation and social support, stroke stigma, hospital anxiety and depression, Athens insomnia, and self-burden

Variable	Social support score	Stroke stigma score	Hospital anxiety and depression score	Athens insomnia scale	Self-perceived burden score
Social alienation score	-0.716**	0.521**	0.715**	0.472**	0.600**
<i>P</i> -value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Note: ** indicates $P < 0.01$ (two-tailed); * indicates $P < 0.05$ (one-tailed)

3.4. Regression analysis of social alienation in relation to demographics, support, stigma, psychological distress, insomnia, and self-burden among young and middle-aged stroke patients

In this study, social alienation was used as the dependent variable, and multiple linear regression analysis was performed using statistically significant independent variables from the univariate analysis (education level, monthly income, residual sequelae, disease duration, self-care ability, whether it was the first onset, social support, stroke stigma, hospital anxiety and depression, Athens insomnia, and self-burden). The results showed that self-care ability, disease duration, residual sequelae, anxiety and depression, stigma, and social support were significant predictors of social alienation ($P < 0.01$), explaining 65.3% of the total variation as shown in **Table 3**.

Table 3. Multiple linear regression analysis of social alienation among young and middle-aged stroke patients ($n=385$)

Independent variable	Unstandardized coefficient (B)	Standard error (SE)	Standardized coefficient (β)	t-statistic	<i>p</i> -value	95% CI
Constant	40.141	2.563		25.641	< 0.001	35.1–45.182
Self-care ability	0.383	0.139	0.093	2.761	0.006	0.11–0.656
Disease course	-0.616	0.253	-0.088	-2.435	0.015	-1.113– -0.119
Sequelae	-0.310	0.095	-0.110	-3.273	0.001	-0.497– -0.124
Anxiety and depression	0.107	0.021	0.254	4.990	< 0.001	0.065–0.149
Stigma	0.038	0.011	0.129	3.567	< 0.001	0.017–0.059
Social support	-0.210	0.030	-0.318	-7.098	< 0.001	-0.268– -0.152

Note: $R^2=0.668$; Adjusted $R^2=0.653$; $F=46.216$; $P < 0.001$

4. Discussion

4.1. Scores of social support, stroke-related stigma, and hospital anxiety and depression among young and middle-aged stroke patients in Dali

The social support score in this study (30.31 ± 5.243) is at a moderate level, consistent with the research by Zhuo *et al.* ^[18]. On one hand, due to responsibilities and dignity, young and middle-aged stroke patients, most of whom are experiencing their first stroke in this study, tend to avoid communication with family and friends because of the panic caused by the disease, hindering the sustainable utilization of social support ^[19]. On the other hand, patients' families have a low level of health literacy regarding stroke, leading to a lower level of support ^[20]. The stroke-related stigma score (35.44 ± 11.815) is also at a moderate level. Compared to elderly stroke patients, young and middle-aged stroke patients may experience greater guilt and shame due to social and family responsibilities. Additionally, due to the high disability rate of stroke, changes in appearance can also bring varying degrees of shame to these patients. The hospital anxiety and depression score (13.21 ± 8.194) indicates significant symptoms. Young and middle-aged stroke patients experience more negative emotions due to changes in physical activity, appearance, family and social responsibilities, as well as economic obstacles caused by difficulties returning to work ^[21].

4.2. Current situation of social alienation among young and middle-aged stroke patients in Dali

The results of this study show that the social alienation score of young and middle-aged stroke patients in Dali is (35.67 ± 3.46), which is consistent with the research by Chen *et al.* ^[22]. As the backbone of society and family, young and middle-aged patients may face difficulties returning to work due to post-stroke dysfunction. Additionally, changes in appearance and multiple burdens exacerbate their social avoidance behavior, thereby reducing treatment and rehabilitation compliance. Healthcare professionals should pay attention to patients' social participation, regularly assess their sense of social alienation, strengthen psychological care, and provide social support.

4.3. Influencing factors of social alienation among young and middle-aged stroke patients in Dali

4.3.1. Disease information

The results of this study show that:

- (1) Young and middle-aged stroke patients with moderate to severe dependence have a higher sense of social alienation, which is consistent with Wang's research ^[23]. This may be because moderate to severe dysfunction affects self-care ability, and at the same time, young and middle-aged patients face family, work, and economic pressures, leading to a decrease in social adaptability.
- (2) Patients with a disease duration of less than 7 days have the heaviest sense of alienation. This is because they are forced to discontinue work during the early stages of the disease, and they worry about family burdens, dysfunction, and prognosis, leading to social avoidance.
- (3) The more sequelae, the heavier the sense of alienation. This is because physical dysfunction or changes in appearance exceed the psychological tolerance of this age group, triggering social avoidance behavior.

4.3.2. Social support

This study confirms that there is a negative correlation between social support and social alienation among young and middle-aged stroke patients, which is consistent with the research by He *et al.* ^[24]. This group has a high demand for

family and social support ^[25]. A good support system can enhance treatment confidence and compliance, and reduce social avoidance behavior. Medical staff should actively evaluate patients' social support levels, provide professional guidance to help patients understand treatment plans and rehabilitation processes, promote effective communication between families and society, and develop intervention measures to enhance patients' social enthusiasm. By improving the social support system, patients' social alienation can be significantly reduced ^[24].

4.3.3. Stigma

The results of this study show that there is a positive correlation between stigma and social alienation among young and middle-aged stroke patients, which is consistent with the research by Jiao *et al.* ^[26]. The dysfunction (such as hemiplegia, aphasia) and appearance changes caused by stroke can significantly damage the patient's image and exacerbate stigma ^[27]. Young and middle-aged patients are more sensitive to their appearance, prone to feelings of inferiority, and thus actively reduce or avoid social interaction, further increasing social alienation. Medical staff should strengthen psychological counseling for patients, especially those with impaired physical function, and conduct health lectures to promote communication between patients and their families. Through knowledge popularization, stigma can be reduced, thereby reducing social alienation ^[26].

4.3.4. Anxiety and depression

This study shows that there is a positive correlation between the level of anxiety and depression and social alienation among young and middle-aged stroke patients, which is consistent with the research by He *et al.* ^[24]. Negative emotions arise from role changes, economic pressures, job uncertainties, and dysfunction, leading to reduced social interest and avoidance behavior, which exacerbates social alienation and affects treatment compliance and prognosis. It is suggested that medical staff strengthen psychological assessment and intervention to promote social participation and reduce alienation.

5. Conclusion

In summary, social alienation among young and middle-aged stroke patients in Dali City is influenced by patients' self-care ability, disease duration, residual sequelae, social support, stigma, and anxiety and depression. Simultaneously, severe social alienation can affect patients' treatment outcomes and prognosis. Therefore, medical staff should actively evaluate the social alienation scores of young and middle-aged stroke patients, further explore and develop measures to reduce patients' negative emotions, stigma, and improve or enhance patients' family social support and self-care abilities, thereby alleviating patients' social alienation. The limitations of this study include a relatively narrow sampling range and a limited number of influencing factor scales included. Therefore, future research should conduct broader sampling, increase the number of influencing factor scales, and further explore the current situation and influencing factors of social alienation among young and middle-aged stroke patients in Dali, providing a scientific basis for developing effective intervention measures, improving patients' mental health and treatment or rehabilitation enthusiasm, and promoting patients' return to society.

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Disclosure statement

The authors declare no conflict of interest.

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Mechanistic Study of Trimebutine Combined with Berberine Hydrochloride in PI-IBS Rat Intervention via the Brain–Gut–Microbiota Axis

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Abstract: This study explored the therapeutic effect of trimebutine maleate dispersible tablets combined with berberine on PI-IBS rats with liver depression and spleen deficiency. Fifty male rats were divided into five groups: normal, model, berberine (XB), trimebutine (QM), and combination (XB+QM). The PI-IBS model was established using maternal separation, TNBS perfusion, and chronic restraint. After 20 days of drug intervention, DAI, CMDI, TDI, AWR scores, histopathology, and expression levels of c-Fos, VIP, NOS, and CHAT in the hippocampus and colon were assessed. The model group showed significant gut and brain changes, while the combination group (XB+QM) improved fecal characteristics, reduced inflammation, regulated brain-gut peptide expression, and alleviated visceral hypersensitivity and colon tissue damage ($P < 0.05$).

Keywords: Postinfectious irritable bowel syndrome; Brain-gut bacterial axis; Trimebutine; Berberine

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1. Introduction

Irritable bowel syndrome (IBS) is a functional disease of the digestive system that affects an average of 22 % of the general population^[1]. The incidence rate in China is 5.2–12%^[2]. Its etiology and pathogenesis are still unclear. Domestic and foreign studies have pointed out that post-infectious irritable bowel syndrome (PI-IBS) is a common type of IBS. IBS may be caused by infectious gastroenteritis identified as PI-IBS. The prevalence of PI-IBS in patients with infectious gastroenteritis is 4–36 %^[3]. The phenotypic frequency of PI-IBS is composed of mixed IBS (IBS-M) 24 %, diarrhea-type IBS (IBS-D) 63 %, and constipation-type IBS (IBS-C) 13 %^[4]. The Rome IV diagnostic criteria provide a new definition for PI-IBS, but the exact mechanism leading to PI-IBS is not yet fully understood. At present, it is generally believed that there is low-grade inflammation or no inflammation in the intestine after gastrointestinal infection, and it is in a state of continuous immune activation, resulting in the symptoms of IBS. The etiology may involve intestinal

motility disorders, visceral hypersensitivity, brain-gut axis disorders, intestinal flora imbalance, psychosocial stress, genetics, and diet. At present, most scholars believe that brain-gut axis regulation disorder is an important pathological basis of IBS^[5-7]. In recent years, the impact of intestinal flora imbalance on IBS has received increasing attention. The intestinal flora and the brain-gut axis undergo complex and subtle interactive regulation, and the concept of “brain-gut-enteric microbiota axis” (BGMA) has been proposed^[8].

Trimebutine (QM) regulates digestive tract motility by modulating smooth muscle activity. It can either stimulate or inhibit movement by affecting K⁺ and Ca²⁺ channels, leading to changes in cell excitability. It also acts on nerve receptors: inhibiting adrenaline release to enhance slow motility, or reducing acetylcholine release to calm excessive activity. Because of the above pharmacological properties, trimebutine maleate has become one of the therapeutic drugs for IBS and some other gastrointestinal motility disorders^[9, 10]. Berberine is an isoquinoline alkaloid extracted from the rhizome of the plant of the genus *Coptis* in the Ranunculaceae family. Traditional Chinese medicine suggests that it has a certain therapeutic effect on intestinal infections and inflammations^[11]. Recent studies show that trimebutine can inhibit intestinal smooth muscle excitation and relieve abdominal pain, with proven clinical effectiveness in treating IBS. Combined with berberine, it shows significant patient benefits, though the exact mechanisms and targets remain unclear.

The brain-gut axis regulates the gastrointestinal tract via brain-gut peptides—small molecules found in both the brain and gut. These peptides, such as 5-HT, Ach, CHAT, NOS, VIP, and others, modulate motility, sensation, and secretion. Acting as both hormones and neurotransmitters, they mediate communication between the gut and central nervous system. Changes in gastrointestinal function in IBS patients are caused by the disorder of brain-gut peptide regulation in the brain-gut axis^[12]. c-Fos is considered to be a key effector of intracellular signaling cascades and can amplify noxious stimulus signals during stress^[13]. With the deepening of our understanding of its biological functions, c-FOS has gradually become an important tool for studying abnormal visceral sensitivity, neural pathways for gastrointestinal noxious signal transmission, how the spinal cord and higher centers regulate, and the origin of key active substances^[14]. VIP is widely present in the central and peripheral nervous systems, especially in the myenteric and submucosal plexuses of the gut. As a key neurotransmitter in the brain-gut axis, it is released from neuron endings to regulate intestinal motility, secretion, and blood flow, mainly by inhibiting gastrointestinal movement through neurotransmitter release^[15].

2. Experimental materials and methods

2.1. Experimental equipment and reagent models, and numbers

- (1) Rotary slicer: model Leica-2016, Germany
- (2) Fully automatic closed tissue dehydrator: model TSJ-II, Changzhou Zhongwei
- (3) Embedding machine: model BMJ-III, Changzhou Zhongwei
- (4) Pathological tissue bleaching and drying instrument: model PHY-III, Changzhou Zhongwei
- (5) Electric constant temperature drying oven: model 202-2AB, Tianjin Test
- (6) Fume hood: model VD-TGF-06, Guangzhou Ruizhi
- (7) Microwave oven: model PTOF20L-DG (S0), Galanz
- (8) Upright microscope: model DM500, Leica (Germany)
- (9) Pure water manufacturing system: model YL-100BU, Yiliyuan (Shenzhen)
- (10) Drug refrigerator: model YPG-260, Qingdao Olex

- (11) Tissue embedding box: Item number 31050102W, Jiangsu Shitai
- (12) Slide: 24mm × 76mm × 1.2mm, Jiangsu Shitai
- (13) Cover glass: 24mm × 24mm, Jiangsu Shitai
- (14) High-efficiency section paraffin: 500 g/box, Sinopharm
- (15) Paraformaldehyde: 500g/bottle, Sinopharm
- (16) PBS phosphate buffer (0.01MPH7.2–7.4): Item number P1010, Solarbio
- (17) SPRabbit&MouseHRPKit(DAB): Item number CW2069S, CWBIO (Jiangsu)
- (18) 30% hydrogen peroxide: Item number 10011208, Sinopharm
- (19) Anhydrous methanol: Comeo (Tianjin)
- (20) Anhydrous ethanol: Comeo (Tianjin)
- (21) Xylene: Comeo (Tianjin)
- (22) Sodium citrate buffer (0.01MPH6.0): Item number C1010, Solarbio (Beijing)
- (23) Hydrochloric acid: Item number 81013, Chongqing Chuandong
- (24) Hematoxylin dye: Item number G1005-1, Servicebio (Wuhan)
- (25) Ultra-clean quick-drying sealing glue: Item number G1404-100ML, Servicebio (Wuhan)

2.2. Methods for animal modeling and intervention

2.2.1. Modeling method (Trimmed to Two-Thirds)

- (1) Mother-child separation: Ten male rats are selected. From day 14, they are separated from their mothers for 3 hours daily until weaning on day 22. The normal group is not separated. At over 6 weeks of age and > 220g, rats proceeded to TNBS modeling.
- (2) TNBS colonic perfusion: Rats fasted for 18 hours (with water). Under anesthesia, 0.3ml of 0.02ml TNBS in 50% ethanol is administered via a 2mm, 12cm enema tube inserted 8–10cm into the colon. Rats are inverted for 30 seconds before being returned to their cages.
- (3) Chronic restraint stress: Two weeks after TNBS perfusion, rats are restrained in a homemade frame for 3 hours daily (9:00–12:00) over 3 weeks. The control group received no restraint and normal feeding.



Figure 1. Binding method

2.2.2. Drug treatment

Trimebutine maleate dispersible tablets combined with berberine are given at a dose of 0.06 g/ kg.d and 0.09 g/kg.d, respectively. Rats in the normal group and the model group are given 15 mL/kg.d of normal saline by gavage, once a day, and the drug intervention lasted for 20 days.

2.3. Model evaluation indicators

2.3.1. General observation

The general condition of the rats (coat color, diet, spirit, activity, and stool) is observed every day, and the body weight is measured and recorded. After one week of drug intervention, the DAI (Disease Activity Index) score is performed, $DAI = \text{body weight loss score} + \text{stool characteristics score} + \text{blood in stool score}$ (**Table 1**).

Table 1. DAI scoring criteria

Weight loss	Stool characteristics	Occult blood or blood in stool	Rating/points
0	Normal	Negative	0
1–5%	Loose stools	Negative	1
6–10%	Loose stools	Positive	2
11–15%	Diarrhea	Positive	3
>15%	Diarrhea	Positive	4

*Note: Normal stool: formed stool; Loose stool: mushy stool that does not stick to the anus; Diarrhea: watery stool that sticks to the anus.

2.3.2. CMDI and TDI scores of colon tissue

The CMDI (colon mucosal injury index) score is based on the Luketal standard (**Table 2**). Dieleman's criteria for TDI (colon histopathology score) scoring is shown in **Table 3**.

Table 2. CMDI scoring criteria

Macroscopic observation of colonic mucosal morphology	Rating/points
No damage to the colon	0
Mild congestion and edema of mucosa, no ulcers	1
Mucosal congestion and edema with thickened intestinal wall, no ulcers	2
A single small ulcer forms, about 0–1 cm in diameter	3
Large ulcer, about 1–2 cm in diameter, but no adhesion between the intestine and surrounding organs	4
The ulcer is about 1–2cm in diameter, the intestine is thickened, and it is severely adhered to the surrounding organs.	5

Table 3. TDI scoring criteria

Pathological changes of colonic mucosa	Rating/points
Normal mucosa	0
1/3 of the basal crypt is missing	1
2/3 of the basal crypt is missing	2
Crypts are absent, leaving only the surface epithelium, with inflammatory cell infiltration	3
Mucosal erosion and ulceration with massive inflammatory cell infiltration	4

2.4. HE staining and immunohistochemistry

The fixed tissue is dehydrated in an automatic dehydrator (dehydration time: 75% alcohol 4h, 85% alcohol 2h,

95% alcohol 1h, 100% alcohol 0.5h, 100% alcohol 0.5h, 100% alcohol 0.5h, 100% alcohol 0.5h, xylene 10min, xylene 10min, paraffin 1h, paraffin 2h, paraffin 3h), embedded, and then sectioned and performed the following operations:

- (1) Oven at 60°C, bake for 30 minutes.
- (2) Dewaxing in xylene for 20 min (2 times); soaking in anhydrous ethanol for 10 min (2 times) → soaking in 95% ethanol for 5 min → soaking in 85% ethanol for 5 min → soaking in 75% ethanol for 5 min → soaking in pure water for 5 min.
- (3) After dewaxing and rehydration, immerse in 3% methanol-hydrogen peroxide at room temperature for 5 min.
- (4) Wash with PBS three times, 5 min each time.
- (5) The slices were immersed in 0.01 M citrate buffer (PH 6.0), heated in a microwave oven at high temperature for 2 min, and then repeated 5 times after a 5-min interval. After cooling, they were washed twice with PBS, each time for 5 min.
- (6) Add goat serum blocking solution and incubate at room temperature for 20 min.
- (7) Add primary antibody and incubate at 4°C overnight.
- (8) Add biotinylated secondary antibody and incubate at 37°C for 30 min.
- (9) Wash with PBS 3 times, 5 min each time.
- (10) DAB color development: Use the DAB color development kit, mix the reagent and drop it onto the slice, color at room temperature, control the reaction time under the microscope, generally about 2 minutes, and wash with distilled water.
- (11) The slides are lightly counterstained with hematoxylin, dehydrated, transparented, and mounted with neutral gum.
- (12) The above specimens are all processed according to the SOP procedures of pathological examination, including dehydration, trimming, embedding, sectioning, staining, sealing, etc., and finally, microscopic examination.

2.5. Image acquisition

An upright microscope (DM500) produced by Leica Microsystems of Germany is used to collect images of the slices. The entire tissue of each slice is first observed at 200 times magnification, and then 2–3 fields of view are selected to collect 400 times microscopic images.

2.6. Data analysis

The Image-Pro Plus 6.0 image analysis system is used to measure the integrated optical density (IOD) and area (Area) of all the collected images, and the mean optical density (MD) of each image is calculated. The average optical density of three images is used to calculate the average to obtain the mean optical density of each sample. SPSS 17.0 statistical analysis software is used to perform one-way ANOVA on the average, and the data are expressed as mean \pm standard deviation ($\bar{x} \pm SD$).

3. Results

For the results, * represents comparison with the normal group, # represents comparison with the model group.

3.1. Effects of trimebutine combined with berberine on the expression of c-Fos protein in hippocampal tissue and colon tissue of model rats

Table 4 shows that compared with the normal group, c-FOS, and VIP protein expression in the hippocampus and colon increased significantly ($*P < 0.05$) in other groups. Drug-treated groups showed a significant decrease ($^{\#}P < 0.05$) compared to the model group. The QM+XB group had significantly lower c-FOS and VIP levels than the XB group ($^{\Delta}P < 0.05$) and the QM group ($^{\S}P < 0.05$). The QM group alone showed no significant change ($P > 0.05$).

Table 4. Statistical results of average optical density of c-FOS and VIP \bar{x} in different tissues of rats in each group (\pm SD)

Group	Rat	c-FOS		VIP	
		Hippocampal tissue	Colon tissue	Seahorse	Colon
	N (only)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)
Normal group	10	0.1377 \pm 0.0046	0.1705 \pm 0.0040	0.1336 \pm 0.0039	0.1693 \pm 0.0046
Model group	10	0.2094 \pm 0.0092 *	0.2597 \pm 0.0102 *	0.1899 \pm 0.0079 *	0.2683 \pm 0.0102 *
XB group	10	0.1866 \pm 0.0105 $^{\#}$	0.2280 \pm 0.0106 $^{\#}$	0.1802 \pm 0.0096 $^{\#}$	0.2274 \pm 0.0091 $^{\#}$
QM group	10	0.1794 \pm 0.0144 $^{\#}$	0.2187 \pm 0.0112 $^{\#}$	0.1721 \pm 0.0083 $^{\#}$	0.2219 \pm 0.0074 $^{\#}$
QM+XB group	10	0.1545 \pm 0.0040 $^{\#}\Delta^{\S}$	0.1946 \pm 0.0061 $^{\#}\Delta^{\S}$	0.1448 \pm 0.0085 $^{\#}\Delta^{\S}$	0.1874 \pm 0.0046 $^{\#}\Delta^{\S}$

Note: Compared with the normal group, $*P < 0.05$; compared with the model group, $^{\#}P < 0.05$; compared with the XB group, $^{\Delta}P < 0.01$; QM+XB group $^{\Delta}P < 0.05$; compared with the QM group, QM+XB group $^{\S}P < 0.05$.

3.2. Effects of trimebutine combined with berberine on NOS protein expression and CHAT expression in hippocampus and colon in model rats

Table 5 showed that compared with the normal group, NOS and CHAT protein expression in the hippocampus and colon of other groups significantly decreased ($*P < 0.05$). Compared with the model group, drug-treated groups showed significant changes in NOS and CHAT expression ($^{\#}P < 0.05$). The QM+XB group had significant changes compared to the XB group ($^{\Delta}P < 0.05$), while the QM group alone showed no significant changes ($P > 0.05$). Compared with the QM group, the QM+XB group showed significant increases in NOS and CHAT expression ($^{\S}P < 0.05$).

Table 5. Statistical results of the average optical density of NOS and CHAT in different tissues of rats ($\bar{x} \pm$ SD)

Group	Rat	NOS		CHAT	
		Seahorse	Colon	Seahorse	Colon
	N (only)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)	OD ($\bar{x} \pm$ SD)
Normal group	10	0.2212 \pm 0.00 55	0.2990 \pm 0.0100	0.2150 \pm 0.00 46	0.2743 \pm 0.0 107
Model group	10	0.1597 \pm 0.0054 *	0.1709 \pm 0.00 46 *	0.1502 \pm 0.0043 *	0.1699 \pm 0.0063 *
XB group	10	0.1846 \pm 0.00 39 $^{\#}$	0.2125 \pm 0.007 4 $^{\#}$	0.1767 \pm 0.00 78 $^{\#}$	0.2222 \pm 0.00 62 $^{\#}$
QM group	10	0.1801 \pm 0.00 48 $^{\#}$	0.2185 \pm 0.0 184 $^{\#}$	0.1820 \pm 0.006 4 $^{\#}$	0.2272 \pm 0.00 90 $^{\#}$
QM+XB group	10	0.2014 \pm 0.00 67 $^{\#}\Delta^{\S}$	0.2545 \pm 0.006 6 $^{\#}\Delta^{\S}$	0.2032 \pm 0.00 59 $^{\#}\Delta^{\S}$	0.2512 \pm 0.00 93 $^{\#}\Delta^{\S}$

Note: Compared with the normal group, $*P < 0.05$; compared with the model group, $^{\#}P < 0.05$; compared with the XB group, $^{\Delta}P < 0.01$; QM+XB group $^{\Delta}P < 0.05$; compared with the QM group, QM+XB group $^{\S}P < 0.05$.

3.3. Effect of trimebutine combined with berberine on TDI, DAI, and CMDI scores of model rats

Based on **Table 6**, there were significant differences between the Model group, QM group, XB group, QM combined with XB group and normal group ($P < 0.05$). There were significant differences between QM group, XB group, QM combined with XB group, and the Model group ($P < 0.05$). There was a significant difference between QM group and QM combined with XB group ($P < 0.05$). There was no significant difference between QM group and XB group ($P > 0.05$).

Table 6. TDI score results after different drug interventions

Project	TDI	DAI	CMDI
Group	Rating /points	Rating /points	Rating /points
Control group	0	0	0
Model group	4.7 ± 0.483	4.7 ± 0.483	4.7 ± 0.483
QM group	3.3 ± 0.483	3.6 ± 0.699	3.5 ± 0.707
XB group	3.1 ± 0.568	3.4 ± 0.699	3.3 ± 1.059
QM Joint XB group	2.5 ± 0.527	2.6 ± 0.966	2.5 ± 0.527

Note: Compared with the normal group, $**P < 0.05$; compared with the model group, $^{##}P < 0.05$; compared with the QM combined with XB group, $P < 0.05$.

3.4. Effect of trimebutine combined with berberine on the abdominal withdrawal reflex score of model rats

Based on **Table 7**, the Control group, the scores of the Model group, QM group, and XB group at the pressure of 1, 1.5, and 2 ml were significantly increased, with significant differences ($P < 0.05$), and there was no significant difference between the QM combined with XB group and the Control ($P > 0.05$). Compared with the Model, the scores of the QM group and the XB group at the pressures of 1, 1.5, and 2 ml were reduced, with no significant difference ($P > 0.05$). Compared with the Model group, the scores of the QM combined with XB group at the pressures of 1, 1.5, and 2 ml were significantly reduced, with significant differences ($P < 0.05$). Compared with the QM group, the scores of the QM combined with XB group at the pressures of 1, 1.5, and 2 ml were significantly reduced, with significant differences ($P < 0.05$).

Table 7. AWR score results after different drug interventions

Group	1ML score /point	1.5ML score /point	2ML score /points
Control group	0.5 ± 0.527	1.4 ± 0.516	2.4 ± 0.516
Model group	1.7 ± 0.483	2.7 ± 0.483	3.7 ± 0.483
QM group	1.6 ± 0.516	2.6 ± 0.516	3.5 ± 0.527
XB group	1.4 ± 0.516	2.4 ± 0.516	3.3 ± 0.483
QM Joint XB group	0.8 ± 0.422	1.8 ± 0.632	2.7 ± 0.483

Note: Compared with the normal group, $**P < 0.05$; compared with the model group, $^{##}P < 0.05$; compared with the QM group, $P < 0.05$.

3.5. Effect of trimebutine combined with berberine on colonic tissue pathological morphology in model rats

HE staining showed the normal group had intact colon mucosa with orderly epithelial cells and no lesions. The model group exhibited mucosal erosion, ulcers, inflammatory infiltration, and crypt atrophy. The QM group had significantly fewer inflammatory cells, regular crypt surfaces, and relatively intact mucosa. The QM+XB group showed notably thickened crypt bases and marked colon tissue improvement compared to QM and XB groups. Refer to **Figure 2** for details.

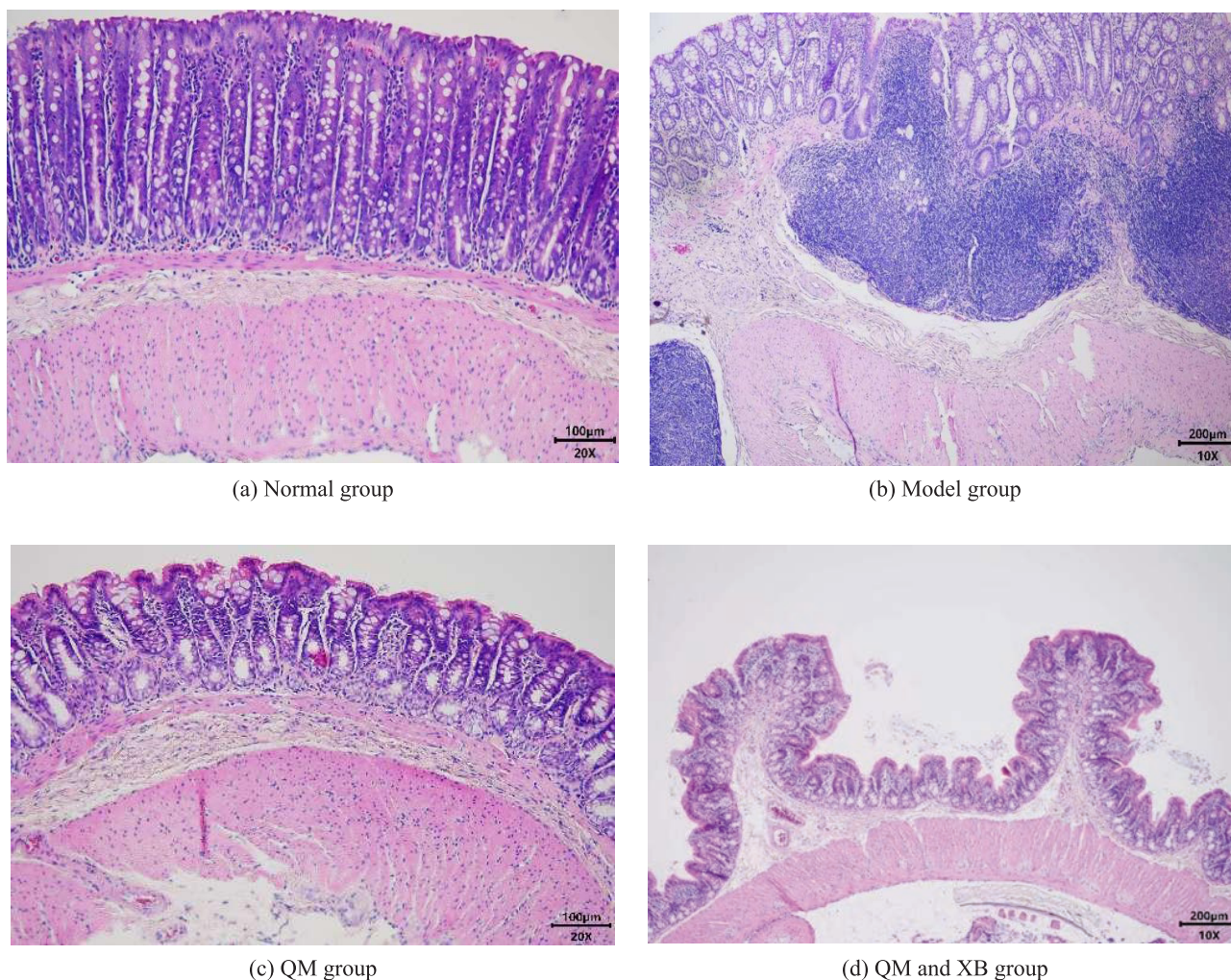


Figure 2. Colon tissue morphology of rats in each group (HE staining, × 100)

4. Discussion

This study found that compared with the normal group, the model group showed increased c-FOS and VIP protein expression in the hippocampus and colon, but decreased NOS and CHAT expression in both regions. Disease indices (TDI, DAI, CMDI) and AWR scores were significantly higher, with mucosal erosion, ulcers, inflammatory infiltration, and crypt atrophy observed. Compared to the model group, the drug-treated groups showed decreased c-FOS and VIP levels, reduced NOS and CHAT expression, lowered disease indices and AWR scores, fewer

inflammatory cells, more regular crypts, and improved mucosal integrity. The QM+XB group had thicker crypt bases and better colon tissue recovery. The study concludes that trimebutine combined with berberine improves intestinal flora and regulates abnormal brain-gut peptide expression, enhancing intestinal barrier integrity and alleviating PI-IBS symptoms.

5. Conclusion

The combination of trimebutine maleate dispersible tablets and berberine demonstrated significant therapeutic efficacy in PI-IBS rats with liver depression and spleen deficiency. The XB+QM group effectively improved fecal characteristics, reduced colonic inflammation, regulated brain-gut peptide expression (c-Fos, VIP, NOS, CHAT), and alleviated visceral hypersensitivity and colon tissue damage compared to the model group ($P < 0.05$). These findings suggest that the combined therapy may offer a promising approach for managing PI-IBS by targeting both gut and brain pathways.

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Disclosure statement

The authors declare no conflict of interest.

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Social Alienation in Adolescents with Depression from an Interaction Perspective: A Qualitative Research

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Abstract: *Objective:* This study aims to explore the experiences of social alienation among adolescents with depression, providing practical guidance for improving their interpersonal relationships and facilitating their reintegration into society. *Methods:* This qualitative research was conducted following the conventional content analysis method. 20 adolescents with depression were employed to select from June to August 2024 for face-to-face semi-structured interviews. The collected data were analyzed using Colaizzi's seven-step method. *Results:* Three themes and eight sub-themes were analyzed and identified: individual level (feelings of helplessness and powerlessness, cognitive distortion, avoidance and withdrawal), family level (lack of family awareness, family conflict), social level (limitations of academic stress and social circle, lack and degradation of skills, generalization of virtual reality, social "stigma"). *Conclusion:* Adolescents with depression experience complex social alienation. Healthcare providers should enhance their self-awareness and social adaptation skills, improve family dynamics, and provide a comprehensive range of services and services to help them to cope with the challenges of depression. Healthcare providers should enhance their self-awareness and social adaptation skills, improve family dynamics, strengthen communication, bolster family support systems, and collaborate to develop comprehensive social networks and psychological services. This will create a supportive social atmosphere to help adolescents gradually alleviate their feelings of social alienation.

Keywords: Depression; Adolescents; Social alienation; The interactive perspective; Qualitative research

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1. Introduction

Adolescent depression is a common psychological disorder characterized by depressed mood and loss of interest and pleasure ^[1]. In recent years, an increasing number of studies have shown that the prevalence of depression among adolescents is rising annually ^[2, 3]. Depression can lead to severe consequences and high mortality, and it

has become the second leading cause of death in this age group. Social alienation is recognized as one of the major risk factors contributing to suicidal behavior ^[4]. Social alienation refers to the difficulty of patients to interact well with the outside world in social interactions due to various reasons, which in turn triggers emotions such as loneliness and helplessness, and behaviors such as social avoidance and refusal of contact ^[5, 6]. Interpersonal Interaction Theory (IIT), proposed by Herman, is a theory that considers that people are interacting with each other and interacting in social interactions, and involves people's attitudes, beliefs, values, and their relationships with others ^[7]. He categorized interpersonal interactions into three levels: inner dialogue, inner-outer dialogue, and outer dialogue. This theory explains that the formation and development of social alienation may be influenced by a combination of personal experience and social environment. There are fewer qualitative studies on social alienation in children with adolescent depression, mostly focusing on quantitative studies in adult patients ^[8–11]. Therefore, the present study conducted in-depth interviews with depressed adolescents to explore their experience of social alienation and to encourage them to participate actively in social activities and gradually return to society.

2. Data and methods

2.1. Design

Every day language is used to describe the experience of social alienation in adolescents with depression, with the aim of providing a foundation for improving their interpersonal relationships and supporting social reintegration. Rather than exploring the underlying nature of the experience or developing a theoretical framework, a descriptive qualitative research design is therefore adopted ^[12, 13].

2.2. Sample

Between June and August 2024, a purposive sampling method is employed to recruit depressed adolescents from The Affiliated Hospital of Hangzhou Normal University. The inclusion criteria are: (1) Meet the International Classification of Diseases (ICD) 10th edition diagnostic criteria for depression; (2) Meet the World Health Organization's age definition of adolescents (10–19 years old); (3) The children had normal comprehension and were able to fully express their feelings; (4) Informed consent and voluntary participation in the study. Patients with serious mental diseases are excluded.

The sample size was not predetermined. Instead, researchers continuously evaluated interview transcripts to determine when data saturation occurred, identified by the repetition of information and the absence of new themes.

2.3. Data collection

By reviewing the literature, a preliminary interview outline is developed in conjunction with the purpose of this study, which was then modified by the discussion and expert consultation of the group (including two psychiatry deputy chief physicians, one psychiatric chief nurse, and one counselor), and two depressed adolescents were selected for pre-interviews, and the outline was further improved and adjusted according to the interview results ^[6, 14]. The finalized interview outline is:

- (1) How were your interpersonal relationships before the illness?
- (2) What do you think about the attitudes of people around you (family, school, society) towards you after the illness?

- (3) How do you feel about these changes? Do you feel helpless or alone? Did you feel accepted? (family, school, society)
- (4) What kind of behavior would you take?
- (5) What kind of help would you like to see from those around you?

The interviews took place in a quiet setting within the Affiliated Hospital of Hangzhou Normal University, utilizing Chinese for communication. To ensure readiness, the student extensively studied qualitative research literature. The advisor, with over three decades of experience in adolescent depression treatment and qualitative research training, has authored multiple peer-reviewed qualitative studies.

Prior to initiating the interviews, participants provided written informed consent. Throughout the sessions, the researchers fostered open communication by employing various interviewing strategies, including probing questions, reflective feedback, and requests for clarification, to enhance the depth and accuracy of the collected data. Each interview, lasting approximately 30 to 45 minutes, is audio-recorded with the participant's permission, facilitating comprehensive data capture and minimizing researcher bias.

2.4. Data analysis

The audio recordings were transcribed into textual data within 24h after the interviews, which are reviewed and analyzed. Categorical coding is carried out with the help of Nvivo 15.0 software, and the data are analyzed with the Colaizzi 7-step analysis method^[15]. The specific steps are as follows:

- (1) The researcher repeatedly read the collected data and fully familiarized with all the contents provided by the respondents.
- (2) Analyzed the data word by word, identified and extracted significant statements related to the research questions.
- (3) Coded the recurring ideas, avoiding the integration of the researcher's own theories and experiences, and realized the "suspension"^[16].
- (4) Summarize the coded ideas, find common concepts, and initially form themes; still need to achieve "suspension".
- (5) Provide detailed descriptions of each of the themes generated in step 4, and extract the original statements from the interviewees.
- (6) repeated comparisons to distill common ideas; construct a concise and meaningful theme.
- (7) Return the collated information to the respondents for confirmation, asking if it reflects their true experience to ensure the accuracy of the results.

In case of deviation, the researcher is supposed to start from the beginning and re-analyze. During the analysis process, the researcher reinforced quality control by keeping a reflective diary. The two researchers convened meetings involving all team members to discuss and critically examine the coding content until consensus is achieved.

2.5. Rigor

The overall quality and credibility of the research is enhanced by adhering to the guidelines of Lincoln *et al.* (1985)^[17]. Regarding credibility, trusting relationships are established with all 20 participants by encouraging them to freely express their viewpoints. Audio recordings and memos are used to verify the data. When

participants' expressions are unclear, researchers proactively initiate inquiries to clarify ambiguous sections, ensuring accuracy. Furthermore, the researchers possessed extensive clinical experience in adolescent psychiatric disorders, which enriched the study's perspective. For transferability, a clear description of the study design, participant selection, data collection, and analysis processes is provided, enabling other researchers to use these methods. For dependability, uncertainties in the audio recordings are addressed by making phone calls to confirm specific details, and the organized text are sent to caregivers for secondary confirmation. Additionally, a rigorous peer-review process provided a solid guarantee for the study's reliability. Team members engaged in in-depth discussions to resolve disputes that arose during the research methodology and data analysis. Data analysis are conducted independently and frequently communicated with their mentor, ensuring the completeness and accuracy of the research findings from multiple perspectives. Finally, self-reflection is maintained throughout the research process and reached consensus on controversial issues through group meetings, effectively reducing bias in the research process.

2.6. Ethical considerations

This study is approved by the Ethics Committee of the Affiliated Hospital of Hangzhou Normal University (20190096). Before the interviews, participants received details about study's objectives and procedures. Interviews ceased instantly if participants felt distress, and psychological support was offered.

3. Results

A total of 20 depressed adolescents were finally interviewed, and the interviewers were replaced by codes A1–A20, and their general information is detailed in **Table 1**.

Table 1. General information of depressed adolescents ($n=20$)

Serial number	Patient information for adolescents with depression					
	Distinguishing between the sexes	Age (years)	Educational attainment	Current state	Duration of depression(months)	Number of hospitalizations
A1	women	10	primary school	be in school	23	1
A2	women	10	primary school	be in school	3	0
A3	male	11	primary school	be in school	12	2
A4	women	11	primary school	be in school	6	0
A5	women	12	primary school	be in school	12	1
A6	male	13	primary school	be in school	24	3
A7	male	13	primary school	suspend schooling	4	0
A8	women	14	junior high school	be in school	36	2
A9	women	15	junior high school	be in school	12	0
A10	male	15	junior high school	be in school	12	1
A11	women	15	junior high school	suspend schooling	36	1
A12	male	16	junior high school	be in school	6	0

Table 1 (Continued)

Serial number	Patient information for adolescents with depression					
	Distinguishing between the sexes	Age (years)	Educational attainment	Current state	Duration of depression(months)	Number of hospitalizations
A13	women	16	junior high school	suspend schooling	45	2
A14	women	16	junior high school	be in school	22	1
A15	male	17	junior high school	be in school	6	0
A16	male	17	senior school	suspend schooling	14	0
A17	women	17	senior school	be in school	6	0
A18	women	18	senior school	be in school	3	0
A19	male	18	senior school	be in school	24	1
A20	women	19	senior school	be in school	3	1

In this study, three main themes and eight sub-themes were identified. Detailed descriptions of these themes are provided below, along with selected quotes from the interviews to illustrate and support each theme. As the participants' quotes were translated from Mandarin to English, the language used may be more sophisticated than that typically used by caregivers.

3.1. Individual level

3.1.1. Feelings of helplessness and powerlessness

Many adolescents reported that when they were depressed, those around them could not provide timely relief and help, and developed the habit of digesting their emotions on their own, as well as being unwilling to confide in the outside world, and gradually losing trust in the outside world.

- (1) "I can't find anyone to talk to, and no one is willing to help me." (A2)
- (2) "I feel that no matter how hard I try, it's useless, I can't change many things." (A5)
- (3) "I've even called the psychiatric hotline, but it's always on a busy line and then I get anxious and can't sleep all night." (A17)
- (4) "I would lose control of my emotions during the night every time, but when I went to my friends they were all asleep and I didn't dare to go to my mom or dad, so I just had to put up with it on my own." (A20)

3.1.2. Cognitive bias

At the adolescent stage, their bodily functions are not yet fully developed, resulting in a lack of sensitivity in judging things: they are prone to make irrational judgments in social situations, so that they interpret the behavior of those around them in a negative way. Most adolescents feel isolated or even perceive rejection. As the cognitive bias worsens, adolescents actively reduce their interaction with others and fall into a vicious cycle of self-isolation.

- (1) "Every time the chatting stops, I wonder in my mind if I said something wrong that made them not want to talk anymore." (A1)
- (2) "I'm worried that people will think I'm boring, so I don't take the initiative to participate in class activities unless those I have to." (A3)

- (3) “I always feel like people don’t like me, a look or a gesture from them gives me the wrong impression, but I can’t figure out why I think that.” (A6)
- (4) “Sometimes I message my friends on WeChat and they ignore me for a long time, so I start to wonder if they don’t want to talk to me. Slowly, I don’t actively look for them anymore.”(A19)

3.1.3. Avoidance and withdrawal

Many adolescents have negative self-perceptions about themselves, including self-denial, illness stigma, and so on. Not only are they skeptical of themselves, but they also care about the opinions of those around them and fear being treated differently because of their mental illness. There is often a tendency for this group of adolescents to avoid and withdraw from situations that make them uncomfortable.

- (1) “I get nervous when I interact with other people, I’m afraid that they’ll laugh at me behind my back if I say something.” (A4)
- (2) “I just want to be left alone, but sometimes I wish I had someone who would be firm with me and would accept me for what I am.” (A9)
- (3) “I feel like I can’t do anything and always mess up everything.” (A11)
- (4) “I’m afraid that people will look at me differently if they know I’m depressed and I don’t want to be around people.”(A18)

3.2. Family level

3.2.1. Lack of family awareness

Most of the interviewed adolescents reported that their parents had limited understanding of depression, and often mistook depression for “adolescent rebellion”. At the same time, due to the generation gap between parents and adolescents, parents were unable to accurately understand and give effective emotional support to adolescents, but instead thought that adolescents were “making a big deal out of it” or tried to correct their behavior by blaming them, causing adolescents to reduce their communication with the family and the outside world.

- (1) “When I tell my parents they just think I’m faking it and don’t want to go to school.” (A1)
- (2) “Every time they talk to me they think I’m faking it and don’t want to go to school.” (A6)
- (3) “When my mom and dad ignore me, I think every time that even they don’t care about me, no one who cares about me, I feel like I don’t have anyone to trust anymore.” (A9)
- (4) “They always think I should be able to handle myself.”(A17)

3.2.2. Family conflicts

Certain adolescents develop a sense of internalized avoidance due to family tensions, such as parental separation and prolonged arguments. These experiences make them skeptical about the stability of interpersonal relationships, thus reducing positive interactions with others. Also, frequent parent-child conflicts can make adolescents resistant to socialization. So family conflict not only affects their social behavior, but also shakes their trust in interpersonal relationships and aggravates the sense of social alienation.

- (1) “They often fight and break things in front of me, so I’m afraid to interact with people outside, I’m afraid of getting into a conflict, and then that person reprimanding me loudly or hitting me.” (A3)
- (2) “My mom and I often get into fights, he doesn’t understand me, and I’m so tired that I don’t want to talk, so I just avoid it.”(A5)

- (3) “My mom and dad fight a lot, sometimes I think they’ll get divorced at any moment and I’m afraid that I’ll be abandoned, so I’m afraid that the people I think are my best friends will leave me behind someday as well, and I don’t dare to imagine a scene like that.” (A8)
- (4) “I always feel like dating my friends will suddenly one day be just as bad as my mom and dad’s and won’t believe in a long-lasting relationship at all.”(A16)

3.3. Social dimension

3.3.1. Academic pressure and limitations of social circles

Heavy academic pressure leaves adolescents with insufficient energy to engage in social activities, resulting in a lack of diverse social experiences. This limited social environment restricts the development of adolescents’ social skills. With increased academic pressure, they choose to avoid socializing and focus on their studies.

- (1) “My daily route is home and school, and I don’t have much time to meet new people.” (A6)
- (2) “They would enroll me in a whole bunch of interest classes, and after the classes were over I just wanted to be left alone.”(A8)
- (3) “It’s hard to have time off, I just want to relax and don’t have the energy to socialize anymore.” (A12)
- (4) “With weekly exams at school, I feel like I don’t have time to do anything else, and I rarely go out with friends now.”(A18)

3.3.2. Lack and degradation of skills

In the current parenting philosophy, many parents pay too much attention to their children’s academic performance at the neglect of their children’s social skills development and lack of diverse social experiences. This limited social environment restricts the development of adolescents’ social skills, resulting in adolescents lacking the ability to cope with social interaction, and thus showing a state of inability to cope in social situations. In addition, some adolescents reported the gradual emergence of social barriers after a prolonged lack of socialization, and resistance and discomfort with social activities.

- (1) “I used to have friends, but now I feel like I don’t know how to make friends.” (A1)
- (2) “I don’t know how to get along with others.” (A4)
- (3) “Socializing is burdensome for me, I try not to interact with others and it makes me feel tired.” (A14)
- (4) “When I come across class reunions, my first thought is that I don’t want to participate because I don’t have close friends in the class and I don’t know who to talk to, and then I don’t want to talk to them.” (A15)
- (5) “Sometimes I don’t know what’s better to say when I talk to my classmates.”(A20)

3.3.3. Generalization of virtual reality

This study found that depressed adolescents indulge more in the internet due to avoidance and withdrawal from reality. Social media has become their main communication platform, which not only provides a convenient way of communication but also offers a new way to establish peer connections. However, due to the immaturity of some teenagers and their weak self-control ability, they are immersed in the Internet and gradually build their own spiritual world in the virtual world, shaping their “ideal selves”. This leads to a high level of anxiety about their own image and interpersonal relationships. When they tried to return to real life, this anxiety was estimated to lead to limited social functioning and further deepened their social withdrawal and alienation.

- (1) “When I play games, I feel very confident and they are all happy to play with me. But interacting with

- others at school makes me feel very unconfident and like I'm not good enough." (A5)
- (2) "I'm very popular online and it's nothing like I am in real life." (A8)
- (3) "I would post interesting photos on social media so people would come to me to comment and chat, but my life was boring." (A14)
- (4) "I can present myself as a college student they won't come and question me." (A19)

3.3.4. Social "stigmatization"

Despite the increasing social attention to mental health issues, psychological problems such as depression among adolescents still face stigmatization, especially in schools and public places. When adolescents talk openly about psychological distress, they encounter cold stares, misunderstanding, and even discrimination from others; they develop a sense of shame and choose to stay away from crowds, reduce interpersonal interactions, and ultimately develop a tendency to social isolation.

- (1) "I don't want to be labeled as 'having a problem,' and as long as I stay away from other people. they won't know I have a mental problem." (A7)
- (2) "When I tell my teachers that I have depressive tendencies, the first thing they think of is to keep me out of school, I feel like I'm being 'isolated' by them." (A9)
- (3) "Once I expressed that I was depressed on the internet, they said they didn't want to play with me." (A10)
- (4) "As soon as I came out of psych, people looked at me differently." (A20)

4. Discussion

4.1. Enhancement of self-knowledge and social adaptation of depressed adolescents

The study found that depressed adolescents exhibited cognitive impairments related to self-perception and social interactions, including negative self-evaluations and a heightened sense of shame. These difficulties may stem from frequent social encounters, limited understanding of their condition, and a tendency to misinterpret others' behaviors. As a result, they often responded with avoidance or rejection in social situations—an outcome consistent with the findings reported in Liu's study^[18]. This phenomenon is consistent with the results of Liu's study. To address these phenomena, healthcare professionals can implement cognitive-behavioral interventions and group self-affirmation training for adolescents to help patients rebuild their thinking styles, correct cognitive misconceptions, improve negative evaluations of the self, and reduce the sense of shame^[19-21]. At the same time, it is necessary to strengthen the disease propaganda of depressive adolescents and improve their knowledge of mental illness, and promote their correct view of mental health problems: correctly view mental health problems^[9]. For the phenomenon of lack and degradation of adolescents' social skills, group training, patient communication, peer support groups and other means can be used to allow adolescents to interact and share their social experiences with each other, helping them to improve and exercise their communication skills, learn social skills, and gradually build up their self-confidence, which will in turn alleviate their sense of social detachment^[22].

4.2. Improving the family atmosphere and upgrading family support systems

It has been found through research that family climate and level of support have a significant effect on social detachment in depressed adolescents. Families with high resilience level and high caring level favor adolescents to be more socially active, cope with stress more effectively, and reduce patients' social alienation^[9, 23-25]. However,

patients who are chronically homebound can exacerbate social alienation ^[26]. Community healthcare workers play a key role between families, hospitals, and schools and are able to integrate resources from all parties ^[27]. Therefore, healthcare and community personnel should strengthen the follow-up mechanism, regularly assess the resilience level of families of depressed adolescents and the level of family cognition, and formulate personalized family intervention programs. Online multi-family intervention groups can also be carried out to allow multiple groups of families to learn from each other, reflect on their own family situation, and create a good family atmosphere ^[28]. As parents, it is important to conduct family education counseling and communication skills training to improve the quality of interaction in order to better understand the needs of adolescents. At the same time, more outdoor socialization with adolescents is needed, which not only promotes parent-child communication and allows parents to understand adolescents' thoughts but also allows adolescents to feel cared for and supported, thus enhancing trust and dependence.

4.3. Multi-party collaboration to improve the social network and psychological service system and create a favorable social atmosphere

The theory of compensatory internet use states that individuals tend to alleviate their emotions in negative environments through virtual online activities, and tend to choose social media that satisfy their needs in order to compensate for social deficits in reality ^[29]. The results of this study show that adolescents use social media to improve their real-life dilemmas, but Internet addiction weakens their social adaptability and functioning, which is consistent with the findings of Sun *et al.* ^[30]. Healthcare professionals can combine Life Skills Training (LST) and Emotional Skills Training (EST) to help adolescents reduce their dependence on social media ^[31]. However, given the uneven quality of information available online and adolescents' limited ability to critically evaluate it, parents should play a leading role by modeling responsible social media use and guiding their children toward healthy online habits. Schools should establish comprehensive internet education programs to enhance students' digital literacy, while the government must strengthen online regulation and work to integrate and optimize internet resources to create a safer and more informative digital environment ^[32, 33]. To foster a positive and healthy media environment for young students, it is essential to uphold and promote mainstream values, ensuring they remain influential and relevant in shaping adolescents' perspectives and behaviors.

In addition, primary and secondary school students face high academic pressure. Schools should implement the "Double Reduction" policy in depth, organize mental health activities regularly, and conduct psychological assessments for students ^[34]. Meanwhile, homeschool cooperation should be promoted to provide students with academic and emotional counseling ^[35]. Schools should actively organize social practice activities to enrich students' extracurricular life and encourage them to participate actively. This study also shows that the public's negative perception of people with mental illnesses makes depressed adolescents feel helpless, so that they are unwilling to seek help, leading to self-isolation and emotional internalization, but the enhancement of the social support system can prevent or reduce the adolescents' sense of social alienation ^[36]. On the one hand, a favorable social atmosphere should be created: educating the public on topics related to depression and guiding the community to view mental illness with an inclusive and open attitude. On the other hand, healthcare professionals should provide professional psychological help, encourage adolescents to face stigmatization positively, and help adolescents to build an effective network of friends and relatives, to enhance psychological adjustment ^[37]. In addition, a few adolescents in the interviews mentioned calling psychological assistance hotlines, but most of the time they could not get through or showed occupied lines. Therefore, the government is called upon to unite

psychological outpatient clinics to carry out relevant hotline services, establish a sound social psychological service system, optimize the allocation of resources, and improve the connection rate.

5. Conclusion

In this study, in-depth interviews revealed that depressed adolescents have complex feelings of social alienation. The results showed that they have complex feelings at the personal, family, and social levels. Therefore, healthcare professionals should focus on enhancing the self-awareness and social adaptability of adolescents with depression, while also working to improve the family environment and strengthen family support systems. Additionally, fostering a supportive social atmosphere through improved social networks and a robust psychological service system—achieved through multi-sector collaboration—can help these adolescents engage more actively in social activities, adjust to social life more effectively, and gradually reduce their feelings of social alienation. However, this study was limited to interviewing adolescents in a tertiary hospital in Hangzhou, storing certain limitations. In the future, it will be extended to different schools and districts to more comprehensively assess the experience of social alienation among depressed adolescents.

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Clinical Efficacy of Modified Shenqi Dihuang Decoction in the Treatment of Early Diabetic Nephropathy and Its Impact on Symptom Scores in Traditional Chinese Medicine

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Abstract: *Objective:* To evaluate the efficacy and symptom scores of early diabetic nephropathy (DKD) treated with modified Shenqi Dihuang Decoction. *Methods:* 82 patients with early DKD who visited the hospital from February 2023 to February 2025 were randomly divided into two groups by drawing. Group A received modified Shenqi Dihuang Decoction + SGLT2 inhibitor, while Group B received SGLT2 inhibitor only. The efficacy, symptom scores, blood glucose, and renal function were compared between the two groups. *Results:* The efficacy of Group A was higher than that of Group B in the treatment of early DKD ($P < 0.05$). The DKD symptom scores of Group A were lower than those of Group B ($P < 0.05$). The fasting blood glucose (FBG), 2-hour postprandial blood glucose (PBG), and glycated hemoglobin (HbA1c) of Group A were better than those of Group B ($P < 0.05$). The serum creatinine (SCr), blood urea nitrogen (BUN), and urinary albumin excretion rate (UAER) of Group A were also better than those of Group B. *Conclusion:* The combination of modified Shenqi Dihuang Decoction and SGLT2 inhibitor dapagliflozin has excellent efficacy in the treatment of early DKD, which can improve renal function, reduce DKD symptoms, and stabilize blood glucose levels.

Keywords: Diabetic nephropathy; Shenqi Dihuang Decoction; Symptom scores; Efficacy

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1. Introduction

DKD is a comorbidity of diabetes, characterized by proteinuria. As the disease progresses, the glomerular filtration rate decreases, leading to end-stage renal disease and increased risk of mortality. Western medicine often treats early DKD with the principle of delaying disease progression and stabilizing the condition, such as using metformin to lower blood glucose. However, these treatments have limited effects on improving renal function. SGLT2 inhibitors, a modern novel therapeutic approach, block the reabsorption of glucose in the kidneys and regulate blood glucose by accelerating urine metabolism. This approach improves cardio-renal outcomes through

metabolic and hemodynamic effects, which is beneficial for protecting cardio-renal function. In traditional Chinese medicine, early DKD is categorized as “consumption-thirst,” which is dialectically considered as a syndrome of Qi and Yin deficiency, with a few patients also experiencing blood stasis syndrome ^[1]. Treatment should focus on removing blood stasis, promoting blood circulation, nourishing the kidneys and liver, and nourishing Yin and Qi. Shenqi Dihuang Decoction can nourish the liver and kidneys, nourish Yin and Qi. Based on this, this article explores the efficacy of modified Shenqi Dihuang Decoction combined with the SGLT2 inhibitor dapagliflozin using 82 patients with early DKD who visited the hospital from February 2023 to February 2025 as samples.

2. Materials and methods

2.1. Materials

Eighty two patients with early DKD visited the hospital from February 2023 to February 2025 and are randomly divided into groups by drawing. The baseline data of early DKD in Group A are compared with those in Group B ($P > 0.05$), as shown in **Table 1**.

Table 1. Baseline data of early DKD patients

Group	<i>n</i>	Gender (%)		Age (years)		Disease duration (years)	
		Male	Female	Range	Mean±SD	Range	Mean±SD
Group A	41	20 (48.78)	21 (51.22)	40–68	58.43 ± 2.11	5–11	7.85 ± 1.26
Group B	41	21 (51.22)	20 (48.78)	40–69	58.41 ± 2.13	5–12	7.81 ± 1.28
X^2/t	-	0.0488 (χ^2)		0.0427 (t)		0.1426 (t)	
<i>P</i>	-	0.8252		0.9660		0.8870	

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Meet the criteria for diabetic kidney disease (DKD) as defined in the “Chinese Clinical Guidelines for the Prevention and Treatment of Diabetic Kidney Disease”, with symptoms of stagnation of meridians due to blood stasis and deficiency of Qi and Yin ^[2].
- (2) Signed informed consent
- (3) Normal nutritional status

2.2.2. Exclusion criteria

- (1) Ketoacidosis
- (2) Urinary tract infection
- (3) Congestive heart failure
- (4) Organ lesions or immune system disorders.

2.3. Treatment methods

Group A received a modified version of Shenqi Dihuang Decoction, with the following composition: 20g of *Poria cocos*; 15g each of *Astragalus*, Cinnamon, *Angelica*, Ginseng, Yam, *Rehmannia*, and *Alismatis*; 13g each of *Coptis*

and *Salviae miltiorrhizae*; 12g of *Rehmannia*; 10g each of Dogwood and Cortex Moutan. Based on syndrome differentiation, 15g of stir-fried *Atractylodes macrocephala* is added for fatigue; 20g of *Coicis Semen* for edema; 10g of Ginseng for Qi and blood deficiency. The herbs are decocted in water to obtain 200 ml of juice, which is taken warm, once in the morning and once in the evening. The herbal treatment lasted for 8 weeks, constituting one course of treatment.

Group B is treated with SGLT2 inhibitor Dapagliflozin tablets, with a single dose of 10mg once a day. The dosage is adjusted based on blood glucose re-examination results. Patients are instructed to follow a low-fat and low-salt diet. The treatment lasted for 8 weeks.

2.4. Observation indicators

- (1) Efficacy: A decrease of more than 70% in the syndrome score for early DKD, stable blood glucose, and normal kidney physiology are considered as markedly effective. A decrease of more than 30% in the syndrome score, lower blood glucose, and improved kidney function indicators are considered effective. A decrease of 30% or less in syndrome score, abnormal blood glucose, and severe kidney damage are considered ineffective.
- (2) Symptom score: Based on the assessment of chest tightness, waist pain, numbness of limbs, dry throat and mouth, fatigue, and other symptoms, scores of 0–3 are assigned for none, mild, moderate, and severe symptoms, respectively.
- (3) Blood glucose: FPG, 2hPBG, and HbA1c are detected using an automatic biochemical analyzer after centrifuging the blood samples and taking the supernatant for testing.
- (4) Kidney function: BUN, SCr, and UAER are detected using a biochemical analyzer after centrifuging the blood samples and taking the supernatant for testing.

2.5. Statistical analysis

Data are processed using SPSS 23.0 software. Count data (%) are tested using the chi-square test, and measurement data ($\bar{x} \pm s$) are tested using the t-test. A comparison difference is considered statistically significant if $P < 0.05$.

3. Results

3.1. Efficacy

The efficacy of early DKD patients in Group A was higher than that in Group B, with $P < 0.05$, as shown in **Table 2**.

Table 2. Comparison of efficacy (n,%)

Group	Markedly effective	Effective	Ineffective	Effectiveness rate
Group A (n=41)	30 (73.17%)	10 (24.39%)	1 (2.44%)	40 (97.56%)
Group B (n=41)	22 (53.66%)	12 (29.27%)	7 (17.07%)	34 (82.93%)
χ^2	-	-	-	4.9865
P	-	-	-	0.0255

3.2. Symptom score

After medication, the early DKD symptom score in group A was lower than that in group B, with $P < 0.05$, as shown in **Table 3**.

Table 3. Comparison of symptom scores ($\bar{x} \pm s$)

Group	Chest/Back pain (points)		Limb numbness (points)	
	Before medication	After medication	Before medication	After medication
Group A ($n=41$)	2.39 ± 0.41	0.67 ± 0.22	2.43 ± 0.39	0.69 ± 0.23
Group B ($n=41$)	2.41 ± 0.43	1.42 ± 0.35	2.45 ± 0.37	1.44 ± 0.32
t	0.2155	11.6167	0.2382	12.1862
P	0.8299	0.0000	0.8123	0.0000

Group	Dry throat/ Mouth (points)		Fatigue (points)	
	Before medication	After medication	Before medication	After medication
Group A ($n=41$)	2.45 ± 0.39	0.64 ± 0.24	2.47 ± 0.38	0.61 ± 0.22
Group B ($n=41$)	2.47 ± 0.38	1.36 ± 0.33	2.48 ± 0.37	1.37 ± 0.29
t	0.2352	11.2984	0.1207	13.3690
P	0.8147	0.0000	0.9042	0.0000

3.3. Blood glucose indices

After medication, the FPG, 2hPBG, and HbA1c indices in group A were lower than those in group B, with $P < 0.05$, as shown in **Table 4**.

Table 4. Comparison of blood glucose ($\bar{x} \pm s$)

Group	FPG(mmol/L)		2hPBG(mmol/L)		HbA1c(%)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Group A ($n=41$)	7.46 ± 0.61	6.25 ± 0.26	10.72 ± 1.02	8.41 ± 0.68	8.61 ± 1.12	6.39 ± 0.43
Group B ($n=41$)	7.48 ± 0.63	6.71 ± 0.41	10.74 ± 1.04	9.53 ± 0.82	8.59 ± 1.14	7.62 ± 0.58
t	0.1460	6.0669	0.0879	6.7321	0.0801	10.9082
P	0.8843	0.0000	0.9302	0.0000	0.9363	0.0000

3.4. Renal function indices

After medication, the BUN, SCr, and UAER indices in group A were better than those in group B, with $P < 0.05$, as shown in **Table 5**.

Table 5. Comparison of renal function indices ($\bar{x} \pm s$)

Group	BUN(mmol/L)		SCr(μ mol/L)		UAER(g/24h)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Group A (n=41)	15.18 \pm 1.29	9.71 \pm 1.06	176.25 \pm 6.28	147.44 \pm 3.29	1.99 \pm 0.51	0.72 \pm 0.21
Group B (n=41)	15.19 \pm 1.31	11.26 \pm 1.15	176.31 \pm 6.31	156.36 \pm 4.11	1.98 \pm 0.55	1.31 \pm 0.36
<i>t</i>	0.0348	6.3458	0.0432	10.8490	0.0854	9.0645
<i>P</i>	0.9723	0.0000	0.9657	0.0000	0.9322	0.0000

4. Discussion

Early DKD is a microvascular complication associated with structural changes and impaired renal function due to hyperglycemia. Lipid, blood pressure, and blood glucose levels can all affect the progression of DKD. Most patients with early DKD do not exhibit pathological manifestations such as edema or proteinuria. However, as the disease progresses, it can lead to proteinuria, swelling, anemia, and renal failure. Western medicine often manages early DKD through blood glucose regulation, commonly using metformin. Metformin can enhance the body's sensitivity to insulin, block the output of hepatic glucose, and increase the utilization rate of glucose by peripheral tissues. It can also relieve insulin resistance and protect renal function ^[3]. However, long-term use of metformin carries the risk of lactic acidosis, which may further damage renal function. Therefore, it is crucial to explore effective strategies for managing early DKD. Dapagliflozin, an SGLT2 inhibitor, can regulate blood glucose, protect renal function, and has a good safety profile, making it an effective option for managing early DKD. Combining this with traditional Chinese medicine can achieve a comprehensive treatment effect that addresses both the symptoms and the root cause.

Based on the analysis of DKD symptoms, traditional Chinese medicine scholars categorize early DKD under the scopes of “edema” and “diabetes with wasting and thirsting syndrome”. They believe that the prolonged and unhealed condition of this disease can lead to the depletion of yin fluid, dysfunction of organs, and disturbance of qi and blood circulation. This, in turn, can generate internal dampness-heat and phlegm-stasis, exacerbating the severity of DKD ^[4]. Additionally, Chinese medicine practitioners consider the initial stage of DKD as a syndrome of Qi and Yin deficiency, which can damage Yang and weaken the spleen and kidneys. As the disease progresses to its later stages, it transforms into a syndrome of both Yin and Yang deficiency, leading to kidney failure and internal stagnation of toxic stasis. Therefore, the disease's location is primarily in the kidneys, manifesting as a syndrome of deficiency in origin and excess in superficiality ^[5]. Traditional Chinese medicine scholars advocate dialectical treatment for early DKD, recognizing the dynamic changes in the pathogenesis of such patients. They suggest that Qi and Yin deficiency is the foundation of the disease, while impairment of Yin fluid and poor Qi and blood circulation can obstruct the kidney meridians. To address this, they recommend the use of herbs that promote blood circulation, remove stasis, strengthen the spleen, and nourish Qi. In this context, Shenqi Dihuang Decoction is selected for treatment ^[6].

Based on the data analysis in this paper, the treatment efficacy of patients with early diabetic kidney disease (DKD) in Group A is higher than that of Group B, and their symptom scores are lower than those of Group B, with $P < 0.05$. The reason for this may be the combined use of Shenqi Dihuang Decoction on the basis of SGLT2

inhibitors. The prescription includes various herbs with different functions: Fuling (*Poria cocos*) can eliminate dampness and strengthen the spleen; Huangqi (*Astragalus membranaceus*) can elevate Yang and tonify Qi; Taizishen (*Pseudostellaria heterophylla*) can moisturize the lungs, generate body fluid, strengthen the spleen, and benefit Qi; Shengdihuang (*Rehmannia glutinosa*) can generate body fluid, nourish Yin, cool blood, and clear heat; Shanyao (*Dioscorea oppositifolia*) can astringe essence, consolidate the kidneys, benefit Qi, nourish the stomach, and tonify the spleen; Shanyurou (*Cornus officinalis*) can consolidate and prolapse, nourish the liver, and nourish the kidneys; Mudanpi (*Paeonia suffruticosa*) can eliminate stasis, promote blood circulation, and clear heat; Danshen (*Salvia miltiorrhiza*) combined with Danggui (*Angelica sinensis*) can relieve pain, promote menstruation, eliminate stasis, and promote blood circulation; Zexie (*Alisma orientale*) can promote urination, drain heat, eliminate dampness, and promote diuresis; Huanglian (*Coptis chinensis*) can detoxify and purge fire; Guizhi (*Cinnamomum cassia*) can warm the meridians, promote blood circulation, and induce sweating ^[7]. The combined use of these herbs in Shenqi Dihuang Decoction can correct metabolic disorders and improve renal blood circulation through multiple targets, promoting the regression of DKD ^[8]. Another set of data shows that the FPG, 2hPBG, and HbA1c indicators of Group A are lower than those of Group B, with $P < 0.05$. The reason for this is that FPG and 2hPBG can objectively and dynamically reflect the blood glucose level in the body, while HbA1c can provide feedback on the average blood glucose level over the past 2–3 months. Patients with early DKD may experience blood glucose fluctuations due to abnormal pancreatic beta-cell function, leading to an increase in the above indicators.

In this paper, the combined treatment with Shenqi Dihuang Decoction includes berberine from Huanglian, which can block hepatic gluconeogenesis and accelerate glucose uptake by peripheral tissues; diosgenin and catalpol from Shengdihuang can improve the body's sensitivity to insulin; *Astragalus* polysaccharides from Huangqi can relieve insulin resistance; polysaccharides and mucin from Shanyao can correct glucose metabolism disorders and inhibit glucose absorption by body tissues; Fuling polysaccharides can correct lipid metabolism disorders, inhibit the accumulation of large amounts of fat in patients, and indirectly reduce insulin resistance; alisol from Zexie can inhibit hyperlipidemia and stabilize blood glucose; salvianolic acid and tanshinone from Danshen can block oxidative stress and protect islet cells; paeonol from Mudanpi has anti-inflammatory and antioxidant effects while protecting islet cells; and Taizishen, Shanyu, and Renshen can nourish the spleen, tonify Qi, and nourish the kidneys, optimizing the body's metabolic function and correcting glucose metabolism disorders caused by deficiency of both liver and kidney Yin ^[9]. Additionally, the modified Shenqi Dihuang Decoction can regulate blood glucose and blood lipids through multiple targets, achieving stable hypoglycemic effects and delaying kidney function damage in early DKD.

Finally, another set of data indicates that the BUN, SCr, and UAER indicators of patients with early DKD in Group A are better than those in Group B, with $P < 0.05$. The reason for this is that an increase in BUN and SCr suggests a decrease in glomerular filtration rate, while an increase in UAER indicates impaired kidney function. The combined use of modified Shenqi Dihuang Decoction as an adjuvant treatment for early DKD includes ingredients such as Huanglian, Shanyao, and Huangqi, which can affect lipid metabolism and blood glucose fluctuations, relieving renal metabolic disorders; Mudanpi, Danshen, and Shengdihuang can accelerate the elimination of free radicals in the human body, inhibit oxidative stress reactions, and protect the kidneys; Zexie and Huanglian combined with Fuling can block the release of inflammatory factors in the body, avoiding kidney damage caused by inflammatory factors; Guizhi combined with Danggui can dilute the blood, stimulate vasodilation, restore normal blood perfusion to the kidneys, and further optimize kidney function; and Danshen combined with Shanyu can

inhibit the progression of renal fibrosis, facilitating the regression of early DKD ^[10]. However, patients with early DKD should follow a proper diet during treatment with the modified Shenqi Dihuang Decoction. Adjust daily calorie intake based on activity level and physical condition to avoid obesity and overweight; reasonably control the intake of vitamins, fats, proteins, carbohydrates, and minerals, increasing the intake of grains, fruits, and vegetables while reducing the intake of high-fat and high-sugar foods. Adjust the proportion of carbohydrate intake, increasing the intake of low-sugar foods such as brown rice and oats to avoid rapid blood glucose elevation after eating. Control daily protein intake, choosing high-quality proteins such as milk, eggs, fish, and lean meat. Additionally, patients should be guided to exercise reasonably, regularly review blood lipids, blood glucose, and renal function indicators, and adjust medication regimens based on the improvement of various indicators.

5. Conclusion

In summary, the treatment of early DKD patients with SGLT2 inhibitors combined with modified Shenqi Dihuang Decoction can protect renal function, reduce renal inflammatory damage, lower blood glucose levels, and optimize the management of early DKD, making it worthy of promotion.

Disclosure statement

The author declares no conflict of interest.

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Analysis of the Clinical Effect of Naomaili Granules in the Treatment of Acute Ischemic Stroke

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Abstract: *Objective:* To explore the clinical efficacy and safety of Naomaili granules in the treatment of acute ischemic stroke. *Methods:* Eighty-eight patients were randomly divided into a treatment group and a control group, with 44 patients in each group. The control group received conventional Western medicine treatment, while the treatment group was additionally administered Naomaili granules at 10g per time, 3 times per day, for 20 days. Neurological function (NIHSS), activities of daily living (BI), inflammatory factors (hs-CRP, IL-6) levels, and adverse reactions were observed before and after treatment. *Results:* After 20 days of treatment, the NIHSS score of the treatment group decreased from (9.20 ± 2.10) to (5.12 ± 1.30) , the BI index increased from (52.30 ± 8.50) to (78.60 ± 9.20) , and hs-CRP and IL-6 decreased to (3.12 ± 1.10) mg/L and (18.20 ± 4.20) pg/mL, respectively, all significantly better than the control group ($P < 0.01$). The incidence of adverse reactions in the treatment group was 4.55%, lower than the 15.91% in the control group ($P < 0.05$). *Conclusion:* Naomaili granules can improve neurological function and living ability, reduce inflammatory response, and have good safety in patients with acute ischemic stroke.

Keywords: Naomaili granules; Ischemic stroke; Acute phase; Neurological function; Inflammatory factors; Safety

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1. Introduction

Ischemic stroke is a clinically common disease, and effective treatment during the acute phase is of great significance. Currently, conventional Western medicine treatment, mainly including antiplatelet aggregation, lipid-lowering and plaque stabilization, and symptomatic support, is the basic approach. However, monotherapy still has room for improvement in reducing neurological deficits, inhibiting inflammatory responses, and promoting neurological repair. According to traditional Chinese medicine theory, Qi deficiency and blood stasis are important pathogenesis of acute ischemic stroke. During this stage, implementing Qi-invigorating and blood-activating therapy can achieve satisfactory results. Modern pharmacological studies have shown that Naomaili granules,

derived from Buyang Huanwu Decoction, can exert neuroprotective effects through multiple pathways, such as improving cerebral blood circulation, inhibiting oxidative stress, and regulating immune and inflammatory responses^[1]. The high-concentration active ingredient extraction process of the drug provides an important material basis for the clinical treatment of acute stroke patients. However, large-sample clinical studies on the treatment of acute ischemic stroke with Naomaili granules are still relatively limited, and its specific effects on neurological function, activities of daily living, and inflammatory markers need further validation. Based on this, this article analyzes the clinical effect of Naomaili granules in the treatment of acute ischemic stroke.

2. Materials and methods

2.1. Baseline information

Eighty-eight patients with acute ischemic stroke admitted from January 8, 2023, to January 8, 2024, are selected. All patients met the diagnostic criteria of the “Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018”. The inclusion criteria are onset time ≤ 72 hours, NIHSS score of 5–15, and syndrome differentiation belonging to Qi deficiency and blood stasis type (consistent with the “Guidelines for the Diagnosis and Treatment of Common Diseases in Traditional Chinese Medicine Internal Medicine”). Patients who received thrombolytic or thrombectomy treatment, or had severe liver and kidney dysfunction, are excluded. They are randomly divided into a treatment group and a control group, with 44 patients in each group. The treatment group consisted of 24 males and 20 females, with an average age of (62.50 ± 8.30) years and an average NIHSS score of (9.20 ± 2.10) . The control group consisted of 22 males and 22 females, with an average age of (61.80 ± 7.90) years and an average NIHSS score of (9.50 ± 1.90) . There were no significant differences in baseline data between the two groups ($P > 0.05$), making them comparable.

2.2. Methods

The control group received conventional Western medicine treatment, specifically including oral administration of Aspirin Enteric-coated Tablets (100mg/time, once a day) for antiplatelet aggregation, Atorvastatin Calcium Tablets (20mg/time, once a day) for lipid-lowering and plaque stabilization. At the same time, targeted control measures are provided based on patients' blood pressure and blood glucose levels (target blood pressure $< 140/90$ mmHg, target blood glucose 7.8–10.0mmol/L), along with symptomatic treatments such as nutritional support and maintenance of water and electrolyte balance. The treatment group received Naomaili Granules (produced by Hefei Heyuan Pharmaceutical Co., Ltd., approval number: Guo Yao Zhun Zi Z20200023) in combination with the control group's treatment, with a dosage of 10g/time, three times a day, dissolved in warm water and taken orally. Continuous administration for 20 days constituted one treatment course. Both groups received interventional treatment for 20 days, during which medication compliance and adverse reactions were strictly recorded. A 3-month outpatient follow-up was conducted after the treatment, including neurological function evaluation, laboratory index detection, and clinical event recording.

2.3. Observation indicators

(1) Neurological function evaluation

The National Institutes of Health Stroke Scale (NIHSS) is used to evaluate the degree of neurological impairment before and after 20 days of treatment. The scale includes 11 items such as level of

consciousness, gaze, facial paralysis, and limb movement, with a total score ranging from 0 to 42. A lower score indicates less severe neurological impairment and better recovery.

(2) Daily life ability evaluation

Concurrently, the Barthel Index (BI) is used to evaluate patients' self-care ability in daily life, covering 10 daily activities such as eating, dressing, walking, and toileting. The total score ranges from 0 to 100, with a higher score indicating stronger independent living ability.

(3) Inflammatory factor detection

Before and after 20 days of treatment, 3ml of fasting venous blood is collected to detect serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels using Enzyme-Linked Immunosorbent Assay (ELISA). The instrument used is a fully automated biochemical analyzer (model: Cobas8000), and the kit is purchased from a biotechnology company in Shanghai. Operations are strictly performed according to the instructions.

(4) Safety observation

During the treatment and within 3 months of follow-up, adverse events such as gastrointestinal reactions (e.g., abdominal distension, nausea, vomiting) and allergic reactions are recorded. Additionally, blood routine tests (red blood cell count, platelet count, neutrophil ratio) and liver and kidney function indicators [alanine aminotransferase (ALT), serum creatinine (Scr), blood urea nitrogen (BUN)] are detected before and after 20 days of treatment to observe any abnormal fluctuations or clinically significant abnormalities.

2.4. Statistical analysis

SPSS 26.0 software is used for data analysis. Measurement data are expressed as mean \pm standard deviation ($\bar{x} \pm s$), and comparisons between groups are performed using the t-test. Count data are expressed as rates (%), and the χ^2 test is used for comparison. A P -value < 0.05 is considered statistically significant.

3. Results

3.1. Neurological function evaluation results

The comparison of NIHSS scores between the two groups before and after treatment is shown in **Table 1**. Before treatment, there was no statistically significant difference in NIHSS scores between the two groups ($P > 0.05$). After 20 days of treatment, the NIHSS scores in both groups were significantly lower than before treatment ($P < 0.01$), and the reduction was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$), as shown in **Table 1**.

Table 1. Comparison of NIHSS scores between the two groups before and after treatment ($\bar{x} \pm s$, scores)

Group	<i>n</i>	Before treatment	After treatment	<i>t</i>	<i>P</i>
Treatment group	44	9.20 \pm 2.10	5.12 \pm 1.30	14.231	< 0.001
Control group	44	9.50 \pm 1.90	6.83 \pm 1.50	9.872	< 0.001
<i>t</i>		0.745	5.862		
<i>P</i>		0.458	< 0.001		

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

3.2. Evaluation results of daily living abilities

The comparison of Barthel Index (BI) scores before and after treatment between the two groups is shown in **Table 2**. Before treatment, there was no statistically significant difference in BI scores between the two groups ($P > 0.05$). After 20 days of treatment, the BI scores of both groups were significantly higher than those before treatment ($P < 0.01$), and the increase was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$), as shown in **Table 2**.

Table 2. Comparison of Barthel Index scores before and after treatment between the two groups ($\bar{x} \pm s$, points)

Group	<i>n</i>	Before treatment	After treatment	<i>t</i>	<i>P</i>
Treatment group	44	52.30 ± 8.50	78.60 ± 9.20	16.123	< 0.001
Control group	44	51.50 ± 8.20	65.40 ± 8.70	10.345	< 0.001
<i>t</i>		0.482	6.231		
<i>P</i>		0.631	< 0.001		

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

3.3. Inflammatory factor test results

The comparison of serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels before and after treatment between the two groups is shown in **Table 3**. Before treatment, there was no statistically significant difference in inflammatory factor levels between the two groups ($P > 0.05$). After 20 days of treatment, the levels of hs-CRP and IL-6 in both groups were significantly lower than those before treatment ($P < 0.01$), and the reduction was more significant in the treatment group. There was a statistically significant difference between the groups ($P < 0.01$).

Table 3. Comparison of inflammatory factor levels before and after treatment between the two groups ($\bar{x} \pm s$)

Group	<i>n</i>	Indicator	Before treatment	After treatment	<i>t</i> -value	<i>P</i> -value
Treatment group	44	hs-CRP (mg/L)	6.85 ± 1.60	3.12 ± 1.10	13.245	< 0.001
		IL-6 (pg/mL)	28.50 ± 5.30	18.20 ± 4.20	10.123	< 0.001
Control group	44	hs-CRP (mg/L)	6.72 ± 1.50	5.05 ± 1.40	5.872	< 0.001
		IL-6 (pg/mL)	27.80 ± 5.10	24.30 ± 5.10	3.215	0.002

Note: Compared with the same group before treatment, $P < 0.01$; compared between groups after treatment, $P < 0.01$.

3.4. Complication rate

The occurrence of complications during treatment in the two groups is shown in **Table 4**. The total incidence of complications in the treatment group was 4.55% (2/44), mainly manifesting as mild abdominal distension (1 case) and nausea (1 case), which resolved spontaneously without special treatment. The total incidence of complications in the control group was 15.91% (7/44), including gastrointestinal reactions (abdominal distension in 3 cases, nausea in 2 cases), and thrombocytopenia (2 cases, platelet count $< 100 \times 10^9/L$). There was a statistically significant difference in the total incidence of complications between the two groups ($\chi^2=3.968$, $P=0.046$), and no severe liver or kidney damage or bleeding events occurred in either group.

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

Group	n	Gastrointestinal reactions	Abnormal blood routine	Abnormal liver/Kidney function	Total incidence
Treatment group	44	2 (4.55)	0 (0.00)	0 (0.00)	2 (4.55)
Control group	44	5 (11.36)	2 (4.55)	0 (0.00)	7 (15.91)
χ^2					3.968
P					0.046

Note: Compared with the control group, $P < 0.05$.

4. Discussion

4.1. Multi-dimensional interpretation of the mechanism of Naomaili granules in the intervention of acute ischemic stroke

The ischemic and hypoxic damage to nerve cells caused by the interruption of cerebral blood flow is a critical core of acute ischemic stroke, accompanied by the synergistic deterioration of inflammatory cascade activation and microcirculation dysfunction^[2]. In this study, the significant improvement of neurologic function by Naomaili granules combined with conventional therapy stems from the synergistic effect of multiple components based on Buyang Huanwu Decoction. *Astragalus* promotes the formation of collateral circulation by regulating vascular endothelial growth factor (VEGF). Motherwort alkaloids reduce blood-brain barrier damage by inhibiting neutrophil adhesion molecules. Paeoniflorin reduces levels of proinflammatory factors such as IL-6 and hs-CRP by blocking the NF- κ B signaling pathway. Qian *et al.* confirmed that Naomaili granules can comprehensively improve perfusion in ischemic areas of the brain by regulating hemorheology and coagulation function, which is closely related to the presence of notoginsenoside^[3]. Cao *et al.* demonstrated that the application of Naomaili granules in patients with this disease can increase VEGF levels and decrease endothelin-1 (ET-1) expression, correcting vascular endothelial dysfunction^[5]. This provides mechanistic support for its use as a “heavy agent for emergency” during the acute phase at the vascular protection level. The multi-target intervention characteristics of this traditional Chinese medicine compound on the ischemic cascade reaction were fully verified in the study by Zhang *et al.*^[7]. Their research showed that these drugs have a significant effect on improving neurologic function in patients with large artery atherosclerotic cerebral infarction, representing a precise correspondence between relevant drug components and ischemic lesions.

4.2. Hierarchical association of clinical value between neurologic function restoration and improvement of daily living abilities

In clinical practice, the NIHSS score and Barthel Index are commonly used to evaluate the effectiveness of disease treatment. These scores accurately reflect the neurologic function restoration and reconstruction of patients' living abilities. In this study, the reduction in NIHSS score (4.08 ± 1.20 points) and the increase in BI index (26.30 ± 9.10 points) in the treatment group were significantly better than those in the control group. This result is consistent with the conclusion reported by Qian *et al.* that Naomaili granules can increase the BI index by 23.6%^[3]. From a mechanistic perspective, drugs mediate neural plasticity through dual pathways: total notoginsenosides and *Astragalus saponins* can improve cerebral blood perfusion and increase local oxygen content in the brain. Additionally, paeoniflorin can activate the BDNF-TrkB signaling pathway, promoting presynaptic vesicle release and axonal myelination. Wang *et al.*'s study further confirmed that Naomaili granules can increase serum BDNF

levels by 41.2%^[8]. This factor enhances hippocampal neurogenesis by regulating cAMP response element-binding protein (CREB) phosphorylation. Clinically, this cascade effect of neuroprotection-functional reconstruction has a temporal advantage. Early intervention within 72 hours of onset in the treatment group can shorten the duration of subsequent interventions entering the treatment time window, thereby achieving the goal of continuous treatment.

4.3. The core target effect of inflammation regulation in the treatment of ischemic stroke

After patients experience ischemic brain injury, changes occur in the levels of hs-CRP and IL-6 in the blood. Under the mediation of inflammatory factors, the blood-brain barrier is damaged, leading to severe neuronal apoptosis^[3, 5]. In this study, the treatment group showed a 36.14% and 54.26% reduction in IL-6 and hs-CRP levels, respectively, which was significantly better than the control group's 12.60% and 24.85% reduction. These results are highly consistent with those reported by Qian *et al.*, where IL-6 decreased by 40.3% and hs-CRP decreased by 52.7% after treatment with Naomaili granules. From a mechanistic perspective, paeoniflorin in Naomaili granules can reduce the binding activity of the IL-6 promoter region by 63.2% by inhibiting the nuclear translocation of the NF- κ B p65 subunit. Leonurine, on the other hand, targets the TLR4/MyD88 pathway, reducing TNF- α by 37.8%, thereby inhibiting both innate and adaptive immune pathways. This compensates for the drawbacks of using Western medicine alone. Aspirin only inhibits COX-2-mediated prostaglandin synthesis and does not directly affect the IL-6/JAK-STAT pathway. Studies by Cao *et al.* further confirm that combination therapy with Naomaili granules can reduce soluble intercellular adhesion molecule-1 (sICAM-1) levels by 29.4%, suggesting that it blocks the pathological process through the entire chain of "inflammation trigger-cascade amplification-tissue damage" by inhibiting leukocyte adhesion and vascular endothelial damage^[5]. This integrated Chinese and Western anti-inflammatory strategy not only reduces neuroinflammatory damage during the acute phase (additional reduction of 1.71 points in NIHSS score) but also reduces the degree of vascular wall inflammation and the risk of stroke recurrence within 90 days.

4.4. Safety characteristics and precise application strategies for the clinical application of Naomaili granules

In this group, compared to the control group, the treatment group had a lower incidence of adverse reactions. Only a few patients in the treatment group experienced gastrointestinal adverse reactions, which is consistent with the conclusion reported by Qian *et al.*, that the adverse reaction rate of Naomaili granules is lower than that of the argatroban treatment group^[3]. This safety characteristic is derived from three levels of protection: Firstly, the modern extraction process of membrane separation combined with macroporous resin adsorption effectively controls the active ingredients such as paeoniflorin ($\geq 18.0\text{mg/g}$) and astragaloside IV ($\geq 0.30\text{mg/g}$), achieving effective dose control while keeping impurity content below 0.5%^[4]. Secondly, the combination of Astragalus and Glycyrrhiza in the prescription can buffer the stimulation of bitter and cold medicines on the gastrointestinal tract. Acute toxicity experiments have verified that its median lethal dose (LD50) is greater than 20g/kg, demonstrating high biosafety^[6]. Thirdly, the drug does not affect platelet aggregation function. In this study, 2 cases of thrombocytopenia (4.55%) occurred in the control group, while no similar events occurred in the treatment group, which is consistent with the conclusion reported by He that combined thrombolytic therapy does not increase the risk of bleeding. In clinical application, the principle of syndrome differentiation and treatment should be followed. The improvement rate of TCM syndrome scores in patients with Qi deficiency and blood stasis syndrome is 31.7% higher than that in the non-syndrome differentiation medication group. Patients need to take the medication 30

minutes after eating to reduce gastrointestinal adverse reactions. Doctors should monitor biochemical indicators for patients with combined hepatorenal insufficiency to improve patient safety during medication.

5. Conclusion

Naomaili granules demonstrate significant therapeutic potential in the management of acute ischemic stroke (AIS). Clinical evidence indicates that this treatment not only improves neurological function and daily living ability but also reduces inflammatory responses, contributing to better patient outcomes. Furthermore, Naomaili granules exhibit a favorable safety profile, supporting their clinical applicability. These findings suggest that Naomaili granules could serve as a promising adjunct therapy for AIS, warranting further large-scale studies to validate long-term efficacy and mechanisms.

Disclosure statement

The authors declare no conflict of interest.

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Research on Clinical Nursing Key Points and Complications Prevention Strategies after Coronary Heart Disease Stent Implantation

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Abstract: With the development of the social economy and the continuous improvement of people's living standards, the number of coronary heart disease patients is on the rise, even affecting some younger groups. When a patient's coronary artery stenosis endangers their life, doctors usually recommend coronary artery stent surgery to effectively improve myocardial ischemia and prevent sudden death. After a successful operation, it is necessary to clarify the key points of clinical nursing and prevent complications. Starting from the situation after coronary heart disease stent implantation, this article analyzes the key points of clinical nursing and proposes specific strategies for preventing complications, aiming to improve the surgical effect and provide a reference for complication prevention activities.

Keywords: Coronary heart disease stent; Post-operative clinical nursing; Complication prevention

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1. Introduction

Coronary heart disease is a common cardiovascular disease in clinical practice. To relieve patients' pain, hospitals recommend stent surgery for some patients as an effective treatment. According to specific clinical data, restenosis is a common problem after coronary heart disease stent implantation, with a relatively high incidence rate, and it may even cause acute in-stent thrombosis. To effectively solve these problems, hospitals need to grasp the clinical nursing requirements after surgery, attach importance to the construction of a scientific nursing system, effectively reduce the risk of complications, protect patients' lives and health, and improve their quality of life.

2. Analysis of key points of clinical nursing after coronary heart disease stent implantation

2.1. Pay attention to post-operative wound care

After coronary heart disease stent implantation, patients will have small puncture points on their bodies, including the wrists and the root of the thighs. Although these wounds are small, the nursing process cannot be taken lightly.

Medical staff need to regularly check the patients' wounds. After the operation, regularly check whether there is bleeding at the puncture site and whether the surrounding tissues are swollen ^[1]. If the patient has swelling and obvious pain, it may be a sign of bleeding or hematoma, and the doctor should be called immediately. At the same time, for the post-operative wounds of patients, attention should be paid to keeping the wounds dry. Before the wounds heal, keep the puncture site dry and avoid contact with water. In particular, the puncture wound on the femoral artery needs to be carefully cared for and maintained for 24–48 hours. In addition, medical staff need to remind the accompanying family members to pay attention to the patient's wound, avoid compression and pulling, do not place heavy objects on the puncture site, and avoid excessive stretching and bending ^[2]. These actions are likely to affect wound healing and may cause pain and bleeding.

2.2. Pay attention to post-operative risk factors

Coronary heart disease is usually caused by the stenosis or blockage of the heart blood vessels, resulting in an insufficient blood supply to the heart muscle. The risk factors involved include hypertension, hyperlipidemia, etc. ^[3]. The presence of these primary diseases can put great pressure on the blood vessels, thus increasing the risk of cardiovascular diseases. After a coronary heart disease stent implantation, hospitals need to develop a good medication plan according to the patient's condition, so that patients can take medications correctly and control their primary diseases. For example, long-term use of anticoagulant drugs can help patients prevent thrombosis ^[4]. Under the guidance of medical staff, patients can avoid reducing or stopping medications without permission, which is helpful for the stability of their condition.

2.3. Maintain a good lifestyle

Medical staff can provide suggestions for patients' post-operative lives, which mainly include the following two aspects: First, pay attention to dietary adjustment. To help post-operative patients recover their wounds, light and easily digestible foods such as rice soup and noodles can be chosen, and spicy and irritating foods should be avoided. ^[5]. At the same time, patients can also eat an appropriate amount of high-protein foods such as beef and eggs to help their bodies recover quickly. The accompanying staff should provide patients with low-salt and low-fat foods and avoid high-fat foods. From the patient's own perspective, they need to temporarily quit smoking and drinking, maintain a good life routine, and avoid staying up late. In addition, patients need to manage their emotions well and maintain a healthy and positive attitude. They should view the stent surgery correctly, understand the precautions for post-operative recovery, strengthen communication with relatives and friends, and engage in appropriate entertainment to maintain a good attitude, which can effectively speed up the recovery process ^[6]. Many patients are prone to anxiety after stent surgery, overly worried about whether there are problems with the stent, which can even affect their normal lives. In this regard, medical staff need to comfort patients, help them understand the principle of the stent, and realize that occasional chest discomfort is a normal phenomenon.

2.4. Conduct regular outpatient reexaminations

For patients' reexaminations, medical staff mainly check their blood pressure, blood lipid, blood sugar, etc., and conduct analysis based on the data. Patients can set a fixed time for reexamination, such as a three-month cycle. If patients experience symptoms such as chest tightness and headache within one month after the operation, they need to seek medical attention promptly ^[7]. Six months after the operation, if they experience chest pain and chest tightness, they also need to be vigilant and understand the possibility of restenosis.

2.5. Give full play to the advantages of the CCU ward and cooperate to carry out in-hospital cardiac rehabilitation

In clinical nursing after coronary heart disease stent implantation, it is of great significance for in-hospital cardiac rehabilitation specialist nurses to cooperate with the rehabilitation department to carry out cardiac rehabilitation work in the early stage. With professional rehabilitation knowledge and skills, specialist nurses communicate closely with the doctors in the department and develop personalized rehabilitation activities according to the individual differences of patients. In the CCU ward, medical staff not only need to pay close attention to the physical recovery of high-risk patients after stent implantation but also need to deeply understand their psychological conditions, conduct psychological counseling promptly, and help patients build confidence to overcome the disease. At the same time, strengthen health education for patients and their families to make them fully understand the value of cardiac rehabilitation. Through early collaborative rehabilitation, formulating personalized rehabilitation plans, and providing comprehensive care for patients' physical and mental health, the rehabilitation effect of high-risk patients after stent implantation can be significantly improved, the incidence of complications can be effectively reduced, and the subsequent quality of life of patients can be effectively guaranteed.

2.6. Organize post-operative exercise activities

Post-operative exercise activities are also an indispensable part of the nursing after coronary heart disease stent implantation. According to the specific conditions of patients, the rehabilitation team will develop suitable exercise plans, such as increasing the walking distance and performing aerobic exercises. These activities can not only promote the blood circulation of patients but also enhance myocardial function and improve the quality of life. At the same time, medical staff can explain in detail the precautions for post-operative exercise activities to patients and their families to ensure that patients can exercise effectively under safe conditions.

3. Complications after coronary heart disease stent implantation and prevention strategies

3.1. In-stent thrombosis

In-stent thrombosis refers to the formation of a thrombus at the stent implantation site due to the influence of the patient's comprehensive quality after stent surgery. The thrombus can cause coronary artery occlusion and a series of clinical manifestations, such as sudden death and unstable angina pectoris. According to the actual situation of patients, in-stent thrombosis can be divided into different types. Taking the formation time as a reference, it includes acute, late, and very-late thrombosis. The main causes of in-stent thrombosis include the following: First, the influence of factors brought by stent implantation. Poor stent apposition is a common factor that can easily cause in-stent thrombosis^[8]. Second, patients stopping the use of anticoagulant drugs too early can easily cause late-stage stent thrombosis. Patient-related factors include many aspects, such as comorbid diabetes, malignant tumors, and comorbid cardiac insufficiency.

In addition, for the complications after coronary heart disease stent implantation, in the face of in-stent thrombosis, corresponding measures can be taken for good prevention and treatment. Hospitals can adjust clinical techniques. According to the patient's situation, select an appropriate-length stent to meet the requirements of coronary heart disease stent surgery, avoid problems such as insufficient stent coverage and poor apposition, and preferably use IVUS or OCT as a guide to effectively place the stent^[9]. At the same time, the hospital catheterization laboratory can perform coronary angiography to identify the early appearance of in-stent

thrombosis. If the cause is considered to be insufficient apposition between the stent and the blood vessel wall, a high-pressure balloon shorter than the stent length can be used to perform PTCA. If the cause of early in-stent thrombosis is determined by angiography, such as intimal tears at the proximal or distal end of the stent, the stent can be reimplanted. Hospitals should attach importance to the implementation of dual-antiplatelet therapy after PCI. According to the patient's situation, check for contraindications and set a fixed time for patients to regularly take aspirin and clopidogrel and adhere to taking them, which can effectively reduce the formation of in-stent thrombosis and help patients with subsequent rehabilitation.

3.2. No-reflow phenomenon or slow flow

After coronary heart disease stent surgery, patients may experience various types of complications, such as the no-reflow phenomenon and slow flow. Specifically, during PCI, the stenosis of the epicardial coronary artery is relieved, and obvious dissection, thrombosis, and other problems are excluded, but the patient shows a significant reduction or loss of coronary blood flow, presenting a problem of no perfusion in the myocardial tissue^[10]. Based on the specific complications, the pathogenesis is judged. The reasons for patients to develop no-reflow and slow flow are as follows: microcirculation embolism, vasospasm, and contraction induced by coronary intervention operations, and individual susceptibility.

In addition, for the prevention and treatment of no-reflow and slow-flow symptoms, the following prevention and treatment methods can be adopted by hospitals: First, carry out drug treatment. Provide patients with medical advice on drug use, including vasodilators, platelet glycoprotein GPIIb/IIIa receptor antagonists, etc. Second, attach importance to the implementation of non-drug treatment. Carry out device-based treatment activities for patients. Based on the recommendations for coronary intervention treatment, clearly identify high-risk acute myocardial infarction patients (AMI) and understand the presence of thrombus-laden lesions. Manual or mechanical thrombus aspiration can be used to carry out good treatment activities^[11]. Through the recommended application of the above methods, it can help patients remove the thrombus in the blood vessels and provide patients with good medical services.

Perform intra-aortic balloon counterpulsation. In the face of patients with acute myocardial infarction, medical staff can promptly use the intra-aortic balloon counterpulsation technique to effectively reduce the area of the infarcted area, so that the patient's coronary artery has a higher blood perfusion volume. By using scientific and reasonable treatment methods, it is helpful to optimize the value of the myocardial microcirculation, reduce the probability of the no-reflow phenomenon, and promote the reduction of the no-reflow myocardial area, which is helpful for the post-operative rehabilitation of patients.

Adjust the diagnosis and treatment process for coronary heart disease patients. To effectively deal with acute coronary syndrome patients (ACS) and improve the treatment effect, hospitals need to pay attention to adjusting the treatment methods for patients^[12]. Specifically, it includes the patient's first-contact medical treatment process, focusing on shortening the time, such as the time from chest pain onset to blood vessel opening. By reducing the ischemic time, the no-reflow phenomenon in patients can be reduced, and timely and effective treatment activities can be carried out.

3.3. Coronary artery dissection

There are many common types of complications after coronary heart disease stent implantation, such as coronary artery dissection. During the PCI process, significant arterial intimal injury can easily cause coronary intimal tear, accompanied by the formation of local thrombus. According to the specific clinical manifestations, this symptom is highly similar to acute coronary syndrome, specifically presenting as angina pectoris, myocardial infarction, etc. It

is difficult for hospitals to effectively distinguish based on symptoms, and mainly rely on coronary angiography. If a patient has a severe coronary artery dissection, it can easily cause large-area ischemia and myocardial infarction, especially in patients with comorbid hypertension.

Analyzing the causes of coronary artery dissection, the specific factors include the following:

3.3.1. Device-related factors

- (1) Guide catheter factors: large-diameter catheter lumen, use of special-type guide catheters, etc.^[13]
- (2) Balloon factors: high-pressure expansion of calcified lesions with ordinary balloons, balloon rupture.
- (3) Guide wire factors: calcified and tortuous lesions of the guide wire can easily cause intimal injury of the blood vessels
- (4) Contrast agent factors: injection of contrast agent can aggravate the dissection^[14].

3.3.2. Operation-related factors

Medical staff's improper selection and operation of devices such as guide catheters and guide wires can easily cause vascular dissection. In addition, the treatment of coronary artery dissection includes specific methods such as medical conservative treatment, coronary stent implantation, and coronary artery bypass grafting. After drug treatment for coronary artery dissection, it usually can heal on its own, but there are still some patients with long-term dissection^[15]. Coronary stent implantation is an important and preferred treatment method for coronary artery dissection. Through coronary angioplasty, the stent covers the dissection to effectively prevent the dissection from expanding and stabilize the vascular lumen. For patients with left main coronary artery dissection and complex lesions, especially those with shock and unsuccessful interventional treatment, emergency coronary artery bypass grafting can be immediately used for treatment.

4. Conclusion

In conclusion, clinical nursing and complication prevention for patients after coronary heart disease stent implantation are of great value. To grasp the nursing key points, it is necessary to carry out meticulous nursing activities for the patients' post-operative wounds, pay attention to various risk factors, and require patients to participate in regular outpatient reexaminations to help patients with subsequent rehabilitation. Specifically, in the process of complication prevention, for coronary heart disease stent surgeries carried out by hospitals, it is necessary to clarify the types of complications, such as in-stent thrombosis and coronary artery dissection, and propose corresponding prevention strategies to effectively reduce the incidence of complications and improve the quality of life of patients.

Disclosure statement

The author declares no conflict of interest.

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Multimodal MRI Enhancement Combined with Diffusion-Weighted Imaging for the Differential Diagnosis of Non-Lactating Mastitis and Breast Cancer

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Abstract: *Objective:* To explore the value of multimodal MRI enhancement scanning and diffusion-weighted imaging in differentiating non-puerperal mastitis (NPM) and breast cancer. *Methods:* From September 2022 to September 2024, 56 patients with breast diseases were selected as samples and grouped according to disease type. Twenty-eight patients with breast cancer were included in Group A, and 28 patients with NPM were included in Group B. All patients underwent multimodal MRI enhancement scanning and diffusion-weighted imaging. The MRI results, time-signal intensity curves, ADC values, lesion intensity, and imaging signs were compared between the two groups. *Results:* There were no significant differences in enhancement characteristics, lymph node enlargement, and margins between Group A and Group B ($P > 0.05$). The proportion of outflow curves in Group A was higher than that in Group B ($P < 0.05$). The ADC value in Group A was lower than that in Group B, and the lesion intensity was higher than that in Group B ($P < 0.05$). There were significant differences in imaging signs, such as abscess or sinus, ascending time-signal curve, and mammary duct dilation between Group A and Group B ($P < 0.05$). *Conclusion:* Multimodal MRI enhancement scanning and diffusion-weighted imaging techniques can be used to diagnose breast diseases. Comprehensive analysis of time-signal intensity curves, lesion intensity, imaging signs, and ADC values can differentiate between NPM and breast cancer.

Keywords: Breast cancer; NPM; MRI; Enhanced imaging; Diffusion-weighted imaging

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1. Introduction

NPM includes various pathological types such as submammary abscess and granulomatous mastitis. Initially, there are no specific inflammatory symptoms, and it is often detected during health screenings. As NPM progresses, patients may develop nodules, lumps, fever, and other symptoms. Some patients experience acute onset, manifesting as breast redness, swelling, pain, and even fistulas^[1]. Currently, the specific pathogenesis of NPM is not yet clear and may be related to duct obstruction, immune system disorders, infections, etc. Breast

cancer progresses rapidly, manifesting as breast lumps, areolar skin itching, nipple discharge, etc. If not treated early, cancer cells can metastasize through the lymphatic and blood systems, potentially threatening life ^[2]. Clinically, surgical biopsy is often used to differentiate between NPM and breast cancer, but biopsy is an invasive procedure and cannot be promoted as a primary screening technique. With the maturity of imaging technology, MRI is gradually being used in the screening of breast diseases, offering advantages of multi-functional and multi-sequence imaging, guiding physicians in the differential diagnosis of breast diseases ^[3]. Based on this, this article explores the diagnostic value of multimodal MRI enhancement scanning and diffusion-weighted imaging using a sample of 56 patients with breast diseases who visited the hospital from September 2022 to September 2024.

2. Materials and methods

2.1. Materials

A sample of 56 patients with breast diseases who visited between September 2022 and September 2024 is selected and grouped according to disease type. Group A consisted of patients aged 32–55 years, with a mean age of (43.19 ± 1.28) years. Among them, 16 cases had left-sided and 12 cases had right-sided breast diseases. Group B consisted of patients aged 33–55 years, with a mean age of (43.21 ± 1.33) years. In this group, 15 cases are left-sided and 13 cases are right-sided. The baseline data of breast diseases in Group A are compared with those in Group B, with $P > 0.05$.

2.2. Inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) First occurrence of unilateral breast lesion
- (2) Pathology suggesting NPM or breast cancer
- (3) Signed informed consent

2.2.2. Exclusion criteria

- (1) Accompanied by other malignancies
- (2) History of breast surgery
- (3) Lactational mastitis

2.3. Methods

MRI examination is performed using a Siemens AVanto 1.5T MRI scanner. Patients are instructed to lie in the prone position correctly, and MRI scanning is initiated according to the principle of head-first, maintaining the natural suspension of both breasts in the coil. Patients are guided to place their arms on both sides of the body, and scanning is performed from the axillary region until images of the lower edge of both breasts are obtained. Breast three-plane localization is performed to acquire T1WI, T2WI, and enhanced scanning images. After completing the pre-enhancement scanning operation, gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA) contrast agent is prepared and injected into the elbow vein, with a dose controlled at 0.2ml/Kg and a flow rate of 3ml/s.

2.4. Observation indicators

Scanning results; recording enhancement features, lymph node enlargement, edges, and other indicators; time-intensity curve, recording outflow, plateau, and ascending curve types; recording ADC values and lesion intensity during MRI scanning; and documenting the detection of imaging signs.

2.5. Statistical analysis

Data are processed using SPSS 23.0 software. Chi-square test is used to analyze categorical data (% recorded), and the t-test is used for continuous data (mean \pm standard deviation recorded). Statistical differences are considered significant at $P < 0.05$.

3. Results

3.1. Scanning results

There was no difference in the proportion of enhancement features, lymph node enlargement, and edges between Group A and Group B ($P > 0.05$), as shown in **Table 1**.

Table 1. Analysis of scanning results (n,%)

Group	Enhancement pattern		Lymph node enlargement		Margin definition	
	Non-mass-like	Mass-like	Present	Absent	Clear	Indistinct
Group A (n=28)	20 (71.43%)	8 (28.57%)	19 (67.86%)	9 (32.14%)	5 (17.86%)	23 (82.14%)
Group B (n=28)	23 (82.14%)	5 (17.86%)	22 (78.57%)	6 (21.43%)	6 (21.43%)	22 (78.57%)
χ^2	0.9016		0.8195		0.1131	
P	0.3424		0.3653		0.7366	

3.2. Time-signal intensity curve

The proportion of outflow-type curves in Group A was higher than that in Group B ($P < 0.05$), as shown in **Table 2**.

Table 2. Analysis of time-signal intensity curves (n,%)

Group	Washout pattern	Plateau pattern	Persistent pattern
Group A (n=28)	12 (42.86%)	14 (50.00%)	2 (7.14%)
Group B (n=28)	4 (14.29%)	12 (42.86%)	12 (42.86%)
χ^2	4.9778	0.1915	8.8889
P	0.0257	0.6617	0.0029

3.3. ADC values and lesion intensity

The ADC value in Group A was lower than that in Group B, and the lesion intensity was higher than that in Group B ($P < 0.05$), as shown in **Table 3**.

Table 3. Analysis of ADC values and lesion intensity (n,%)

Group	ADC value ($\times 10^{-3}$ mm ² /s)	Lesion intensity
Group A (n=28)	1.05 \pm 0.21	433 \pm 32
Group B (n=28)	1.38 \pm 0.36	425 \pm 43
t	4.1898	0.7898
P	< 0.0001*	0.4331

3.4. Imaging signs

There were significant differences in imaging signs such as abscess or sinus, ascending time-signal curve, and mammary duct ectasia between Group A and Group B ($P < 0.05$), as shown in **Table 4**.

Table 4. Analysis of imaging signs (n,%)

Factor		Group A (n=28)	Group B (n=28)	χ^2	P
Abscess/Sinus tract	Yes	2(7.14)	22(78.57)	20.7407	0.0000
	No	26(92.86)	6(21.43)		
Boundary	Clear	5(17.86)	4(14.29)	0.1383	0.7100
	Blurry	23(82.1)	24(85.71)		
Vascular tortuosity and thickening at the center of the lesion	Yes	13(46.43)	14(50.00)	0.0461	0.8300
	No	15(53.57)	14(50.00)		
Swollen lymph nodes	Yes	19(67.86)	20(71.43)	0.0319	0.8582
	No	9(32.14)	8(28.57)		
Ascending time signal curve	Yes	4(14.29)	24(85.71)	17.7778	0.0000
	No	24(85.71)	4(14.29)		
Mammary duct dilation	Yes	3(10.71)	23(82.14)	19.1453	0.0000
	No	25(89.29)	5(17.86)		
Morphology	Regular	4(14.29)	2(7.14)	0.4978	0.4805
	Irregular	24(85.71)	26(92.86)		

4. Discussion

NPM belongs to the category of chronic inflammatory lesions of the breast, with pathological features including hyperplasia, deterioration, and exudation of breast tissue on the affected side. It exhibits non-caseating necrosis and non-bacterial infectious lesions, and the inflammatory lesions have blurred boundaries with adjacent glands. Breast cancer, on the other hand, is a malignant tumor-like lesion. During its growth, cancer foci stimulate the body to produce large amounts of proteolytic enzymes, which can damage healthy glandular structures. The edges of the lesions appear spiculated or crab-like, and lymph node metastasis occurs as the disease progresses^[4]. The treatment options for NPM and breast cancer are different, and clinical diagnosis often relies on pathological examination to analyze the nature of breast diseases. However, this is an invasive procedure that some patients with breast diseases cannot tolerate^[5]. With the development of imaging technology, MRI technology has gradually matured, allowing for the analysis of breast disease properties from multiple aspects such as hemodynamics, morphology, and differences in water molecule diffusion during scanning. This approach has a high accuracy rate in differential diagnosis^[6]. However, relying solely on multimodal MRI-enhanced scanning to observe blood flow changes can lead to misdiagnosis if NPM and breast cancer patients exhibit overlapping hemodynamic features. Similarly, focusing only on diffusion-weighted imaging to observe water molecule diffusion in patients with breast diseases can also result in misdiagnosis if NPM and breast cancer patients have similar ADC values. Therefore, to improve diagnostic efficacy, this article adopts a combined diagnostic method of multimodal MRI enhancement and diffusion-weighted imaging to distinguish between NPM and breast cancer.

Based on the data analysis in this article, there is no difference in the proportion of enhancement features, lymphadenopathy, and margins between Group A and Group B ($P > 0.05$). The reason for this is that although multimodal MRI enhanced scanning can obtain hemodynamic information, the differences in scan results between NPM and breast cancer patients are not significant due to variations in fat content, glandular density, and tissue structure among patients with breast lesions ^[7]. Another set of data indicates that the proportion of outflow curves is higher in Group A than in Group B ($P < 0.05$). The reason for this is that during diffusion-weighted imaging, the focus is on observing microscopic changes in water molecule movement in breast tissue. There is a high sensitivity to observe favorable water molecule flow and diffusion, which can objectively reflect histological changes and cancer lesion typing characteristics. Therefore, scanned data can serve as a basis for physicians to qualitatively analyze breast diseases. Enhanced scanning provides dynamic feedback on patients' blood flow characteristics, allowing for the identification of lesion properties by observing changes in the time-signal intensity curve. For example, an outflow curve often suggests malignant breast lesions, while a plateau curve suggests benign breast lesions. However, to ensure the accuracy of MRI scan results, patients should remove metal objects from their bodies before scanning, as they can alter the uniformity of the magnetic field and affect the examination results. Patients should also inform the physician of any allergies to contrast agents or medications and should schedule appointments 7–14 days after menstruation ^[8].

Another set of data indicates that Group A has a lower ADC value and higher lesion intensity than Group B, with $P < 0.05$. This suggests that doctors can assist in differentiating between NPM and breast cancer by analyzing changes in ADC values and lesion intensities in patients with breast diseases. In this paper, multi-modal MRI enhanced scanning technology is selected for differential diagnosis of diseases, and hemodynamic fluctuation data of the affected breast is obtained. The immediate time-signal intensity curve can objectively feedback the internal proliferation process of breast lesions. Combined with diffusion-weighted imaging scanning, the analysis of water molecule diffusion movement, and quantitative analysis of tissue lesions with ADC values can guide clinical diagnosis in multiple aspects. Furthermore, the combined scanning of multi-modal MRI enhanced scanning and diffusion-weighted imaging technology can avoid image artifacts and deformations, and has high image spatial resolution and signal-to-noise ratio, which is beneficial for improving imaging clarity ^[9]. The final set of data shows significant differences in imaging signs such as abscess or sinus formation, ascending time-signal curves, and breast duct dilation between Group A and Group B, with $P < 0.05$.

The analysis of the reasons reveals that patients with NPM have severe inflammatory reactions in their bodies, which can easily generate inflammatory granulation tissue, abscesses, and even sinuses to facilitate the discharge of inflammatory secretions. However, breast cancer lesions are invasive, and during disease progression, breast tissue undergoes necrotic and liquefied changes without the formation of abscesses or sinuses. NPM lesions progress in a localized manner, resulting in relatively clear lesion boundaries, while breast cancer proliferates rapidly and infiltrates adjacent tissues, leading to relatively blurred boundaries. However, the boundary characteristics of the two diseases are not significant in the early stages of the disease. Long-term inflammatory stimulation in NPM patients can cause vasodilation and thickening, while the growth of breast cancer lesions increases the demand for blood, leading to an increase in the number of local new blood vessels with tortuous and thickened features to support lesion growth. Therefore, there is no difference in the signs of vascular tortuosity and thickening between the two groups of patients. NPM patients experience inflammatory factor-induced continuous stimulation of lymph nodes, leading to symptoms of enlarged lymph nodes with soft texture, strong activity, and pain. Breast cancer patients may also experience enlarged lymph nodes due to cancer metastasis, but the masses

are hard, immobile, and painless.

NPM is a benign breast lesion, so during MRI scanning, the signal gradually increases after the contrast agent enters the body, and the time-signal curve can be maintained for a long time. However, in breast cancer patients, changes in vascular permeability and rapid increases in the number of blood vessels cause the signal to gradually decrease after the contrast agent enters the body. Under inflammatory stimulation, NPM patients experience breast hyperplasia and edema on the affected side, leading to increased duct pressure and prone to duct obstruction and stenosis, manifesting as duct dilation. Furthermore, continuous secretion of inflammatory factors in the body can further increase duct pressure and exacerbate duct dilation symptoms, while duct dilation is not obvious in breast cancer patients. Under the influence of increased inflammatory factor secretion, NPM patients may experience changes in tumor morphology. However, there are differences in the range and direction of inflammatory factor diffusion among different patients, which can stimulate breast tissue swelling and cause irregular breast morphology. Breast cancer patients may also experience changes in breast morphology due to the infiltrative growth of tumor lesions, so there is no difference in breast morphology changes between the two groups^[10].

5. Conclusion

In summary, multi-modal MRI enhanced scanning and diffusion-weighted imaging technology can assist doctors in the differential diagnosis of NPM and breast cancer. Observing changes in imaging signs, ADC values, lesion intensity, and time-signal intensity curves provides high accuracy and has promotional value.

Disclosure statement

The author declares no conflict of interest.

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Clinical Efficacy and Safety Evaluation of Continuous Blood Purification in the Management of Critically Ill Sepsis Patients in the Intensive Care Unit

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Abstract: *Objective:* To observe and explore the effectiveness and safety of continuous blood purification intervention in the clinical treatment of patients with severe sepsis in the Intensive Care Unit (ICU). *Methods:* Medical records were collected from March 2024 to March 2025, including a total of 54 patients with severe sepsis in the ICU. The patients were divided into two groups using a random number table method: the conventional group (27 patients receiving conventional treatment) and the observation group (27 patients receiving continuous blood purification in addition to conventional treatment). C-reactive protein, arterial lactate, mean arterial pressure, respiration, and heart rate were measured. The Sequential Organ Failure Assessment (SOFA) score was compared, and adverse reactions were observed. *Results:* The observation group had lower levels of C-reactive protein, arterial lactate, respiration, heart rate, and total SOFA score compared to the conventional group, while the mean arterial pressure was higher ($P < 0.05$). The incidence of adverse reactions during treatment was lower in the observation group than in the conventional group ($P < 0.05$). *Conclusion:* The use of continuous blood purification in the clinical treatment of patients with severe sepsis in the ICU is effective. It can alleviate the disease, improve vital signs, reduce inflammatory damage, and reduce adverse reactions.

Keywords: Sepsis; Blood purification; Adverse reactions

Online publication: July 7, 2025

1. Introduction

Sepsis occurs due to trauma or infection, causing toxic metabolites and pathogenic bacteria to breach the body's defense mechanisms and spread throughout the body via the bloodstream^[1]. This triggers the immune system, leading to a systemic inflammatory response that can affect critical organs such as the abdominal cavity, lungs, kidneys, and urinary system, potentially resulting in death due to multiple organ failure^[2]. Continuous blood purification technology can improve the prognosis by removing toxic metabolites and inflammatory mediators,

assisting the body in enhancing the stability of its internal environment ^[3,4]. This study included 54 patients with severe sepsis in the ICU and specifically aimed to evaluate the treatment with continuous blood purification for reference.

2. Materials and methods

2.1. General information

Medical records are collected from March 2024 to March 2025, including 54 patients with severe sepsis in the ICU. The patients are randomly divided into two groups: the conventional group (27 patients) and the observation group (27 patients). Inclusion criteria are: meeting the diagnostic criteria for severe sepsis, staying in the ICU for ≥ 24 hours, no blood system diseases, and normal coagulation and immune function. Exclusion criteria included blood transfusion or anticoagulation therapy in the past 6 months, pregnancy, lactation, organ transplantation, heart, liver, or kidney dysfunction, cachexia or malignancy, personality disorders, or mental disability.

2.2. Methods

The conventional group received conventional treatment, including broad-spectrum antimicrobial treatment based on drug sensitivity results, electrolyte balancing, dynamic monitoring of respiratory, blood pressure, pulse oxygen, and heartbeat changes, intravenous infusion of compound sodium acetate Ringer's injection for fluid resuscitation, and nutritional, respiratory, and circulatory support as prescribed.

The observation group received continuous blood purification in addition to conventional treatment. This involved initiating continuous venovenous hemofiltration (CVVH) treatment mode, controlling blood flow rate at 150–200 ml per minute, and adjusting replacement fluid and dialysis fluid rates hourly. The blood filter is replaced every 12 to 24 hours. Both groups are evaluated for efficacy after 72 hours of continuous treatment.

2.3. Observation indicators

- (1) Before and after treatment, blood was drawn from the median cubital vein to prepare serum. The serum C-reactive protein is measured using immunoturbidimetry at a low speed of 3000 rpm per minute, 9cm radius, and for 10 minutes. Simultaneously, arterial blood lactate is detected using a blood gas biochemical analyzer (Guangzhou Wondfo Biotech, Guangdong Medical Device Registration No. 20172220716, Instrument Model BGA-102).
- (2) Heart rate and respiration are monitored using a multi-parameter monitor (Beijing Taeyang Electronics Technology, Beijing Medical Device Registration No. 20192070420, Instrument Model SOLAR6000B). Mean arterial pressure is measured using a hemodynamic analyzer (Jiangxi Yiludeli Medical Technology, Jiangxi Medical Device Registration No. 20192070181, Instrument Model HM92-03A).
- (3) Before and after treatment, the Sequential Organ Failure Assessment (SOFA) score is used for quantitative evaluation. The scoring range is from 0 to 24, and a lower score indicates a less severe condition.
- (4) Adverse reactions are observed during the treatment process.

2.4. Statistical processing

The observation indicators in this study are analyzed using statistical software (SPSS version 22.0). The incidence of adverse reactions, described as $[n(\%)]$, is compared between the two groups using the chi-square test (χ^2) to

determine any differences. The C-reactive protein, arterial lactate, mean arterial pressure, respiration, heart rate, and total SOFA score, described as mean \pm standard deviation ($\bar{x} \pm s$), all met the requirements of the Shapiro-Wilk normal distribution test. The t-test is used to compare these variables between the two groups and assess any differences. The significance level (α) is set at 0.05. When the test result P is less than 0.05, the statistical significance is established.

3. Results

3.1. Comparison of C-reactive protein and arterial lactate between the two groups

There were no significant differences in the levels of C-reactive protein and arterial lactate between the two groups before treatment. However, after treatment, the levels of C-reactive protein and arterial lactate in both groups further decreased, but the observation group showed a more significant decrease compared to the conventional group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of C-reactive protein and arterial lactate between the two groups ($\bar{x} \pm s$)

Group	Number of cases	C-reactive protein (mg/L)		Arterial blood lactate (mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation Group	27	94.88 \pm 8.87	25.63 \pm 5.75*	5.56 \pm 0.60	1.88 \pm 0.22*
Conventional group	27	94.86 \pm 8.75	50.16 \pm 3.23*	5.55 \pm 0.61	2.43 \pm 0.26*
<i>t</i>		0.008	19.326	0.060	8.391
<i>P</i>		0.993	< 0.001	0.952	< 0.001

Note: * denotes $p < 0.05$ compared with pre-treatment

3.2. Comparison of mean arterial pressure, respiration, heart rate, and total SOFA score between the two groups

The mean arterial pressure, respiration, heart rate and total SOFA score of the two groups before treatment did not show any significant difference. The mean arterial pressure of the two groups after treatment further increased, but the observation group increased significantly more than the conventional group. The respiration, heart rate and total SOFA score of the two groups further decreased, but the observation group decreased significantly more than the conventional group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of mean arterial pressure, respiration, heart rate, and total SOFA score between two groups ($\bar{x} \pm s$)

Group	Number of cases	Mean arterial pressure (mmHg)		Respiration (breaths/min)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	27	50.52 \pm 6.77	59.16 \pm 1.98*	26.88 \pm 2.01	16.07 \pm 1.61*
Conventional group	27	50.55 \pm 6.78	54.08 \pm 2.33*	26.82 \pm 2.02	19.95 \pm 1.63*
<i>t</i>		0.016	8.632	0.109	8.799
<i>P</i>		0.987	< 0.001	0.913	< 0.001

Table 2 (Continued)

Group	Number of cases	Heart rate (beats/min)		Total SOFA score (points)	
		Before treatment	After treatment	Before treatment	After treatment
Observation Group	27	128.36 ± 8.89	79.75 ± 3.63*	6.75 ± 1.55	2.02 ± 0.38*
Conventional group	27	128.33 ± 8.87	99.04 ± 3.34*	6.72 ± 1.46	2.88 ± 0.47*
<i>t</i>		0.012	20.319	0.073	7.393
<i>P</i>		0.990	< 0.001	0.942	< 0.001

Note: * indicates $P < 0.05$ compared with pre-treatment

3.3. Comparison of adverse reactions occurring in the two groups

Less adverse reactions occurred in patients in the observation group than in the conventional group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of adverse reactions occurring in the two groups [n (%)]

Group	Number of cases	Dizziness	Yellowing of the skin	Bleeding	Infection	Total occurrence
Observation Group	27	2(7.41%)	0	0	1(3.70%)	3(11.11%)
Conventional group	27	5(18.52%)	1(3.70%)	1(3.70%)	3(11.11%)	10(37.04%)
χ^2						4.964
<i>P</i>						0.026

4. Discussion

Septicaemia has a very high lethality, due to a large number of inflammatory mediators, toxic metabolites in the organism for a long time synergistically or singly, and thus strongly stimulate the abdominal cavity, liver, kidney, lungs, urinary system, etc., so that each organ cannot withstand and out of control, the formation of systemic inflammatory response syndrome, and even cause organ failure ^[5]. Conventional anti-infective treatment, fluid resuscitation, immunomodulation, nutritional support, respiratory and circulatory support, and other therapeutic measures are of limited benefit and time-consuming, and it is difficult to effectively constrain the underlying factors of sepsis, so that the clinical efficacy is not very satisfactory ^[6]. While continuous blood purification has good biocompatibility, the process of removing toxic metabolites and inflammatory mediators is gentle and stable, and it can be continuously purified for 24 hours a day, which is better able to meet the needs of the human physiological state, maintain the stability of the internal environment, and promote the recovery of the prognosis ^[7].

In this randomized controlled study, the observation group showed significantly lower levels of C-reactive protein, arterial blood lactate, respiratory rate, heart rate, and total SOFA score compared to the conventional group, while the mean arterial pressure was significantly higher ($P < 0.05$). To analyze the reasons, the continuous blood purification treatment technology based on the convection principle has significant advantages in the removal of medium and small molecule solutes, which can better help patients to remove toxic products from the body, reduce the content of inflammatory factors in the body, reduce the body's burden, and alleviate hyperthermia. It can also accurately control the fluid balance, correct the electrolytes, improve the internal circulatory environment, and promote the restoration of vital signs ^[8]. Continuous blood purification therapy has

a sustained and stable effect, and can provide continuous support for the patient's condition regression in order to prevent deterioration and aggravation of the condition ^[9].

In this randomized controlled study, the incidence of adverse reactions during treatment in the observation group was only 11.11%, significantly lower than the 37.04% observed in the conventional group ($P < 0.05$). The improved safety of continuous blood purification can be attributed to its isotonic, slow, and uniform removal of toxic substances, which minimizes the negative impact on effective circulating blood volume. This helps patients maintain relatively stable hemodynamics and enhances treatment safety. Moreover, the therapy allows for timely and precise adjustment of treatment parameters based on the patient's condition, reducing the risk of adverse reactions caused by internal environment disturbances. Combined with continuous monitoring by a professional medical team, this approach provides comprehensive safety assurance for patients ^[10].

5. Conclusion

In conclusion, continuous blood purification therapy has idealized clinical effects, can assist ICU patients with severe sepsis to alleviate their condition, stabilize haemodynamics, improve vital signs, reduce inflammatory damage, and reduce adverse reactions, and can be recommended.

Disclosure statement

The author declares no conflict of interest.

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Application of CBL Combined with PBL Teaching Model in Teaching Medical Imaging to Undergraduate Students Majoring in Clinical Medicine

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Abstract: *Objective:* To explore the application effect of Case-based Learning (CBL) combined with Problem-Based Learning (PBL) in the teaching of medical imaging to undergraduate students majoring in clinical medicine. *Methods:* Undergraduates of clinical medicine majoring in the School of Clinical Medicine of Hebei University were selected as the research subjects and divided into the experimental group (CBL combined with PBL teaching mode) and the control group (traditional teaching mode), and the teaching effect was evaluated by the examination results and questionnaires. *Results:* The test scores of the experimental group were significantly better than those of the control group ($P < 0.05$), and the satisfaction of the students in the experimental group reached more than 90%. *Conclusion:* CBL combined with PBL teaching mode can effectively improve the teaching quality of medical imaging in clinical medicine specialty.

Keywords: CBL; PBL; Medical imaging; Clinical medicine; Teaching models

Online publication: July 8, 2025

1. Introduction

Medical imaging is an important pillar of clinical medicine, but the traditional teaching mode exists “heavy theory light practice”, “image analysis ability is insufficient” and other problems, need to further improve the teaching mode, from the actual needs of students, mobilize students’ enthusiasm and cultivate clinical diagnostic thinking, to improve the quality of teaching^[1]. Case-based Learning (CBL) emphasizes clinical context reduction, and Problem-Based Learning (PBL) focuses on independent inquiry, and the combination of the two may make up for the shortcomings of the traditional teaching mode, providing a new hybrid teaching mode reference for the teaching of medical imaging to undergraduate students of clinical medicine^[2,3]. This study aims to investigate the teaching effect of CBL combined with PBL teaching mode applied in medical imaging for undergraduate students of clinical medicine.

2. Subject and methodology of the study

2.1. Subjects of study

Class 4 ($n=80$) of the undergraduate clinical medicine program of Hebei University in the class of 2020 was selected as the experimental group, and class 1 ($n=80$) is selected as the control group. There is no statistically significant difference in the comparison of general information (gender and age) between the two groups of students ($P < 0.05$).

2.2. Teaching methods

The control group adopts the traditional teaching mode, which is mainly the theoretical lecture method. The experimental group used CBL combined with PBL teaching mode, CBL link selected typical clinical cases for analysis and interpretation, PBL link teacher put forward clinical problems, students group discussion, independent review of information, and report the results of the analysis, and finally the teacher summarized the imaging features and differential diagnosis points.

2.3. Evaluation indicators

The quantitative indicator is the final exam grade. Qualitative indicators are questionnaires, including overall satisfaction, improved interest in learning, improved diagnostic imaging skills, improved communication skills, and improved independent learning skills.

2.4. Statistical methods

SPSS 22.0 software is used, and the measurement information is expressed as $\bar{x} \pm s$. The t-test is used for comparison between groups. Differences between the two groups will be considered statistically significant when $P < 0.05$.

3. Results

3.1. Comparison of examination results

In the experimental group, 10.00% of the students' grades were excellent (90–100 points) while there were none in the control group. In the experimental group, 40.00% of the students had good grades (80–89 points), which was significantly higher than the 26.25% in the control group. In addition, there were no students with failing grades in the experimental group compared to 7.50% in the control group (**Table 1**).

Table 1. Comparison of test scores

Distribution of results	Experimental group	Control subjects
Excellent (90–100 points)	8 (10.00%)	0
Good (80–89 points)	32 (40.00%)	21 (26.25%)
Medium (70–79 points)	25 (31.25%)	37 (46.25%)
Pass (60–69 points)	15 (18.75%)	16 (20.00%)
Failing (< 60 points)	0	6 (7.50%)

Further comparing the test scores, the experimental group's test scores averaged 78.98 ± 9.22 compared to 73.90 ± 8.32 in the control group, and the difference between the two groups was statistically significant ($P < 0.05$) (Table 2).

Table 2. Comparison of test scores

Theoretical results	Experimental group ($n=80$)	Control group ($n=80$)	<i>P</i> -value
	78.98 ± 9.22	73.90 ± 8.32	< 0.05

3.2. Results of the questionnaire survey

The overall satisfaction of teaching in the experimental group was 95.00%, and the students thought that the teaching mode of CBL combined with PBL improved learning interest, diagnostic imaging ability, and communication ability, and the students were more willing to actively participate in the study of medical imaging. In the control group, the overall satisfaction of the teaching was 73.75%, and the students thought that the traditional teaching mode could partially improve the diagnostic imaging ability, and was limited in improving the learning interest, communication ability, and independent learning ability.

4. Discussion

Medical imaging involves anatomy, pathology, physiology, and other disciplines. The traditional teaching mode is mainly based on theoretical teaching, teacher-student interaction is insufficient, the teaching effect is poor, it is difficult to stimulate interest in learning, and the feedback from the students is poor^[4, 5]. CBL focuses on the accuracy of case analysis, while PBL evaluates the problem-solving process, which can comprehensively assess knowledge mastery, logical reasoning, and expression ability. Meanwhile group discussion can simulate Multi-Disciplinary Treatment (MDT), integrate knowledge from various disciplines to solve complex problems, promote multi-perspective communication, improve teamwork ability, and strengthen the combination of theory and practice^[6-10].

The CBL and PBL teaching mode adopted in this study, through the combination of real case analysis and clinical problems, students need to comprehensively analyze the imaging manifestations, medical history and laboratory examination, to cultivate and strengthen the integrated thinking of "imaging-clinical", emphasize the practicality and promote the combination of theory and practice, which is conducive to the construction of clinical diagnostic thinking of the students. Comparison results show that the final theoretical scores of students using CBL and PBL teaching mode are significantly higher than those of the control group, and they show higher motivation for learning, and this mode also cultivates students' clinical diagnostic thinking and differential diagnosis ability, which improves the overall quality of teaching. CBL provides a large amount of typical and atypical image data, and students can improve their sensitivity to key signs and enhance their ability of image interpretation through repeated training. PBL teaching method is student-centered and teacher-guided, focusing on cultivating students' innovative thinking ability and independent learning ability. Students' overall satisfaction with CBL combined with PBL medical imaging teaching is high, and the open-ended questions of PBL allow students to consider a variety of possibilities, which can be applied to the differential diagnosis of homozygous and heterozygous images to reduce the risk of clinical misdiagnosis.

To further improve the quality of CBL combined with PBL teaching mode applied to medical imaging, it is

necessary to train teachers to master the dual-mode guidance skills to avoid PBL discussion deviating from the topic or CBL flowing on the surface. It is also necessary to build a high-quality case bank covering common, difficult and misdiagnosed cases, and to design progressive problem chains. There are also some limitations to this study, and the long-term instructional effects need to be further tracked.

5. Conclusion

The teaching mode of CBL combined with PBL has advantages in the teaching of medical imaging for undergraduate students majoring in clinical medicine, realizing the complementary advantages of case anchoring and problem driving, which can help students to improve their diagnostic imaging ability and motivation to learn, and is a suitable and effective teaching mode to help cultivate compound medical talents in line with the needs of modern healthcare, which is worthy of popularizing and applying to the teaching of medical imaging.

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Application and Evaluation of Common Clinical Imaging Techniques in Cancer Diagnosis

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Abstract: With the reform and opening up entering a new era, China's modern civilization and technology are "rolling forward". In the medical field, innovative changes in radiology imaging technology have presented unprecedented value opportunities in tumor diagnosis. Therefore, this article explores the classification of radiological imaging techniques, specifically including X-ray imaging, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and ultrasound imaging. Furthermore, it analyzes the practical application of these key technologies in tumor diagnosis and propose new ideas. In the end, the advantages and characteristics of radiology imaging technology are evaluated, and two limitations are also pointed out, which deserves profound reflection.

Keywords: Radiology; Imaging technology; Tumor diagnosis; Application; Evaluate

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1. Introduction

In the past, tumors posed a serious threat to human life and health, and if left untreated in the early stages, the survival rate was extremely low. But with radiological imaging technology, it can provide certain technical guidance to make judgments on the location, size, shape, and surrounding tissues of tumors, assisting doctors in diagnosis and treatment. Especially in recent years, with the rapid development of technology, radiological imaging technology can provide more and more important information related to diseases, which is of great medical research value. Therefore, a deep understanding of the application characteristics and value of various radiological imaging techniques in tumor diagnosis is of great practical significance for optimizing the tumor diagnosis process and improving diagnostic accuracy.

2. The application direction of radiological imaging technology in tumor diagnosis

2.1. X-ray imaging

X-ray imaging uses X-rays to penetrate the human body, presenting black and white contrast images of different density

tissues on film or detectors. In the diagnosis of bone tumors, X-ray plain films can clearly display the morphological and structural changes of bones, and can detect typical manifestations of bone tumors such as bone destruction, periosteal reactions, and soft tissue masses. This is of great significance for the preliminary diagnosis of common bone tumors such as osteosarcoma and giant cell tumor of bone ^[1]. In terms of lung tumor screening, chest X-ray can detect larger lung space-occupying lesions, which is one of the commonly used methods for preliminary screening of lung cancer. However, X-ray imaging also has significant limitations. Due to its two-dimensional imaging, tissue overlap can affect the observation of lesion details and easily miss small lesions. For nodules with a diameter less than 1cm in some diseases, the detection rate of X-rays is low, which can easily lead to missed diagnosis. Moreover, X-ray imaging has low resolution for soft tissue, making it difficult to distinguish subtle differences between tumors and surrounding soft tissue, and accurately determine the boundaries and extent of tumor infiltration ^[2, 3].

2.2. CT scan

CT imaging uses X-rays to perform cross-sectional scans of the human body. The detector can receive X-ray attenuation signals from different angles and generate cross-sectional images of the human body through computer reconstruction algorithms. In the diagnosis of lung cancer, CT technology can accurately display detailed information such as the size, shape, edge features, and internal density of lung nodules, which plays a crucial role in evaluating the benign and malignant nature of nodules. Specifically, CT manifestations such as lobulation sign, spiculation sign, and vacuolar sign often indicate that the nodule is a malignant tumor ^[4]. Enhanced CT scanning, by injecting contrast agents, can further observe the blood supply of tumors, help identify the nature of tumors, and also detect lymph node metastasis in the hilum and mediastinum, accurately determine tumor staging, and provide key basis for developing treatment plans. CT also has a positive significance in displaying tumors in various organs of the abdomen, with a particularly high detection rate for liver cancer. Plain scan can detect low-density occupying lesions inside the liver, and enhanced CT scan shows significant enhancement of arterial phase tumors, presenting a typical manifestation of “fast in and fast out”.

2.3. MRI

MRI imaging technology, as shown in **Figure 1**, relies on the principle of nuclear magnetic resonance, which applies radio frequency pulses to hydrogen nuclei in a strong magnetic field to excite them and generate resonance signals, thereby achieving imaging.

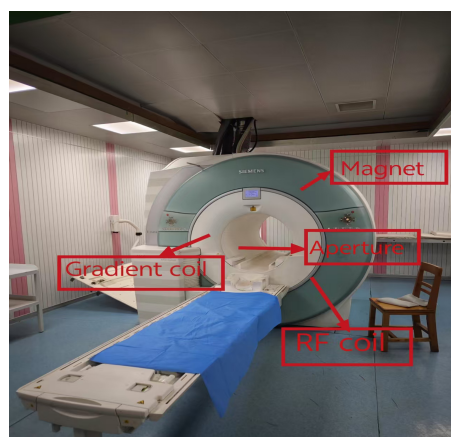


Figure 1. A photo of a certain brand of MRI equipment in clinical practice

Unlike the two aforementioned techniques, MRI has extremely high resolution for soft tissue and also has unique advantages in tumor diagnosis. In the diagnosis of brain tumors, MRI can clearly display the location, size, shape, boundary, and relationship with surrounding brain tissue of tumors, which is of great value for the diagnosis and differential diagnosis of common brain tumors such as gliomas, meningiomas, and pituitary tumors. MRI imaging of different sequences (such as T1WI, T2WI, FLAIR, etc.) can provide rich tissue information and help determine the nature of tumors. MRI also plays a similar role in the diagnosis of breast tumors, pelvic tumors (such as cervical cancer, endometrial cancer), spinal cord tumors, etc., but the examination time is relatively long, the patient's cooperation requirements are high, and the cost is also high, which limits its application in some underdeveloped areas and is also an important aspect of future research and practice ^[5-8].

2.4. PET

PET imaging (as shown in **Figure 2**) belongs to nuclear medicine imaging technology and is generally combined in series with CT in clinical practice as a PET/CT scanner. PET utilizes the high uptake of glucose and other metabolites by tumor cells through injection of radioactive tracers, displaying the metabolic activity of tumor cells and functionally imaging each cell. In terms of early diagnosis of tumors, PET can detect metabolic abnormalities in tumor cells before morphological changes occur, which helps to detect early small tumor lesions. Early cancer cell concentration, on the other hand, has a slightly better therapeutic effect. For MRI and CT that use anatomical imaging principles, cancer is detected relatively late, and the choice of treatment methods for advanced cancer is often limited, and most treatment outcomes are also poor. It is of great significance for the early screening and diagnosis of lung cancer, breast cancer, colorectal cancer, and other common tumors.

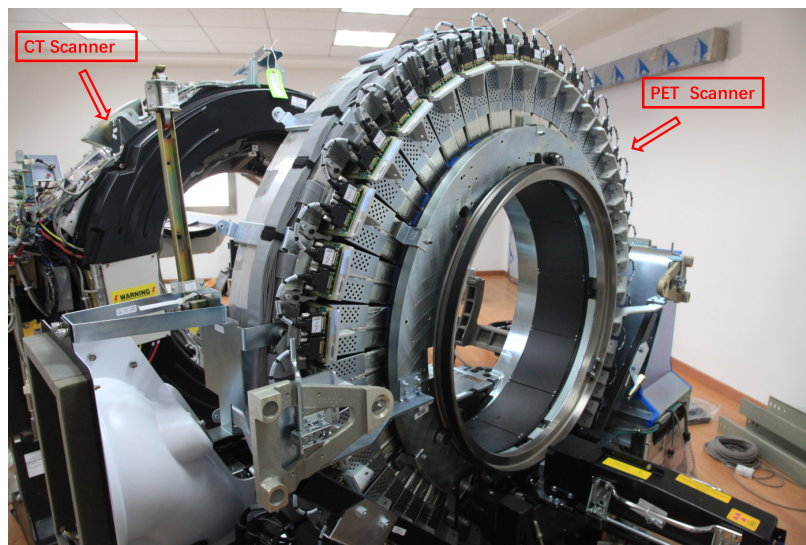


Figure 2. Photo of the internal scanning ring of a certain brand PET/CT in clinical practice

For tumor staging, PET can comprehensively evaluate the distribution of tumors throughout the body, accurately detect distant metastases, avoid errors in tumor staging due to missed metastases, and provide a reliable basis for developing reasonable treatment plans ^[9]. In terms of follow-up treatment evaluation, PET can timely and accurately determine the treatment effect by observing the changes in tumor cell metabolic activity before and after treatment, which helps to adjust the treatment plan. However, PET examination is expensive and radioactive

tracers have a certain level of radioactivity, which poses potential radiation hazards to patients and operators and requires strict protection.

2.5. Ultrasonic imaging

Ultrasonic imaging technology constructs detailed images of internal organs and tissues of the human body by utilizing physical phenomena such as reflection, refraction, and scattering generated when ultrasound propagates through human tissues. For example, in the diagnosis of thyroid tumors, ultrasound examination has become the preferred diagnostic method due to its ability to clearly display key features such as the size, shape, edges, internal echoes, and blood flow status of thyroid nodules. Including but not limited to low echo, unclear boundaries, irregular morphology, aspect ratio greater than 1, microcalcifications, and rich blood flow signals, ultrasound findings often indicate that the nodule is a malignant tumor. However, the accuracy of ultrasound imaging largely depends on the skill level and experience of the operator, and the examination results of different doctors may vary ^[10]. The quality of ultrasound images is easily affected by elements such as gases and bones. For gas-containing organs such as the lungs and gastrointestinal tract, as well as tumors located behind the bones, the display effect of ultrasound examination is often unsatisfactory, and its diagnostic value is relatively limited.

3. Application of radiology imaging technology in cancer treatment

3.1. Image-guided radiotherapy

Image-guided radiotherapy (IGRT) can be regarded as a major breakthrough in modern radiotherapy technology. This technology utilizes advanced imaging equipment to provide real-time or near real-time imaging monitoring of patients before, during, and after radiotherapy. Before radiotherapy, high-precision CT scans are used to obtain detailed three-dimensional anatomical information of the patient's tumor and surrounding tissues. Based on imaging information, doctors can develop personalized radiotherapy plans, accurately planning parameters such as the direction of radiation, dose distribution, and irradiation time, to ensure that the radiation can cover the tumor target area to the maximum extent possible while minimizing exposure to surrounding normal tissues ^[11, 12].

In the subsequent radiotherapy process, this technology can also play a real-time monitoring role. Taking lung cancer radiotherapy as an example, the impact of respiratory movement on the location of lung tumors is extremely significant. At this point, 4D-CT imaging technology synchronously records the patient's respiratory signals during CT scanning, divides the respiratory cycle into multiple phases, and obtains the dynamic motion trajectory of the tumor throughout the entire respiratory cycle, allowing doctors to make real-time adjustments to the entire radiotherapy plan. By using respiratory gating technology, the radiotherapy equipment will only emit radiation when the tumor moves to a predetermined safe position, ensuring that the radiotherapy radiation always accurately hits the tumor and avoiding irradiation deviation caused by tumor position movement. This significantly reduces the incidence of radiation therapy complications and greatly improves the quality of life of patients.

3.2. Interventional radiotherapy

Interventional radiation therapy is an advanced treatment method that uses minimally invasive techniques such as puncture and intubation, guided by imaging equipment, to directly deliver treatment instruments or drugs to the lesion site, achieving targeted treatment. Using transarterial chemoembolization (TACE) and real-time clear guidance from digital subtraction angiography (DSA) equipment, doctors puncture the patient's femoral artery

and gradually insert a thin catheter along the vascular path into the hepatic artery branch that supplies blood to the tumor^[13]. Injecting high concentrations of chemotherapy drugs through a catheter can instantly reach extremely high drug concentrations in the tumor tissue, directly exerting a powerful killing effect on tumor cells. Subsequently, embolic agents are injected to completely block the tumor's blood supply artery, cutting off the tumor's blood supply and causing tumor cells to gradually die due to ischemia and hypoxia. Clinical practice has shown that for patients with advanced liver cancer who cannot be surgically removed, after standardized TACE treatment, the tumor volume of some patients can be significantly reduced, tumor marker levels can be significantly decreased, and survival can be effectively prolonged.

In addition to TACE technology, thermal ablation technology in interventional radiation therapy has also demonstrated significant advantages in early cancer treatment. Taking early small liver cancer as an example, under the precise guidance of ultrasound or CT, doctors will percutaneous puncture the ablation needle into the tumor. Radiofrequency ablation technology utilizes the resistance heat generated by radiofrequency current in tumor tissue to rapidly raise the temperature of the tumor tissue to 60 °C–100 °C, leading to protein denaturation and membrane rupture of tumor cells, ultimately resulting in coagulative necrosis. Compared with traditional surgical resection, the hospitalization time of patients treated with thermal ablation is significantly shortened. Generally, patients can be discharged within 1–2 days after surgery, and the impact on the function of organs such as the liver is relatively small. Patients can recover their normal life and work faster^[14]. For some early cancer patients who cannot tolerate surgical resection due to their advanced age and poor physical condition, this technology also provides them with safer and more effective treatment options.

3.3. Image-guided surgery

The emergence of image-guided surgery has brought unprecedented opportunities for transformation in cancer surgical treatment, making surgical treatment more precise and safe. In traditional cancer surgery, doctors mainly rely on preoperative imaging data and their own clinical experience to determine the location, extent, and relationship with surrounding tissues of the tumor. During the surgical process, due to factors such as changes in patient position, tissue tension, and bleeding, the actual anatomical structure often undergoes certain changes, resulting in deviations between preoperative images and intraoperative conditions, undoubtedly increasing the difficulty and risk of the surgery.

Intraoperative magnetic resonance imaging (iMRI) technology plays a significant role in neurosurgery, especially in brain tumor resection surgery. Due to its unique location, brain tumors are surrounded by complex neural and vascular structures, and even a slight carelessness during surgery can lead to severe neurological dysfunction. IMRI equipment can obtain high-resolution brain images in real-time during surgery, clearly displaying the boundaries, internal structures, and adjacent relationships with surrounding nerves and blood vessels of tumors. For example, when removing gliomas located near functional areas of the brain, with the help of iMRI technology, doctors can observe the real-time removal of the tumor during the surgery. When residual tumor boundaries are found, surgical operations can be adjusted in a timely manner to further remove residual tumor tissue, while avoiding damage to important nerve functional areas around the patient, maximizing the protection of the patient's nerve function, and reducing the incidence of postoperative complications^[15]. Clinical studies have shown that using iMRI-guided brain tumor resection surgery can increase the total tumor resection rate by 15–20%, while reducing the incidence of postoperative neurological dysfunction by 10–15%.

4. Evaluation of the application of radiology imaging technology in tumor diagnosis

4.1. Advantages

X-ray imaging has multiple advantages, such as simple equipment and facilities, fast examination speed, etc., and is very common in current clinical work. CT has high spatial resolution and unique advantages, playing a key role in tumor localization and staging. MRT has high contrast and can clearly distinguish soft tissues, providing diverse information even without the use of ionizing radiation. It also plays an important role in tumor localization, staging, and differential diagnosis, and is one of the important technologies for testing and treatment. PET can reflect the metabolic activity of tissues and is an important technology for tumor detection and diagnosis, but it can also be used for efficacy evaluation. Finally, let's take a look at ultrasound imaging, which has the advantage of no radiation and real-time imaging. It has a positive effect on tumor screening in the thyroid, breast, liver, and other areas, and is worth exploring and practicing in depth.

4.2. Limitations

4.2.1. False positives and false negatives

Some radiology imaging techniques have false-positive and false-negative results. For example, in lung cancer screening, about 20–30% of small lung nodules detected by low-dose spiral CT are false positives, indicating that the nodules are not malignant tumors but require further examination and follow-up to confirm the diagnosis. This may lead to unnecessary anxiety and a waste of medical resources for patients. For some early-stage small tumors or special types of tumors, due to atypical imaging findings, false negative results may occur, leading to a missed diagnosis.

4.2.2. Technical and equipment limitations

The development of imaging technology relies on advanced equipment and professional technical personnel for support. In general, some primary healthcare institutions may lack high-end CT, MRI, and other equipment, or have outdated and outdated equipment, which affects image quality and diagnostic accuracy. Similarly, there may also be a lack of high-level, high-quality, experienced, and professionally qualified physicians, leading to inconsistent diagnostic results that must be improved and transformed.

5. Conclusion

Overall, radiological imaging technology is constantly advancing and developing. It is believed that in today's era of technology and medical industry integration, promoting transformation and upgrading, there will be increasingly better solutions for combating malignant tumors and diagnosis and treatment. Frontline clinical and scientific researchers should also actively explore and practice key technology applications based on actual situations to achieve precise diagnosis and personalized treatment of tumors.

Disclosure statement

The author declares no conflict of interest.

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A Study of Staged Differences in the Needs of Lymphoma Patients throughout the Service under the Care Perspective

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Abstract: Based on the perspective of caring, this study constructs a whole-cycle management programme for lymphoma patients, and systematically explores the pathway of patients' health management from diagnosis to recovery by integrating literature analysis, clinical practice research, and multidisciplinary experts' consensus. Focusing on the differentiated needs of patients, the study proposes a dual-track management framework of 'precise diagnosis and treatment standard' and 'humanistic care practice', and innovatively designs a multidisciplinary collaborative mechanism, an information-based follow-up platform, and a social support network. Through the role of 'care consultant', the programme connects the medical team with the individual needs of patients, strengthens treatment compliance and improves the quality of life, and provides a theoretical basis and practical reference for the optimization of the whole management mode of lymphoma patients.

Keywords: Lymphoma patients; Holistic management; Patient needs

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1. Introduction

Lymphoma is one of the common malignant tumours in China, with the incidence rate increasing year by year and showing a trend of youthfulness. Although advances in diagnostic and treatment technologies have significantly improved the survival rate of patients, the long treatment cycle and complex treatment methods still bring continuous pressure on patients physically and mentally ^[1]. Existing management models focus on the treatment of the disease itself, but it lacks dynamic attention to the needs of patients throughout the entire course of their illness, resulting in some of their needs not being responded to in a timely manner, which affects the overall effectiveness of treatment and quality of life ^[2]. Therefore, this study systematically analyses the differences in the core needs of

lymphoma patients during the diagnosis, treatment, and rehabilitation stages from a caring perspective, to provide theoretical support for the construction of a more humanistic and caring whole-course management model.

2. Theoretical framework and research design

2.1. Theoretical foundation

From the individual-environment interaction perspective, the health ecology model highlights that patients' needs are shaped by both internal factors (physical and psychological) and external factors (family, healthcare system, and policy environment) ^[3]. It offers a dynamic framework to assess how lymphoma patients' needs align with available resources across different disease stages.

Meanwhile, patient empowerment theory emphasizes patients' active role in care through information, skills, and emotional support, enhancing their control, adherence, and quality of life ^[4]. This study applies the theory to explore patient demands for information, psychological care, and social support, supporting a doctor-patient co-managed model of care.

2.2. Research subjects and data sources

This study takes lymphoma patients admitted to a tertiary hospital in Hubei Province as the main research subjects. Inclusion criteria include: (1) Patients with lymphoma diagnosed by pathology; (2) Age 18–70 years old; (3) Conscious and with basic communication ability ^[5]. The exclusion criteria included: (1) Patients with severe organ dysfunction or mental illness; (2) Patients whose survival period was expected to be less than 6 months ^[6]. Finally, a total of 276 valid cases were included, and the patients were predominantly over 45 years of age (67.15%), with the time of diagnosis concentrated within 1 year (78.47%), and non-Hodgkin lymphoma accounted for 66.42% of the cases. Meanwhile, semi-structured interviews were conducted with 24 haematology staff (8 doctors and 16 nurses) with 2–35 years of working experience, covering junior, middle, and senior titles.

A mixed-method study was conducted from Jan 2023 to Feb 2024, using both paper and online questionnaires with a valid return rate of 98.56%. The survey covered patient demographics, perceptions of the management process, and needs assessment. Semi-structured interviews (15–30 minutes each) were conducted with 24 hematology staff (8 doctors [D1–D8], 16 nurses [N1–N16]) with 2–35 years of experience, focusing on practical experiences and suggestions for improving TMS implementation. Interviews were recorded, transcribed, and analyzed using NVivo12. Ethics approval was obtained, and informed consent was signed by all participants. The study included 276 lymphoma patients admitted to a tertiary hospital in Hubei Province. Inclusion criteria: pathologically diagnosed lymphoma, aged 18–70, conscious, and communicative. Exclusion criteria included: severe organ dysfunction, mental illness, or expected survival < 6 months. Most patients were over 45 years old (67.15%), diagnosed within 1 year (78.47%), and had non-Hodgkin's lymphoma (66.42%).

Data were collected from a mixed-method study (Jan 2023–Feb 2024), using paper-based and online questionnaires on patient demographics, management perceptions, and needs, achieving a valid return rate of 98.56%. Semi-structured interviews (15–30 minutes each) explored healthcare professionals' experiences and suggestions for TMS improvement, transcribed and analyzed via NVivo12. The study received ethics committee approval, and all participants provided informed consent to ensure compliance and privacy protection.

2.3. Criteria for the division of phases

2.3.1. Diagnostic period (0–1 month)

The time boundary is taken as the time from the first appearance of symptoms in patients to the pathological confirmation of the diagnosis and the formulation of the preliminary treatment plan ^[7]. This stage covers imaging examination, pathological biopsy, typing diagnosis, and the formulation of treatment plans, and it is the period when the patient's psychological impact is the most significant and the need for information is the most urgent ^[8]. The delineation is based on the clinical diagnosis and treatment pathway; 78.47% of patients are diagnosed within 1 year, and the staging assessment and treatment plan decision-making need to be completed within 1 month after the initial diagnosis.

2.3.2. Treatment period (1–6 months)

The treatment period is centered on receiving standardized chemotherapy, radiotherapy, or targeted therapy, covering 2–8 standard treatment cycles ^[9]. In this stage, patients face multiple challenges such as drug side effects, treatment compliance, and family economic pressure, and need to dynamically monitor physiological indicators and psychological status ^[10]. The division refers to the recommended treatment cycles in CSCO Lymphoma Guidelines 2024, and combines with clinical data showing that 51% of patients need to go through multiple hospitals to confirm the diagnosis, suggesting the importance of treatment consistency.

2.3.3. Rehabilitation phase (more than 6 months)

The starting point is to enter the follow-up monitoring after completing the standardized treatment, focusing on the prevention of recurrence, management of long-term complications, and promotion of social function recovery ^[11]. The quality of patient survival in this stage is closely related to long-term follow-up services, and 22.26% of patients have the need for a rehabilitation period of more than 3 years. The classification is based on the International Consensus on the Management of Survivors of Lymphoma, which emphasizes the need for continued attention to relapse risk and health behavior interventions for 5 years after the end of treatment ^[12].

3. Analysis of differences in demand by stage

3.1. Core demand in diagnostic period

In the diagnostic period, the service demand of lymphoma patients mainly focuses on the outpatient consultation session itself, with a lower reliance on the appointment and waiting process ^[13]. According to the data in **Table 1**, in the outpatient consultation session, 22.63% of the patients considered it very necessary, and 21.53% considered it relatively necessary, indicating that patients generally attach importance to the quality and efficiency of the services in the actual consultation process. For outpatient appointments and pre-admission appointments, although around 22% of patients said they needed it very much, more than 43% of patients chose 'not very much', indicating that the overall demand for appointment-based services was not prominent. Similar trends were observed for arrival and waiting procedures, with only 20.80 per cent of patients indicating 'very much' and 44.89 per cent 'not much'. These data suggest that patients are most concerned with obtaining effective, timely, and clear medical information and professional judgement during the diagnostic phase of the consultation process, rather than the process itself.

Table 1. Outpatient visits and examinations

	Very little	Not much	Fair	More	Very much
Outpatient Appointments	4.01%	43.43%	10.95%	19.34%	22.26%
Outpatient Visits	2.55%	45.99%	7.30%	21.53%	22.63%
Pre-admission Outpatient Appointments	2.92%	44.16%	6.93%	22.99%	22.99%
Arrival at Hospital, etc.	2.19%	44.89%	8.39%	23.72%	20.80%

The interviews further corroborated this focus on need. Healthcare professionals generally agreed that effective communication at the initial diagnosis stage plays a key role in patient understanding and treatment adherence, with D1 noting that ‘it is important to guide the patient himself to have a general understanding of his disease and an expectation of the prognosis’ and D6 emphasizing that “at the beginning of his diagnosis, if we can comprehensively and better inform him about the disease and popularize it with him”. This suggests that what patients urgently need during the diagnostic period is the transparent communication of information about the disease and support at the psychological level to help them build initial awareness and trust in the midst of the unknown and anxiety. In contrast, process services, such as appointment booking and waiting, are of lower priority during the diagnostic period, and more service improvement should be focused on improving the quality of interaction and the ability of scientific communication during face-to-face consultation.

3.2. Core demand in the treatment period

In the treatment period, patients’ demand for various services in the inpatient treatment process shows a high degree of concentration, especially in the key nodes such as admission confirmation and ward entry ^[14]. The data in **Table 2** shows that 26.28% of the patients think that they ‘need it very much’ in the service node of ‘notification and confirmation of hospital admission’, and as high as 26.64% of the patients think that they ‘need it very much’ in the service node of ‘arrival at the inpatient ward’. In the ‘arrival at the inpatient ward’ section, as many as 26.64% of patients chose ‘very necessary’, suggesting that patients are extremely concerned about communication and process confirmation in the early stages of hospitalization. Meanwhile, although 21.90% and 20.80% of the patients in the data considered ‘very necessary’ for the examination procedure and hospital waiting procedure respectively, more than 43% of the patients indicated that these procedures were ‘(not very necessary)’, indicating that the patients’ needs for functional processes are relatively balanced. This shows that patients’ needs for functional processes are relatively balanced, while the real focus is on the quality of service and smoothness of processes actually experienced during hospitalization. In addition, the data on information and communication needs show that about 24.82% of patients very much hope that healthcare professionals can explain treatment plans and side effect management in easy-to-understand language, reflecting the actual needs of patients for professional explanations and timely responses during the treatment period.

The interviews further reflected the important impact of treatment services on patients’ overall adherence to treatment and psychological support. By ‘providing patients with a clear description of the disease and treatment expectations at the initial consultation stage’, healthcare professionals help patients to develop correct perceptions and lay a foundation of trust for the successful implementation of the treatment period. In addition, the interviews also emphasized the care for patients’ financial burden and treatment outcome, indicating that during the treatment period, healthcare professionals not only focused on the quality of treatment, but also on providing personalized financial and psychological support to patients.

In **Table 3**, there is also a relatively high concentration of demand for ‘consistent standards of care’ and ‘continuous nursing guidance’ (26.28% and 24.45% of patients said ‘very much needed’, respectively), indicating that nursing care is not only focused on the quality of treatment, but also on providing personalized financial and psychological support to patients during the treatment period. “This shows that the quality and coordination of care services is an important part of improving patient satisfaction and treatment adherence. By optimizing communication and coordinating treatment and care services at all stages, healthcare professionals seek to build an integrated service system that focuses on medical technology and meets the emotional and economic needs of patients, thus truly reflecting the concept of holistic management from a caring perspective.

Table 2. Hospitalization treatment

	Very little	Not much	Fair	More	Very much
Waiting for inpatient admission	2.92%	43.80%	6.57%	25.91%	20.80%
Inpatient admission notification and confirmation call	2.55%	44.53%	5.47%	21.17%	26.28%
Blood test procedures	2.55%	43.07%	6.93%	25.55%	21.90%
Arriving at hospital and waiting for admission	3.65%	43.07%	6.57%	20.80%	25.91%
Admission to ward	4.01%	44.16%	5.47%	23.72%	22.63%
Arrival at inpatient ward	4.01%	43.07%	6.57%	19.71%	26.64%

Table 3. Treatment and nursing needs

	Very little	Not much	Fair	More	Very much
I expect a consistent standard of care at different stages of treatment	4.01%	38.69%	8.76%	22.26%	26.28%
I need healthcare professionals to provide ongoing nursing guidance during treatment	1.82%	36.86%	12.41%	24.45%	24.45%
I expect healthcare professionals to coordinate services at different stages of treatment	2.55%	35.40%	13.50%	26.28%	22.26%
I need healthcare professionals to provide rehabilitation guidance after treatment	1.82%	37.96%	9.49%	28.83%	21.90%
I expect healthcare professionals to provide advice on pain management	2.55%	35.77%	12.77%	27.01%	21.90%

3.3. Core needs in the rehabilitation phase

In the rehabilitation phase, the service focus of lymphoma patients gradually shifted from inpatient treatment to post-discharge continuity support and inter-agency co-management, showing a shift in the focus of needs ^[15]. The data in **Table 4** shows that in terms of discharge processing, only 28.10% of patients indicated that they needed the service ‘very much’, while as many as 43.07% of patients indicated that they needed it ‘not too much’. Similarly, at the point of ‘leaving the hospital’, 24.10% of patients indicated that they needed the service ‘very much’, while 43.07% of patients indicated that they needed it ‘not too much’. Similarly, 24.45% of patients indicated that they needed the service ‘very much’ at the point of ‘leaving the hospital’, while 44.89% indicated that they needed it ‘not too much’, reflecting the overall low demand of patients for discharge procedures. This phenomenon shows that the majority of patients have a basic understanding of and are able to adapt to the discharge process, but their real concern is the continuous medical support and health management after discharge.

Table 4. Discharge

	Very little	Not much	Fair	More	Very much
Discharge	3.65%	43.07%	6.20%	18.98%	28.10%
Leaving the hospital	2.92%	44.89%	6.57%	21.17%	24.45%

Most patients showed a strong demand for continuity and coordination in medical services (**Table 5**). Specifically, 28.83% indicated they “somewhat needed” and 21.17% “very much needed” continuous care, reflecting concerns about consistency across treatment stages. For coordination between different healthcare institutions, 25.18% expressed a strong need and 23.36% a moderate need, highlighting expectations for smooth inter-agency collaboration. Additionally, 25.91% of patients “very much needed” follow-up plans and guidance, while 27.37% emphasized the importance of timely updates to treatment records, showing that follow-up and information sharing remain key concerns during the rehabilitation phase.

Table 5. Service coordination and continuity requirements

	Not at all needed	Not much needed	Neutral	Somewhat needed	Very much needed
I need medical staff to ensure continuity of care	2.19%	35.40%	12.41%	28.83%	21.17%
I hope medical staff can coordinate services across different institutions	2.55%	36.50%	12.41%	23.36%	25.18%
I need medical staff to provide follow-up plans and guidance	2.19%	36.13%	12.77%	22.99%	25.91%
I hope medical staff can update my treatment records in a timely manner	1.46%	31.02%	16.79%	23.36%	27.37%

Interviews with healthcare professionals similarly highlighted practical dilemmas and professional reflections on services during the rehabilitation period. D4 mentioned that ‘many patients may be lost behind just after the end of treatment’, pointing out the risk of patients being easily disengaged from the management of the healthcare system after discharge. D3, on the other hand, bluntly stated that “follow-up is the most difficult, firstly, there has to be a person and then that person must also have a spirit of sacrifice”, revealing the reality of the challenge of manpower investment in follow-up.

Nonetheless, healthcare professionals demonstrated a positive attitude towards continuous improvement of services during the recovery period, with some departments extending their health management services by setting up public numbers and conducting regular lectures. Especially in terms of updating and sharing treatment information as shown in **Table 6**, 27.37% of the patients said that they ‘very much need’ healthcare professionals to update their treatment records promptly, highlighting the high demand for transparent and continuous information services. Regarding follow-up planning and guidance, 25.91% were ‘very necessary’ and 22.99% were ‘quite necessary’, further confirming that the focus of rehabilitation services has clearly shifted to post-discharge care and extended services for chronic disease management. Therefore, from a caring perspective, the rehabilitation period should not be regarded as the end of medical services, but rather as a service re-linking stage that requires great attention and determines the quality and effectiveness of long-term health management for patients.

Table 6. Service coordination and continuity requirements

	Very little	Not much	Fair	More	Very much
I need healthcare professionals to ensure continuity of treatment services	2.19%	35.40%	12.41%	28.83%	21.17%
I want healthcare professionals to co-ordinate services between different healthcare providers	2.55%	36.50%	12.41%	23.36%	25.18%
I need healthcare professionals to provide follow up plans and guidance	2.19%	36.13%	12.77%	22.99%	25.91%
I want healthcare professionals to keep my treatment records up to date	1.46%	31.02%	16.79%	23.36%	27.37%

4. Management countermeasures under the perspective of care

4.1. Theoretical logic

Guided by the concept of whole-person health (“physical, mental, social, and spiritual”), lymphoma management requires a shift from disease-centered to patient-centered care. Integrating MDT and narrative medicine, the model combines clinical pathways with humanistic care through information sharing, psychological support, and social connection. The caring consultant bridges patients and the medical team, enhancing treatment adherence and quality of life, ultimately promoting a management model that unites medical precision with human warmth.

4.2. Staged intervention strategies:

4.2.1. Diagnostic period: Establishing the mechanism of ‘stepped release of information’

Intervention in the diagnostic period is centered on progressive information transfer, and cognitive guidance and emotional comfort are achieved through the collaboration of doctors and nurses. During the first consultation, the nurse in charge uses layman’s language to explain the characteristics of lymphoma, and combines graphic manuals and three-dimensional animation demonstrations to eliminate the patients’ misunderstanding of “cancer = terminal disease”. The attending physician informs the patients of the classification, treatment plan, and prognosis indexes in a graded manner after the diagnosis is confirmed by pathology, and at the same time, provides a standardized Diagnostic and Treatment Navigator’s Manual to specify the examination process and time nodes. In response to patients’ individual questions, the multidisciplinary team will conduct targeted Q&A within one week after diagnosis, and dynamically adjust communication strategies in combination with the emotional assessment of the counsellor to ensure the simultaneous advancement of information absorption and psychological adaptation.

4.2.2. Treatment period: constructing ‘family-healthcare’ collaborative symptom management

The treatment period focuses on symptom control and treatment adherence, and dynamic management is achieved through the empowerment of family caregivers and remote monitoring technology. The nursing team provides family members with training in symptom recognition, such as early warning signs of fever, and supplies an electronic “Symptom Log” for real-time documentation of chemotherapy-related reactions, including nausea and myelosuppression. Utilizing a mobile medical platform, a 24-hour direct symptom reporting channel is established, enabling patients or caregivers to report abnormal signs through visual descriptions or standardized assessment scales. Specialist nurses respond within two hours with graded interventions: green for consultation and guidance, yellow for outpatient evaluation, and red for emergency intervention. At the same time, a multidisciplinary support

team was formed to discuss complex symptoms (e.g. neurotoxicity, immune-associated pneumonia) weekly by video conference, and personalized nursing video tutorials were simultaneously pushed to the family to form a closed-loop management of “symptom identification - professional intervention - family implementation”, to reduce the risk of unplanned hospital admission.

4.2.3. Rehabilitation: Implementing a ‘community embedded’ social support network

Rehabilitation management focuses on the reconstruction of social functions and long-term health monitoring, and connects medical resources and community services through a hierarchical diagnosis and treatment system. With community health service centers as the hub, a collaborative team of family doctors, specialist nurses and social workers has been set up to establish dynamic health records for patients, and carry out regular home follow-up visits (routine blood tests, assessment of immune function) and home care guidance (PICC maintenance, nutritional programmes). In collaboration with the civil affairs department and by integrating community resources, a “Lymphoma Rehabilitation Station” has been established to offer vocational training and psychological counselling services. Additionally, patients who have been in remission for over five years have been recruited to form a “Peer Support Group,” aimed at easing the anxiety of reintegration into society through shared experiences and mutual support. At the same time, a mobile rehabilitation management module has been developed, integrating data from smart bracelets (such as heart rate and step count) and a review reminder function. The system enables automatic alerts for abnormal indicators and allows one-click activation of a green referral channel to the nearest medical facility. This supports the construction of a three-tier linkage network connecting hospital, community, and family care.

5. Conclusion

Based on the pain points of clinical practice, this study constructed a patient-need-oriented lymphoma management programme, which deeply integrates humanistic care into the whole cycle of disease management. The program innovatively combines multidisciplinary collaboration mechanism and information technology, which not only ensures the standardization of diagnosis and treatment, but also realizes individualized health management through the role of caring consultant, and provides an operable practical path to enhance patients’ adherence to treatment and improve the quality of long term survival, which is of great value in promoting the transformation of China’s oncology patients’ management mode from “disease-centred” to “life-cycle care”.

Disclosure statement

The authors declare no conflict of interest.

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The Effect of Venetoclax Combined with Azacitidine on the Clinical Efficacy, Immune Function, and Adverse Reactions in Elderly Patients with Acute Myeloid Leukemia

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Abstract: *Objective:* To evaluate the immune function and safety of Venetoclax combined with Azacitidine in the treatment of elderly patients with acute myeloid leukemia (AML). *Methods:* Sixty-eight elderly AML patients who visited the hospital from January 2021 to December 2024 were selected as samples and randomly divided into two groups. Group A was treated with Venetoclax and Azacitidine, while Group B was treated with Azacitidine alone. Immune indicators, inflammatory factors, tumor markers, and adverse reactions were compared between the two groups. *Results:* The levels of CD3⁺, CD4⁺, and CD8⁺ in Group A were higher than those in Group B ($P < 0.05$). The tumor necrosis factor- α (TNF- α) level in Group A was lower than that in Group B, while the interferon- γ (IFN- γ) level was higher ($P < 0.05$). The levels of cyclooxygenase-2 (COX-2), lactate dehydrogenase (LDH), and vascular endothelial growth factor (VEGF) in Group A were lower than those in Group B ($P < 0.05$). The adverse reaction rate in Group A was lower than that in Group B ($P < 0.05$). *Conclusion:* The combination of Venetoclax and Azacitidine in the treatment of elderly AML patients can improve immune function, inhibit inflammation, delay disease progression, and is safe and efficient.

Keywords: Acute myeloid leukemia; Venetoclax; Azacitidine; efficacy

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1. Introduction

AML is a malignant disease of the blood system that often occurs in the elderly population. It is related to factors such as organ degeneration, intolerance to chemotherapy, and comorbidities in the elderly population. Additionally, drug resistance of leukemic cells can affect the prognosis of AML ^[1]. Furthermore, many elderly AML patients have DNA methylation issues, so demethylating drugs such as Azacitidine should be selected, which can optimize patients' hematopoietic function and prolong their survival. However, the effect of monotherapy is limited. Bcl-

2 is a common analyte that regulates tumor cell apoptosis and is a target drug for modern diagnosis and treatment of leukemia. Venetoclax can inhibit Bcl-2, and its pharmacological components can activate T cells, block the formation of respiratory chain supercomplexes in the body, thereby increasing the amount of reactive oxygen species generated in the patient's body and enhancing T cell function ^[2]. Based on this, this study explores the efficacy of Venetoclax combined with Azacitidine using 68 elderly AML patients who visited the hospital from January 2021 to December 2024 as samples.

2. Materials and methods

2.1. Materials

Sixty-eight elderly AML patients who visited the hospital from January 2021 to December 2024 are selected as samples and randomly divided into two groups. The baseline data of elderly AML patients in Group A are compared with those in Group B ($P > 0.05$), as shown in **Table 1**.

Table 1. Baseline data analysis of elderly AML patients

Group	<i>n</i>	Gender (%)		Age (years)		Duration of illness (months)	
		Male	Female	Mean	Range	Mean	Range
Group A	34	20(58.82)	14(41.18)	66–87	77.28 ± 2.11	8–15	10.25 ± 1.43
Group B	34	21(61.76)	13(38.24)	66–88	77.31 ± 2.13	8–16	10.28 ± 1.45
X ² /t	-	0.0614		0.0583		0.0859	
<i>P</i>	-	0.8043		0.9536		0.9318	

2.2. Inclusion and exclusion criteria

The inclusion criteria are: (1) Meet the criteria for AML in the “Chinese Guidelines for the Diagnosis and Treatment of Adult Acute Myeloid Leukemia (Non-Acute Promyelocytic Leukemia)” ^[3]; (2) Signed informed consent; (3) Molecular, cytological, and blood routine tests suggest AML; (4) Newly diagnosed AML patients who are difficult to tolerate chemotherapy.

Meanwhile, the exclusion criteria includes: (1) History of demethylating agent treatment; (2) Cardiovascular and cerebrovascular diseases; (3) Central nervous system diseases.

2.3. Treatment methods

Group A is treated with Venetoclax tablets (produced by AbbVie Ireland NL B.V, National Medical Approval Number HJ20200054; 100mg) in combination. The doses for the first day, second day, and 3–28 days were 100mg, 200mg, and 400mg, respectively. Administration for 28 days is considered one treatment course. Regular monitoring of blood routine is performed during the treatment. Bone marrow puncture is repeated from day 21 to 28 of administration. In case of disease progression or severe side effects, the medication is stopped for monitoring. If Hb is less than 60g/L and PLT is less than 20X10⁹/L, blood products are transfused.

Group B received Azacitidine (produced by Chia Tai Tianqing Pharmaceutical Group Co., Ltd., National Medical Approval Number H20193278, 100mg) via subcutaneous injection. The single dose is 75mg/m², administered for 7 days. Targeted hydration and alkalization adjuvant therapy are provided during the treatment. It is noted that after the initial administration, the white blood cell count of AML patients is monitored, and

appropriate amounts of hydroxyurea are given until the white blood cell count returns to normal.

2.4. Observation indicators

- (1) Immune indicators: 5ml of venous blood was collected, and CD3+, CD4+, CD8+, and other detections were completed using a flow cytometer.
- (2) Inflammatory factors: 5ml of venous blood was collected, and TNF- α , IFN- γ , and other detections were completed using enzyme-linked immunosorbent assay.
- (3) Tumor markers: 5ml of venous blood was collected, and COX-2, LDH, VEGF, and other detections were completed using enzyme-linked immunosorbent assay.
- (4) Adverse reactions: Abnormal liver function, gastrointestinal reactions, infections, and other morbidities in AML patients were recorded.

2.5. Statistical analysis

Data are processed using SPSS 21.0 software. Measurement data are recorded as $\bar{x} \pm s$ (t-test), and count data are recorded as percentages (χ^2 test). Statistical significance is considered at $P < 0.05$.

3. Results

3.1. Immune indicators

After treatment, the levels of CD3+, CD4+, and CD8+ in elderly AML patients in Group A were higher than those in Group B ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of immune indicators in elderly AML patients ($\bar{x} \pm s$)

Group	CD3+(%)		CD4+(%)		CD8+(%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=34$)	51.28 \pm 1.82	56.71 \pm 2.46	36.28 \pm 1.88	43.48 \pm 2.48	21.38 \pm 1.52	25.68 \pm 1.88
Group B ($n=34$)	51.27 \pm 1.79	54.36 \pm 2.11	36.24 \pm 1.91	39.53 \pm 2.16	21.39 \pm 1.53	23.22 \pm 1.68
t	0.0228	4.2280	0.0870	7.0033	0.0270	5.6893
P	0.9818	0.0001	0.9309	0.0000	0.9785	0.0000

3.2. Inflammatory factor indicators

After treatment, the TNF- α level of elderly AML patients in Group A was lower than that in Group B, while the IFN- γ level was higher than that in Group B ($P < 0.05$), as shown in **Table 3**.

3.3. Tumor marker indicators

After treatment, the levels of COX-2, LDH, and VEGF in elderly AML patients in Group A were lower than those in Group B ($P < 0.05$), as shown in **Table 4**.

Table 3. Comparison of inflammatory factor indicators in elderly AML ($\bar{x} \pm s$)

Group	TNF- α (pg/ml)		IFN- γ (pg/ml)	
	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=34$)	258.14 \pm 3.87	86.49 \pm 1.58	38.61 \pm 1.82	74.29 \pm 2.42
Group B ($n=34$)	258.19 \pm 3.91	126.02 \pm 2.09	38.59 \pm 1.79	57.58 \pm 2.03
<i>t</i>	0.0530	87.9755	0.0457	30.8467
<i>P</i>	0.9579	0.0000	0.9637	0.0000

Table 4. Comparison of tumor marker indicators in elderly AML ($\bar{x} \pm s$)

Group	COX-2(ng/L)		LDH(U/L)		VEGF(pg/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A ($n=34$)	55.16 \pm 2.17	35.17 \pm 1.25	132.42 \pm 3.29	105.43 \pm 1.89	156.95 \pm 5.26	76.14 \pm 3.26
Group B ($n=34$)	55.19 \pm 2.19	40.82 \pm 1.68	132.39 \pm 3.31	117.36 \pm 2.43	156.99 \pm 5.31	86.43 \pm 4.29
<i>t</i>	0.0567	15.7329	0.0375	22.5967	0.0312	11.1357
<i>P</i>	0.9549	0.0000	0.9702	0.0000	0.9752	0.0000

3.4. Adverse reaction indicators

The adverse reaction rate of elderly AML patients in Group A was lower than that in Group B ($P < 0.05$), as shown in Table 5.

Table 5. Comparison of adverse reactions in elderly AML (n,%)

Group	Abnormal liver function	Gastrointestinal reaction	Infection	Incidence rate
Group A ($n=34$)	0(0.00)	1(2.94)	0(0.00)	1(2.94)
Group B ($n=34$)	1(2.94)	3(8.82)	2(5.88)	6(17.65)
χ^2	-	-	-	3.9813
<i>P</i>	-	-	-	0.0460

4. Discussion

AML accounts for a relatively high proportion among the many pathological types of leukemia, and it predominantly affects the elderly population. Most patients have a poor prognosis. The main treatment option for AML is intensive chemotherapy. However, due to the weak physical functioning and poor tolerance to chemotherapy among elderly patients, issues such as poor prognosis and shortened lifespan may arise. Additionally, the immune function of elderly patients declines, leading to a reduction in T-cell production and higher treatment requirements. Elderly AML patients may experience problems such as increased adipose cells and decreased osteoblast count, which can affect the proliferation of leukemic cells. Coupled with the impact of chronic diseases, this can exacerbate inflammatory responses in the body. Therefore, it is crucial to explore effective management strategies for elderly AML patients^[4].

Azacitidine is a commonly used drug for managing elderly AML. It exerts a demethylating effect, disrupting

the structure of deoxyribonucleic acid (DNA) in cancer lesions and inhibiting DNA repair and transcription processes. When used as prescribed, it can accelerate the differentiation of bone marrow cells and optimize the function of hematopoietic stem cells ^[5]. However, the efficacy of Azacitidine monotherapy in treating elderly AML is limited, and it is difficult to prolong patient survival. Venetoclax can inhibit Bcl-2, blocking the process of Bcl-2 binding to proteins. It can also activate cell signaling molecules, accelerate damage to the mitochondrial membrane, and induce tumor cell apoptosis ^[6]. Combining these drugs for the treatment of elderly AML can synergistically inhibit AML cell proliferation, enhance anti-tumor efficacy, and improve the prognosis of AML patients.

The active ingredient of Venetoclax can directly act on T-cells, enhancing the immune system's anti-leukemia efficacy. When combined with Azacitidine, it can increase the sensitivity of AML cells to T-cells. CD3+ represents an independent or endogenous immune response to malignant cells; CD4+ can reflect the peripheral homeostatic state and tolerance to self-antigens, while also suppressing harmful immune responses and even inhibiting tumor-specific T-cells; CD8+ provides feedback on the clearance of leukemia cells and stimulates the body to produce immune factors ^[7]. Data presented in this study shows that the levels of CD3+, CD4+, and CD8+ in Group A are higher than those in Group B, with $P < 0.05$. This indicates that Venetoclax combined with Azacitidine treatment can improve immune function in elderly AML patients. Another set of data shows that TNF- α is lower in Group A than in Group B, while IFN- γ is higher in Group A, with $P < 0.05$. TNF- α , which originates from the serum and bone marrow of elderly AML patients, reflects the level of inflammation. Excessively high levels of TNF- α in the body can activate the NF- κ B signaling pathway, stimulate the activation of leukemia cells, inhibit hematopoietic stem cell proliferation, induce myelosuppression, damage the bone marrow microenvironment, and exacerbate AML.

Impaired immune function in elderly AML patients can reduce IFN- γ levels. IFN- γ has anti-tumor and anti-leukemia cell proliferation effects, and it can also enhance the activity of immune cells, delaying the progression of AML ^[8]. In this study, Azacitidine treatment is chosen based on its pharmacological mechanism, which can inhibit the production of proteins in lesions and bind to the DNA of lesion cells, generating 5-Aza-2'-deoxycytidine. This blocks the demethylation process in patients' bodies and inhibits tumor proliferation. However, the efficacy of Azacitidine alone may be weakened by tumor cell heterogeneity, especially in a few subtypes with gene mutations that can block Azacitidine's DNA generation and even methylation processes. Therefore, combination therapy with Venetoclax is necessary. The active ingredients of Venetoclax can accelerate tumor cell apoptosis, enhance the activity of cell apoptosis signals, damage tumor cell membranes, increase cell membrane permeability, activate caspases, and inhibit the body's release of inflammatory factors ^[9]. Additionally, the combination of Azacitidine and Venetoclax can inhibit oxidative damage to tumor cells and enhance anti-inflammatory effects.

COX-2 belongs to the category of proteolytic enzymes, which are inducible and can participate in the regulation of tumor cell proliferation. VEGF, a growth factor with specificity, can accelerate the formation of blood vessels in tumor cells and promote their spread. LDH can block immune response, and abnormally elevated LDH levels suggest the spread and proliferation of cancer cells in elderly patients with AML. Based on the data analysis in this study, the levels of COX-2, LDH, and VEGF in Group A were lower than those in Group B ($P < 0.05$). This suggests that the combination therapy of Azacitidine and Venetoclax can inhibit tumor progression and delay the increase in tumor marker levels. In addition, Azacitidine exerts its effects on tumor cell DNA in elderly AML patients, inhibiting tumor proliferation through demethylation, thereby reducing COX-2 levels. The active ingredients of Venetoclax can bind to Bcl-2, specifically inhibiting the anti-tumor apoptosis pathway, damaging

and destroying tumor cell blood vessels, and accelerating vascular dissociation, thus reducing LDH and VEGF levels in elderly AML patients^[10].

Furthermore, the synergistic effect of Azacitidine and Venetoclax allows for rapid and efficient regulation of tumor marker levels. The final set of data shows that the adverse reaction rate in Group A was lower than that in Group B ($P < 0.05$). The analysis suggests that the combined use of Azacitidine and Venetoclax, with complementary mechanisms of action, can inhibit the toxic effects of single high-dose drug administration, reduce toxicity to healthy cell tissues while enhancing tumor cell killing, and generate synergistic effects through Azacitidine's sensitization of tumor cells to apoptosis and Venetoclax's induction of apoptosis in tumor cells. Combined drug use can also improve the targeting of active ingredients, inhibit damage to the hematopoietic system caused by drug toxicity, and reduce the risk of bone marrow suppression. Additionally, different mechanisms of action can avoid the risk of drug resistance associated with single-drug administration, ensuring the safety of medication for elderly AML patients. However, this study included a limited number of elderly AML patients and did not explore the long-term efficacy of Azacitidine plus Venetoclax treatment across multiple centers. Future research should increase the number of elderly AML patients to ensure data reliability.

5. Conclusion

In summary, the combination therapy of Azacitidine and Venetoclax for elderly AML patients can improve immune function, inhibit inflammatory responses, and reduce tumor marker levels without increasing drug toxicity, making it a safe and effective treatment option.

Disclosure statement

The author declares no conflict of interest.

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