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Experimental and computational processes in surgery, 2nd Edition

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ORIGINAL RESEARCH
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Model-Based Computational Analysis on the Effectiveness of Enhanced Recovery after Surgery in the Operating Room with Nursing

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Objective: In order to better understand the relative surgical process, this work used a model-based computational analysis on the effectiveness of enhanced recovery after surgery (ERAS) in the operating room with nursing.

Methods: A total of 360 surgical patients in the First Affiliated Hospital, Sun Yat-sen University, from the period June 2020 to March 2021, were randomly divided into two groups, namely, observation group and control group, with 180 cases in each group. Routine nursing was used in the control group, while ERAS was implemented in the observation group from the point of view of four aspects, namely, preoperative visit, intraoperative cooperation, postoperative return visit, and psychological intervention.

Results: Postoperative complications, average hospital stay, nursing satisfaction, and postoperative quality of life in the observation group were significantly better than those in the control group (all $p < 0.05$).

Conclusion: The application of ERAS for surgical patients can enhance team awareness, optimize the process of cooperation, reduce surgical complications and improve nursing quality, and prognosis, and it is worth popularizing in the operating room.

Keywords: surgery, operating room nursing, enhanced recovery after surgery, complication, satisfaction

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INTRODUCTION

Surgery refers to the treatment that doctors use with knives, scissors, needles, and other medical instruments to cut off and sew parts of the human body to maintain or even save the patient's health. This surgical treatment is commonly known as "operation". The purpose is to treat or diagnose diseases to improve the body's function and shape, such as removing diseased tissues (1, 2), repairing injuries (3, 4), and organ transplantation (5, 6). Early surgery is limited to cutting and suturing on the body surface by simple manual methods such as abscess drainage, tumor resection, and trauma suturing. With the development of surgery, the field of surgery has been expanding, and today, it can be performed in any part of the human body (7–10). In addition, it has been reported that surgery has greater efficacy than non-surgical treatments in curing some human diseases (11, 12).

However, various intraoperative complications and postoperative complications may occur due to injury, bleeding, or infection caused by surgical treatment (13–15). In addition, when patients undergo surgery, they have to experience the stimulation of anesthesia and surgical trauma. Their body will be in a state of stress, which will lead to both psychological and physiological burden (16). Therefore, some kind of good and effective perioperative nursing is required to provide patients with holistic physical and mental care so that they can successfully spend their perioperative period in the best frame of mind (**Figure 1**). Such nursing also plays an extremely important role in preventing or reducing postoperative complications (17).

The theory of Enhanced Recovery after Surgery (ERAS) was proposed systematically by Danish surgeon Professor Kehlet (18) for the first time in 1997, which refers to the adoption of a series of perioperative optimization measures with evidence-based medical evidence to block or reduce the stress response of the body. It can promote the accelerated recovery of patients after surgery and achieve the purpose of shortening the patient's hospitalization time so as to reduce postoperative complications and also the risk of readmission and death (19). It has been verified that ERAS has a very positive application (20, 21). The purpose of this study is to research and analyze the effect of ERAS on perioperative nursing and provide a reference for further study.

MATERIALS AND METHODS

General Description

A total of 360 (223 males and 137 females) surgical patients in the First Affiliated Hospital, Sun Yat-sen University, from the period June 2020 to March 2021, were selected as the research objects. All the selected patients underwent elective surgery, following which all of them could actively cooperate with perioperative nursing guidance. The whole study was carried out with the informed consent of these patients and approved by the hospital ethics committee.

All patients were randomly divided into two groups, 180 in each group. Of these, 118 males and 62 females with age ranging from 61 to 78 years and an average of (62.50 ± 15.60) years were in the observation group, in which ERAS was implemented in the form of preoperative visit, intraoperative cooperation, postoperative return visit, and psychological intervention. A total of 105 males and 75 females with age ranging from 51 to 81 years and an average of (62.70 ± 14.60) years were in the control group, in which routine nursing was implemented. There was no significant difference between the two groups in the general data such as gender, age, and gastrointestinal diseases (all $p < 0.05$), which indicated that they were comparable in this study.

Materials

Routine Nursing

The control group was given routine nursing care. Preoperative nursing was carried out for the purpose of education. Patients were required to fast for 8–12 h and abstain from drinking for 4 h (7). After entering the operating room, the patients were checked, and venous access was established. After general anesthesia, the patients were placed in the operating position. They could eat after anal exhaust, the complications of which were observed and recorded.

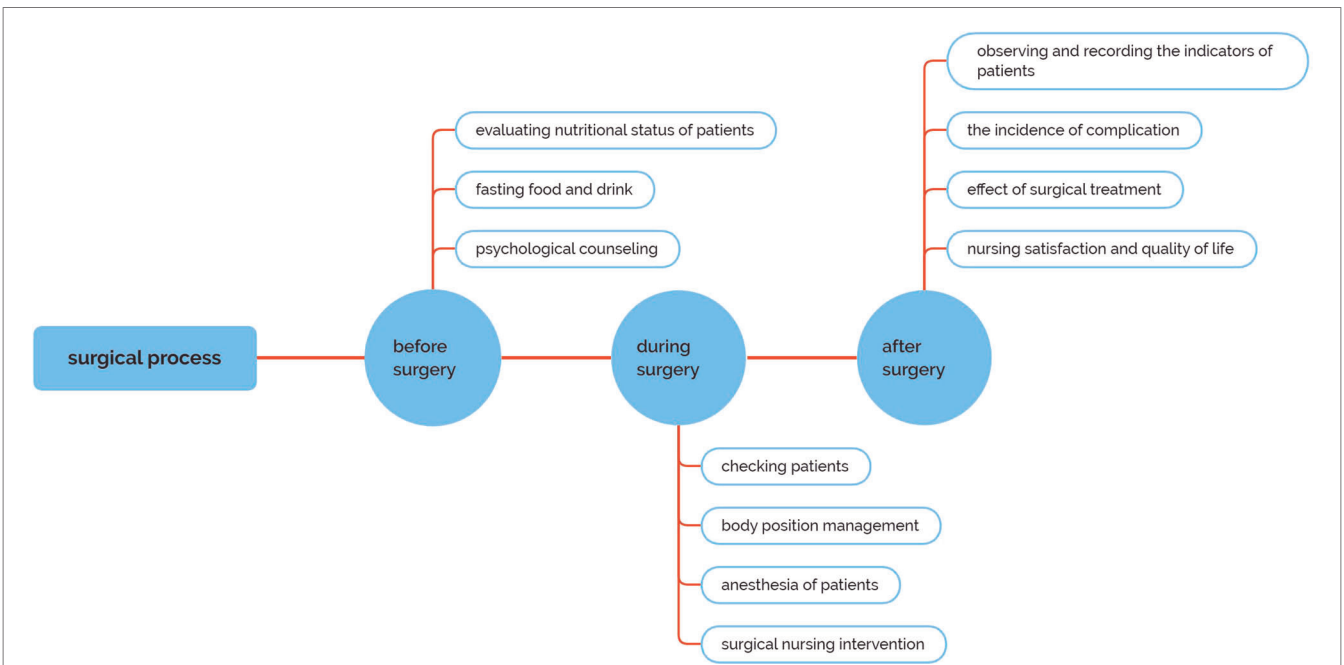

FIGURE 1 | General surgical process during the perioperative period.

ERAS Pathway

The observation group received routine nursing and the corresponding nursing intervention combined with ERAS, including preoperative nursing, operation room nursing, and postoperative nursing, which are described in the following paragraphs.

Preoperative Nursing

In the ERAS pathway, good preoperative preparation and psychological nursing play a key role in the smooth conduct of operation. Nurses should visit patients 1 day before operation and give them appropriate diet and psychological nursing.

Psychological Nursing. Surgery is an invasive operation, which causes serious psychological burden to patients. Anxiety is a common psychological condition of patients before surgery. Psychological counseling should be done well before surgery to enhance the confidence of patients during surgery.

Self-Care Ability. The self-care ability of the patients were evaluated according to the inputs provided by the patients in the self-care ability evaluation form. Self-care ability was divided into four levels, namely, no dependence, mild dependence, moderate dependence, and severe dependence. The self-care ability of these levels was evaluated as none needed for care, a few needed care, most needed care, and all needed care, respectively. Dynamic evaluation was made according to the changes in the patients' condition and nursing levels, and corresponding nursing measures such as secondary care, primary care, and special care were implemented.

Diet Nursing. The nutritional status of the patients was evaluated. Patients without gastrointestinal motility disorder were required to fast solid food for 6 h and liquid food for 2 h before operation. They were required to take two bottles of "Suqian beverage" (a kind of maltose fructose drink made in China) of approximately 800 ml orally at 22:00 and one bottle of approximately 400 ml 2 h before operation. Reducing the hunger, thirst and anxiety of patients can lower the incidence of postoperative nausea and vomiting, which will accelerate their recovery.

Operating Room Nursing

The bladder of the patients should be confirmed empty while the nurse brings them into the operating room. An equilibrium liquid of approximately 30 drops/min was given to the patients after confirming the standby state of the indwelling needle and slowly dripping it for maintenance (22, 23). The roving nurse and the workers jointly verified the general information of the patients and handed over their intraoperative medication, imaging data, special supplies, and medical records. After signing the printed operation handover form, the patients were sent to the operating room.

The patients were under anesthesia during the operation. Excessive blood loss and fluid loss may be caused by long operation time and trauma. Therefore, it is highly important to implement operating room nursing intervention in the ERAS pathway. The infusion channel should be reasonable, and the appropriate venous catheter should be selected. In case of significant blood loss and fluid loss during the operation, the large-diameter venous channel and central venous catheters anti-infection catheter should be selected and the three-way pipe should be managed well. It is reported that the pollution rate of the three-way pipe during the operation can reach 23%. The integrated board was used to prevent infection. In addition, body position management should be standardized. The exposed field should be convenient for the operator to conduct the operation. The body should be placed gently and the functional position should be maintained after the body is placed. Personalized body position should be adopted to avoid skin damage and nerve damage. Physical preventive measures such as elastic socks and intermittent pressurizing devices can be used to avoid low blood volume. A specialist group should be set up, with a specialist nurse as the team leader. Daily staff should be arranged by the specialist group every day. Operational materials should be prepared well according to the doctor's instructions, and the staff should actively cooperate with the surgeons to shorten the operation time.

Postoperative Nursing

The patients went back to the ward after anesthesia. Evaluation and handover were made according to the observation record sheet of the anesthesia recovery room (PACU). The handover contents mainly include the following: identity confirmation, vital signs, consciousness, respiration, circulation, oxygen saturation, the patient's limb mobility, oral and lip color, infusion, urinary catheter, medication, drainage and wound dressing, and skin.

Observation Indicators

The incidence of postoperative complications, treatment effect, nursing satisfaction, and quality of life were compared between the two groups (22–24). According to the questionnaire of patient satisfaction in the operating room developed by our hospital, the patients scored on the spot to judge their nursing satisfaction during the postoperative return visit. Satisfaction rate = very satisfied + satisfied (the total number of people).

Statistical Method

SPSS 26.0 statistical software was used to analyze the data. The measurement data were expressed by average ($\bar{x} \pm s$) and the t-test was used. The counting data were expressed by percentage (%) and the X^2 test was used. The difference was statistically significant ($p < 0.05$).

RESULTS AND DISCUSSIONS

As shown in **Table 1**, complications such as skin injury, shiver, and incision infection occurred in both groups, which include

13 cases in the observation group (7.22%) and 35 cases in the control group (19.44%). The number of patients with complications in the observation group was significantly less than those in the control group, which indicated better nursing effect on ERAS ($p < 0.05$). One of the concepts of ERAS is to reduce the incidence of postoperative complications and promote the recovery of patients' physical and psychological health (25), which is consistent with the results in **Table 1**. Nursing staff made a comprehensive evaluation of the preoperative visits of the patients in the observation group before the operation. The infusion pipeline was well managed during the operation, and the operation position was correctly placed to prevent hypothermia. In addition, a series of nursing interventions to prevent deep vein thrombosis and control incision infection were adopted, which significantly reduced the complication rate of the patients.

Generally, surgical patients experienced moderate and severe pain. Good postoperative analgesia can relieve their tension and anxiety. In the ERAS pathway, a return visit was made to correctly evaluate the patients' pain after the operation. It is beneficial for wound healing and will speed up recovery if analgesia is given in a preventive, timely, and multimode manner (26). ERAS has been shown to allow patients to move out of bed sooner (27, 28) and reduce the length of stay in hospital (29, 30). From **Table 2**, it can be seen that the patients in the observation group were significantly better than those in the control group in terms of exhaust time, free movement time out of bed, and average length of hospital stay ($p < 0.05$), which showed consistency with the previous report.

As shown in **Table 3**, patients' satisfaction with nursing in the observation group (98.30%) was significantly higher than that in the control group (85.00%), and the difference was statistically significant ($p < 0.05$). Compared with patients who underwent routine nursing, the time of fasting food and drink of those who adopted ERAS was shortened. The patients' hunger, panic, and fear caused by long-term fasting were avoided. Effective communication with the patients was made before the operation. The patients could more clearly understand the purpose and time of fasting so that they could more actively cooperate during the perioperative period. Therefore, nursing satisfaction was improved (31).

Quality of life was positively correlated with the score. The higher the total scores, the higher the quality of life. As shown in **Table 4**, the scores of quality of life after nursing in the observation group were significantly higher than those in the control group ($p < 0.05$) after psychological intervention. It was reported that ERAS can significantly improve patients' mental health and physical health, which was basically

TABLE 1 | Comparison of postoperative complications between two groups ($n = 360$, %).

Groups	Skin injury	Shiver	Incision infection	Incidence rate (%)
Observation group	4	6	3	7.22
Control group	12	14	9	19.44
X^2-value	8.226	8.126	4.232	
p-Value	0.005*	0.002*	0.001*	

*$p < 0.01$.

TABLE 2 | Comparison of therapeutic effects between two groups ($n = 360$, $\bar{x} \pm s$).

Groups	Anal exhaust time (h)	free movement time out of bed (h)	Average length of hospital stay (days)
Observation group	33.30 ± 3.26*	19.80 ± 4.26*	9.07 ± 1.26*
Control group	64.50 ± 3.28*	33.72 ± 2.32*	18.01 ± 2.26

*$p < 0.05$.

TABLE 3 | Comparison of nursing satisfaction between two groups ($n = 360$, %).

Groups	Number	Very satisfied	Satisfied	Dissatisfied	Degree of satisfaction (%)
Observation group	180	108	69	3	98.30*
Control group	180	58	95	27	85.00*

*$p < 0.05$.

TABLE 4 | Comparison of quality of life after nursing care between two groups ($n = 360$, $\bar{x} \pm s$).

Groups	Physiological functioning	General health	Mental health	Vitality	Bodily pain	Role-emotional	Social functioning
Observation group	87.35 ± 6.31	78.39 ± 5.76	70.20 ± 5.12	82.14 ± 6.21	75.21 ± 5.21	79.02 ± 5.21	81.62 ± 6.06
Control group	72.37 ± 6.35	72.32 ± 5.26	63.21 ± 4.98	74.21 ± 6.09	70.11 ± 5.31	73.21 ± 5.06	76.22 ± 5.26
t-Value	9.903	5.721	4.226	4.781	4.919	5.121	5.266
p-Value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

*$p < 0.01$.

consistent with the conclusion in **Table 4** of this study (32). Moreover, psychological intervention can improve the patient compliance following the ERAS after operation.

CONCLUSIONS

In this study, the effects of routine nursing and ERAS on perioperative nursing were compared. The results indicated that the ERAS pathway can not only reduce postoperative complications and shorten the length of hospital stay, but also improve patients' quality of life. From this study, we can see that for patients, the application of the ERAS theory during the perioperative period can shorten the operation time and reduce their postoperative complications so as to improve the prognosis and enhance their overall satisfaction with the quality of care. For surgeons, ERAS can enhance the awareness of the operation team and optimize the operation process of cooperation, which is worth popularizing.

With the development of medical technology, minimally invasive surgery and precise medications have led to fewer contraindications for surgical treatment. Surgery, as the main method of invasive treatment, has a great impact on the status of patients' psychology and physiology. In order to alleviate patients' anxiety and fear before operation, improve nursing quality, and reduce postoperative complications, operating room nursing staff are required to keep pace with the times and garner new ideas to serve patients. However, due to a wide range of departments involved in ERAS, multiteam and multidisciplinary assistance are required. In our study, ERAS proved to be an effective way to help patients recover quickly and comprehensively, thus providing a good reference and theoretical basis for studying ERAS and changing traditional nursing concepts to devise more effective nursing measures.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

WL and SH conceptualized and designed the study and wrote the first draft of the manuscript. YX, GC, and JY were involved in data collection and analysis. YY contributed in terms of manuscript revision, reading, and project management. All authors contributed to the article and approved the submitted version.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethical approval for this work was obtained from The Ethical Review Committee of The First Affiliated Hospital, Sun Yat-sen University. The patients/participants provided their written informed consent to participate in this study.

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Observation of Anesthetic Effect of Dexmedetomidine Combined With Intraspinal Anesthesia in Hip Arthroplasty and its Effect on Postoperative Delirium and Stress Response

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Objective: To observe the anesthetic effect of dexmedetomidine combined with spinal anesthesia in hip arthroplasty, and to analyze the effects of dexmedetomidine on postoperative stress response, incidence of delirium, immune function and inflammatory indicators.

Methods: A total of 42 patients who underwent hip replacement in our hospital from March 2020 to June 2021 were selected as the research subjects and randomly divided into the control group and the observation group, 21 cases in each group. The control group was given intraspinal anesthesia, and the observation group was given dexmedetomidine on this basis. The onset time and maintenance time of sensory and motor nerve block were recorded. Stress response indexes [cortisol (Cor), blood glucose (Glu), adrenaline (E), noadrenaline (NE)], T lymphocyte subsets (CD3+, CD4+, CD8+, CD4+/CD8+), inflammatory indexes [tumor necrosis factor -α (TNF-α) and interleukin-6 (IL-6)] were detected before and after operation, and the incidence of postoperative delirium in both groups was recorded.

Results: The onset time of sensory nerve block and motor block in the observation group were lower than those in the control group, and the retention time of sensory nerve block and motor nerve block were higher than those in the control group ($P < 0.05$). After surgery, the levels of Cor, Glu, E and NE in the observation group were lower than those in the control group ($P < 0.05$). After surgery, the incidence of postoperative delirium in the observation group (4.79%) was lower than that in the control group (28.57%) ($P < 0.05$). After surgery, the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ in the observation group were higher than those in the control group ($P < 0.05$). After surgery, the levels of TNF-α and IL-6 in the observation group were lower than those in the control group ($P < 0.05$).

Conclusion: The combined use of dexmedetomidine and intraspinal anesthesia has good anesthesia effect in hip joint replacement, which can greatly reduce the stress response of

patients, reduce the incidence of postoperative delirium, and effectively restore the immune function of patients, reduce the level of inflammatory response, and has high clinical application value.

Keywords: hip replacement, dexmedetomidine, intraspinal anesthesia, anesthetic effects, stress response, delirium, immunologic function

INTRODUCTION

Hip is the area where the trunk and legs are connected, which can make the trunk and legs move forward, backward and laterally independently. Since the hip is the center of a series of body movements, you are more likely to get injuries in your daily life (1, 2). Hip fracture is common in older people over 60 years old, who are often accompanied by osteoporosis and are prone to hip fracture when suffering from low energy trauma (3, 4). Hip replacement is a surgical method for the treatment of hip diseases such as hip fracture in the elderly, which can effectively correct hip deformity, relieve hip pain, help patients recover hip function, improve the quality of life, and significantly improve the clinical symptoms and clinical manifestations of patients (5, 6). The choice of anesthesia in clinical practice is determined by different factors, such as patient differences, pre-operative complications, risk of post-operative complications, and doctors' clinical experience (7, 8). As there are many chronic basic diseases in the elderly patients due to pathological and physiological changes, anesthesia has a greater impact on the postoperative prognosis of elderly patients, so the choice of anesthesia brings challenges to clinical work (9, 10). Intraspinal anesthesia is one of the current anesthesia methods for hip fracture, and it is commonly used in China. However, when the anesthesia level of elderly patients is too high, it can lead to severe hypotension, or even affect respiratory function. The application of intraspinal anesthesia to hip fractures in the elderly is limited by the fact that degenerative lumbar intervertebral stenosis and ligament calcification can lead to difficulty or failure in puncture in the elderly (11, 12). Dexmedetomidine is a highly selective α2- adrenoceptor agonist, which has sedative, analgesic,, anti-anxiety, inhibition of sympathetic nerve activity, and stability of hemodynamics. Studies have found that dexmedetomidine can enhance the effect of propofol and opioids, stabilize cerebral blood flow, and has a neuroprotective function (13–15). The purpose of this study was to investigate the anesthesia effects of dexmedetomidine combined with intraspinal anesthesia in hip joint replacement and analyze its effects on postoperative stress response, the incidence of delirium, immune function and inflammation indexes of patients.

MATERIALS AND METHODS

Patients

A total of 42 patients who underwent hip replacement in our hospital from March 2020 to June 2021 were selected as the research subjects. Inclusion criteria: age ≥60 years old; All patients underwent hip replacement; All patients met the standards of spinal anesthesia; American Society of Anesthesiologists (ASA) grades II to III; Patients with normal cardiopulmonary function. Exclusion criteria: With coagulation disorders; Patients with hematopoietic system diseases; Patients with arrhythmia and severe conduction block; Patients with history of delirium and dementia before operation. All the patients were randomly divided into a control group and an observation group, 21 cases in each group. There was no significant difference in general information between the two groups ($P > 0.05$). As shown in **Table 1**.

Treatment Methods

After preoperative preparation and exclusion of surgical contraindications, the patient was sent to the operating room for hip replacement. Routine intravenous channels were opened before surgery, blood pressure, heart rate, pulse, blood oxygen saturation and Electroencephalogram (EEG) dual frequency index were continuously detected, and oxygen inhalation by mask was continued during surgery. During the operation, oxygen was continuously inhaled through face mask. In the control group, intraspinal anesthesia was adopted. The patient was in the lateral decubitus position, and epidural puncture was performed using the intervertebral space of L2 and L3 as the puncture points. After successful puncture, a tube was inserted into the epidural space with the catheter pointing towards the head end. The spinal anesthesia was performed with 1 ml of 0.5% bupivacaine (Shandong Hualu Pharmaceutical Co., LTD., National Drug Approval: H37022107), and the anesthesia plane was controlled below the 10th thoracic vertebra (T10) plane. On the basis of the control group, patients in the observation group were additionally sedated with dexmedetomidine: The method of intraspinal anesthesia was the same as above. After the spinal canal was fixed with the anesthesia plane, dexmedetomidine (Jiangsu Nhwa Pharmaceutical Co., Ltd., National Drug Approval Code: H20110085) hydrochloride injection at 1 μg/kg was given, and the infusion pump was connected after intravenous infusion for 10–15 min, for continuous intravenous pumping at the rate of 0.2 μg/(kg·h).

Both groups were given automatic intravenous analgesia to relieve postoperative pain. The analgesic formula was 0.9% sodium chloride injection 100 ml and 2 μg/kg sufentanil. If the patient has severe postoperative pain, 40 mg parecoxib can be injected intravenously to keep the patient's postoperative pain visual analog score below 4 points.

TABLE 1 | Comparison of general data of patients between the two groups.

Group	Gender		Age (years)	BMI (kg/m^2)	ASA		Disease site		Course of disease (years)
	Male	Female			II	III	Left	Right	
Control group	28	21	69.53 ± 5.16	23.46 ± 2.19	16	5	11	10	6.08 ± 2.04
Observation group	30	19	69.68 ± 5.29	23.59 ± 2.24	14	7	9	12	5.96 ± 2,15
t/χ^2	0.383		0.142	0.291	0.467		0.382		0.186
P	0.536		0.887	0.772	0.495		0.537		0.854

Observation Indicators

Anesthesia Effect index

The onset time and maintenance time of sensory and motor nerve block in the two groups were recorded.

Stress Response Indicators

The levels of serum cortisol (Cor), blood glucose (Glu), epinephrine (E) and norepinephrine (NE) in the two groups were measured preoperatively and 1d after operation using an automatic biochemical analyzer (Mindray Automatic Biochemical analyzer BS-280).

Occurrence of Delirium

3 days after operation, the incidence of postoperative delirium in the two groups was recorded, and the incidence of delirium was calculated. Incidence of delirium = cases of delirium/total cases × 100%.

Immune Function Indicators

The levels of T lymphocyte subsets (CD3+, CD4+, CD8+, CD4+/CD8+) were measured by FACSCount flow cytometry produced by BD Company in the United States and supporting reagents.

Inflammatory Indicators

The levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in serum of both groups were detected by ELISA before and 1d after surgery. The above kits were purchased from Shanghai Enzyme-linked Biotechnology Co., LTD.

Adverse Reactions

Postoperative observation was made for nausea, vomiting, dizziness and other adverse reactions in both groups.

Statistical Methods

All data were processed with SPSS 22.0 statistical software. The enumeration data were examined by X^2 test and expressed by [n (%)], the measurement data were examined by t-test and expressed by ($\bar{x} \pm s$). The difference is statistically significant when $P < 0.05$.

RESULTS

Comparison of Anesthesia Effect Indexes Between the Two Groups

The onset time of sensory and motor block in the observation group was lower than that in the control group, and the retention time of sensory and motor block was higher than that in the control group ($P < 0.05$). As shown in **Figure 1**.

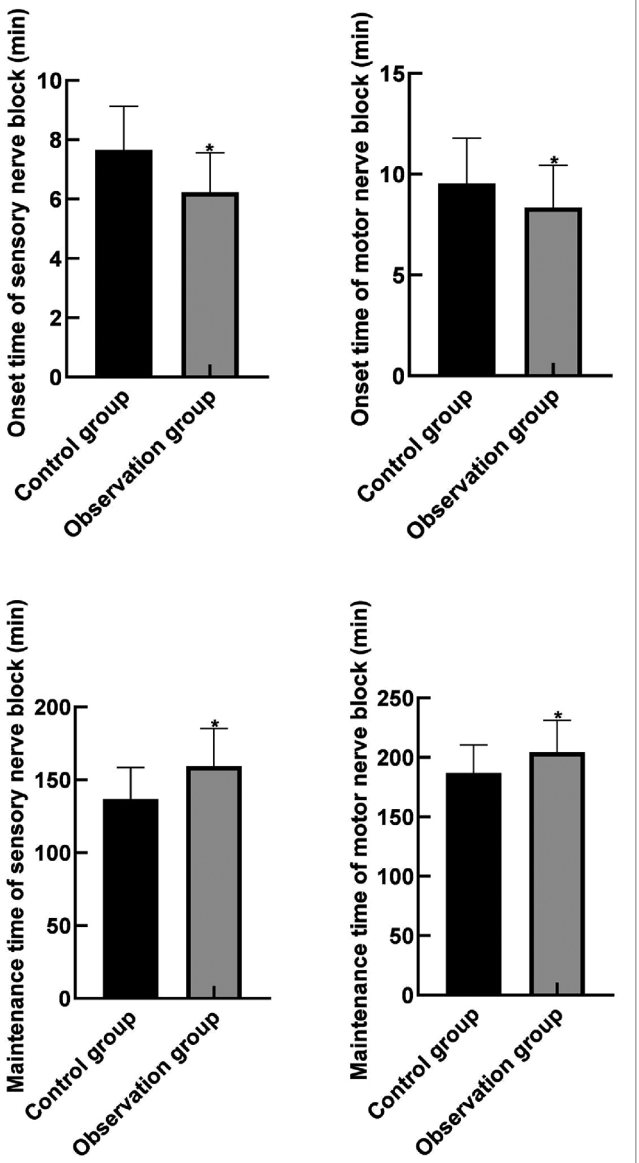

FIGURE 1 | Comparison of anesthesia effect indexes between the two groups. Note: Compared with the control group, *$P < 0.05$.

Comparison of Stress Response Indicators Between the Two Groups

After surgery, the levels of Cor, Glu, E and NE in the two groups were higher than those before surgery, and the levels of Cor,

Glu, E and NE in the observation group were lower than those in the control group ($P < 0.05$). As shown in **Figure 2**.

Comparison of Delirium Occurrence Between the Two Groups

After surgery, the incidence of delirium in the control group and the observation group was 28.57% (6/21) and 4.79% (1/21), respectively. The incidence of postoperative delirium in the observation group was lower than that in the control group ($P < 0.05$).

Comparison of Immune Function Indicators Between the Two Groups

After surgery, the levels of CD3+, CD4+, CD8+, and CD4 +/CD8 + in the two groups were lower than those before surgery, and the levels of CD3+, CD4+, CD8+, and CD4 +/CD8 + in the observation group were higher than those in the control group ($P < 0.05$). As shown in **Figure 3**.

Comparison of Inflammatory Indexes Between the Two Groups

After operation, the levels of TNF-α and IL-6 in both groups were higher than those before operation, and the levels of TNF-α and IL-6 in observation group were lower than those in control group ($P < 0.05$). As shown in **Figure 4**.

Adverse Reactions of the Two Groups

After operation, there were 2 cases of nausea, 1 case of vomiting, 1 case of dizziness and 1 case of hypotension in the control group, and the total incidence of adverse reactions was 23.81% (5/21). In the observation group, there was 1 case of nausea, 1 case of dizziness and 1 case of hypotension, and the total incidence of adverse reactions was 14.29 (3/21). The incidence of adr in observation group was slightly lower than that in control group, but the difference was not statistically significant ($P > 0.05$). As shown in **Table 2**.

DISCUSSION

Elderly patients undergoing hip replacement are prone to stress reaction during the operation because they often suffer from various basic diseases of the system, such as diabetes and hypertension, and the decline of body organ function, resulting in low compensatory function of the cardiovascular system and reduced regulation ability of the circulatory system. In addition, due to slow drug metabolism, patients are

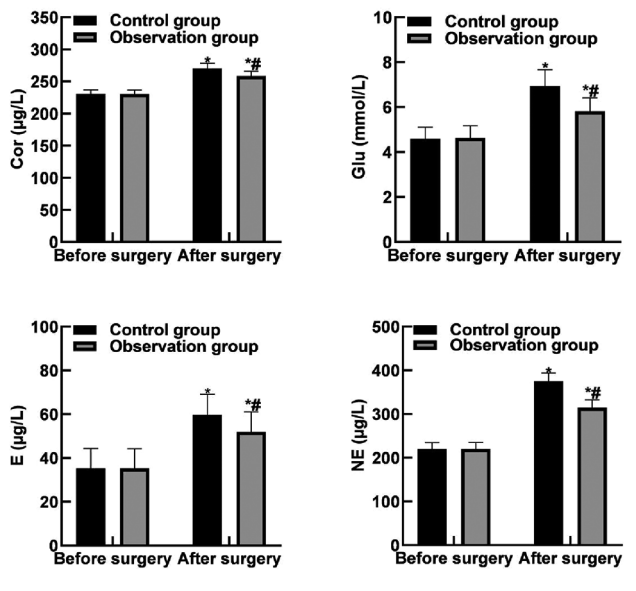

FIGURE 2 | Comparison of stress response indicators between the two groups. Note: Compared with before surgery, $^{*}P < 0.05$. Compared with the control group, $^{\#}P < 0.05$.

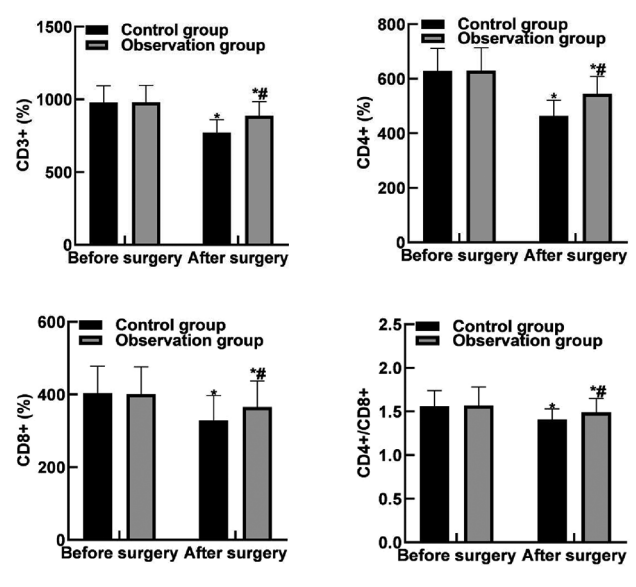

FIGURE 3 | Comparison of immune function indicators between the two groups. Note: Compared with before surgery, $^{*}P < 0.05$. Compared with the control group, $^{\#}P < 0.05$.

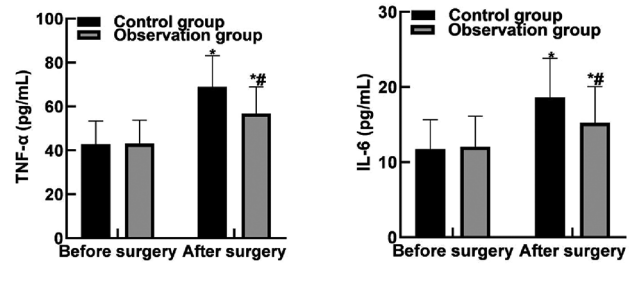

FIGURE 4 | Comparison of inflammatory indexes between the two groups. Note: Compared with before surgery, $^{*}P < 0.05$. Compared with the control group, $^{\#}P < 0.05$.

TABLE 2 | Adverse reactions of the two groups.

Group	Nausea	Vomiting	Dizziness	Hypotension	Total incidence
Control group	2	1	1	1	5 (23.81)
Observation group	1	0	1	1	3 (14.29%)
χ^2					0.618
P					0.432

prone to delayed awakening or even temporary brain dysfunction after surgery, which increases the risk of complications and affects the patient's rehabilitation (16, 17). Previous studies have found that intraspinal anesthesia has the characteristics of good analgesic effect, small drug consumption, and the block range is limited to one side, which can effectively reduce the sympathetic activity and reduce vasodilation, thereby reducing the damage to the circulatory system and the occurrence of adverse events, and effectively meeting the basic needs of hip replacement in the elderly (18, 19). Our patient avoided endotracheal intubation and mechanical ventilation with relatively low respiratory complications; The incidence of nausea and vomiting is low; Epidural analgesia can be performed with good postoperative analgesic effect. However, for the routine use of anticoagulants during perioperative period, the use of epidural analgesia is limited to a certain extent due to the risk (20, 21). In addition, the change of body position during anesthesia may result in the displacement of the fracture end, causing damages to the peripheral nerves and blood vessels, or even aggravation. Moreover, patients under simple intraspinal anesthesia are in a awake state and easily suffer from tension, anxiety and other bad emotions. With the use of traditional sedative auxiliary drugs, elderly patients are often more sensitive, which finally leads to different degrees of inhibition of respiratory cycle, thus affecting the safety during the operation (22, 23). Therefore, effective sedation is still need to stabilize that patient's vital signs.

The results of this study showed that the onset time of sensory and motor block in the observation group was lower than that in the control group, and the retention time of sensory and motor block was higher than that in the control group. It indicated that dexmedetomidine combined with intraspinal anesthesia had better anesthesia effect in hip joint replacement. The reason for this analysis is that dexmedetomidine has a high selectivity for α2- adrenergic receptor agonists, and therefore it works more quickly and is less toxic. Dexmedetomidine can enhance the anesthetic effect in the spinal canal by inhibiting the central and peripheral sympathetic nerves, and can also block the release of neurotransmitters by acting on presynaptic C fibers and spinal motor neurons (24, 25).

Stress response is a series of physiological and psychological changes generated by the human body in response to external stimuli. Moderate stress response is conducive to the body to adapt to the external stimuli, while excessive stress response can cause various system dysfunction, or even life-threatening (26, 27). Due to the degradation of body function, the sensitivity of various systems of the body to external stimuli is decreased in elderly patients, and they are more likely to have stress responses. Surgical trauma and pain are the stress source of elderly patients with hip replacement. If the stress response of patients is not effectively controlled, it is likely to induce cardiovascular events and other accidents, increasing the risk of surgery and anesthesia. Cor is an adrenocortical hormone that can effectively regulate the relationship between immune cells and inflammation, blood vessels and blood pressure, and its abnormal expression is often closely related to stress response. Glu is an important source of energy. Under stress state, the excitability of sympathetic nervous system will be enhanced, and the secretion of glucocorticoids and catecholamine will be increased, resulting in the decrease of glucagon and insulin contents, as well as the initiation of hepatic glycogen decomposition and gluconeogenesis, further resulting in the elevation of blood glucose. E mainly comes from adrenal gland, and can cause increased heart rate, increased cardiac output, and enhanced myocardial contractility, with the increased content suggesting that the body was stimulated by injuries. NE is not only a neurotransmitter but also a hormone, which can cause the contraction of venules and arterioles by acting on α receptor, and increase the peripheral resistance, leading to an increase in blood pressure and slow heart rate. The serum content of NE is positively correlated with the degree of stress response (12, 28). The results of this study showed that after surgery, the levels of Cor, Glu, E and NE in the observation group were lower than those in the control group. These results indicated that dexmedetomidine combined with intraspinal anesthesia could reduce the stress response of surgery and the change amplitude of stress hormones after surgery. The reason for this was analyzed as follows: Dexmedetomidine can directly act on the posterior horn of gray matter in the spinal cord of patients, thus triggering the hyperpolarization of postsynaptic membrane and inhibiting the convergence of noxious mediators, thus greatly reducing the pain of patients and relieving stress response of the body.

Delirium is a cognitive or sensory disorder associated with inattention that develops over a short period of time and fluctuates over time. Postoperative delirium is a heterogeneous disorder characterized by dramatic changes in mental status, such as changes in attention and consciousness (29, 30). Postoperative delirium has a high incidence in patients undergoing hip replacement, especially in patients with hip fractures, which is as high as 35% to 65%. The incidence of delirium is generally high because preoperative fractures (acute trauma), pain, chronic inflammation and subsequent surgical treatment can all be contributing factors to systemic reactions, and because hip replacements are generally performed in older patients (31, 32). The results of this study showed that the incidence of postoperative delirium in the observation group was lower than that in the control group. These results indicated that dexmedetomidine combined with intraspinal anesthesia could reduce the incidence of postoperative delirium in patients. The reason was analyzed as follows: The sleep state induced by dexmedetomidine was natural

non-oculomotor sleep, which could effectively promote the recovery and repair of nervous and immune system of elderly patients, avoid the impairment of cognitive function and physiological function, thus shorten the awakening time and reduce the incidence of postoperative delirium. Dexmedetomidine combined with intraspinal anesthesia can produce a synergistic effect, which is conducive to reducing the stress source, reducing the stress state of patients, and improving the safety of surgery.

T-lymphocyte level can reflect the changes of immune function in patients and directly affect complications, rehabilitation and prognosis of patients. CD3+, CD4+, CD8+, and CD4+/CD8+ are common cellular immune indicators (33, 34). CD3+ mainly exists on the cell surface and is involved in T cell activation signal transduction, thus initiating the immune response. CD4+ can assist the expression of T cells, which can guide the body's resistance to inflammatory cells, so as to enhance the body's anti-toxicity ability. The results of this study showed that after surgery, the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ in the observation group were higher than those in the control group. These results indicated that dexmedetomidine combined with intraspinal anesthesia could improve the postoperative immune function of patients and inhibit the expression of T lymphocyte subsets. The results of this study showed that the levels of TNF-α and IL-6 in the observation group were lower than those in the control group. These results indicate that dexmedetomidine combined with spinal anesthesia can effectively reduce the inflammatory response level caused by surgical trauma. The reason is analyzed that dexmedetomidine can regulate the release of inflammatory factors by macrophages and monocytes, exert anti-inflammatory effect by reducing the chemotaxis of inflammatory cells and enhancing cell-mediated immune response, and inhibit the TOLL-like receptor 4 inflammatory pathway, thereby exerting anti-inflammatory effect.

CONCLUSION

Dexmedetomidine combined with intraspinal anesthesia has good anesthesia effect in hip joint replacement, which can greatly reduce the stress response of patients, reduce the incidence of postoperative delirium of patients, and effectively restore the immune function of patients, reduce the level of inflammatory response, and has high clinical application value.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by This study was approved by the Ethics Committee of Yiwu Central Hospital (2020004). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YS and CW are the mainly responsible for the writing of the article. XZ is mainly responsible for research design. YW is mainly responsible for data analysis. YS is responsible for the guidance of the entire research. The corresponding author is XH, and she is responsible for ensuring that the descriptions are accurate and agreed by all authors. All authors contributed to the article and approved the submitted version.

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ORIGINAL RESEARCH
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Effect of Silver Nanoparticles With Thermoplastic Polyurethane on Postoperative Rehabilitation of Diabetic Patients With Open Fracture of Lower Extremities

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Objective: This retrospective study aims to explore the effect of silver nanoparticles with thermoplastic polyurethane (TPU/NS) on the rehabilitation of diabetic patients with open fracture of lower extremities.

Methods: Diabetic patients ($n = 98$) with open fracture of lower extremities treated in our hospital were analyzed retrospectively from June 2015 to December 2021. TPU/NS nanocomposites were prepared for postoperative treatment of diabetic patients with open fracture of lower extremities. First, the cultured *Staphylococcus aureus* and *Escherichia coli* were used to test the antibacterial effect of TPU/NS dressing *in vitro*. After using TPU/NS dressing (observation group) and traditional dressing (control group), the inflammatory reaction, clinical treatment, functional rehabilitation, and adverse reactions in patients were compared.

Results: TPU/NS dressing effectively inhibited the growth of bacteria with a minimum inhibitory concentration of 2 μg/mL. The usage of TPU/NS dressing reduced the inflammatory reaction by reducing positive rate of bacteria after the dressing on the seventh day postoperatively. Besides, the times of dressing, stopping time of wound exudation, wound healing time, length of hospital stay, and VAS score in the observation group were lower than those in the control group; the incidence of adverse reactions after treatment was lower in the observation group as compared with the control group (17.07% vs. 35.09%). Meanwhile, the functional rehabilitation and life quality of patients in the observation group were better TPU/NS dressing treatment.

Conclusion: TPU/NS dressing has the function of promoting the postoperative recovery of patients by inhibiting the bacterial infection of the wound, thus improving the limb function and life quality. As a result, there was a tremendous potential to apply the

constructed TPU/NS membrane to diabetic patients with open fractures, especially those with soft tissue injury.

Keywords: nano-silver, open fracture, diabetes mellitus, rapid rehabilitation, postoperative recovery

INTRODUCTION

Poorly controlled diabetes mellitus (DM), a common metabolic disease, negatively affects outcomes associated with several lower extremity orthopedic conditions and complications including fractures (1, 2). Moreover, higher baseline fracture risks in both type I (T1MD) and type II diabetes (T2MD) were reported to result in a higher overall incidence of fractures in women (3). There was an expected rise to 366 million individuals with DM by 2030 worldwide; therefore, the incidence of open fractures of the lower limb is also on the rise (3, 4). The wounds have the characteristics of foreign body pollution, serious tissue defects, and poor blood supply, which are easily associated with infection, especially in patients with diabetes (5). If wound infection occurs after fixation surgery, it may lead to delayed healing, multiple debridements, bone and soft tissue defects, and joint stiffness, resulting in permanent loss of function and even amputation (6, 7).

It is generally believed that most of the pathogens causing the infection are introduced during injury or surgery (8). Infection means that there are sufficient numbers of toxic microorganisms, which can destroy the local defense mechanism of patients (9). Once the bacteria invade, any given systemic antibiotics are difficult to play the effective roles (10). Therefore, we are looking for a postfracture wound dressing to effectively prevent infection of fracture wounds.

Nanosilver (NS) as one type of excellent antibacterial agent has strong and broad-spectrum antiviral activity against both Gram-positive and -negative bacteria, including multiple drug tolerance bacteria, for example, methicillin-resistant *Staphylococcus aureus* (MRSA) (11). What is more, there is some proposal that NS suppressed bacteria *via* various mechanisms, such as cell membrane destruction, DNA replication interference, and respiratory function inhibition without causing drug resistance (12). Therefore, NS may be an appropriate antibacterial agent contained in biological materials. However, choosing a suitable wound dressing is still a question that needs to be explored (13). Thermoplastic polyurethane (TPU) is a type of biocompatible and biodegradable elastomer that has been approved by the Food and Drug Administration (FDA) and has been widely used in biomedical sciences (14), which does not only display significant chemical stability but also good mechanical behavior (15). These excellent properties indicate that TPU has the potential to become a kind of wound dressing (16).

In this study, prepared TPU/NS antibacterial wound dressings were applied to the postoperative wounds of open fracture patients with DM to observe and analyze its effect on rehabilitation and pain improvement.

MATERIALS AND METHODS

Clinical Information

The clinical data of patients with open fractures of lower limbs treated in our hospital from June 2015 to December 2021 were retrospectively analyzed. Inclusion criteria are as follows: (1) the clinical symptoms and imaging examination met the diagnostic criteria in *Guidelines on Diagnosis and Treatment of Open Fractures in China (2019 Edition)* (17); (2) DM was confirmed in line with the *Diagnosis and Classification of Diabetes Mellitus published by* American Diabetes Association (18); (3) all patients had new lower limb fractures and met the surgical treatment standards; (4) Gustilo grade: type II and type IIIA; (5) age > 18 years. Exclusion criteria are as follows: (1) patients had malignant tumors and pathological fracture; (2) wound debridement of patients were in grade C; (3) patients had coagulation dysfunction, vascular diseases, and autoimmune diseases; (4) patients had diabetic ulcers; (5) patients had mental disorders, cognitive dysfunction, or Alzheimer's disease; (6) patients had renal or severe cardiopulmonary dysfunction; (7) patients were allergic to nanosilver; (8) patients had a preoperative infection; and (9) patients whose soft tissues hardly be second-stage sutured even if skin- muscle flap transfer, free skin grafting nor vacuum suction device. A total of 98 patients were included, including 59 males and 39 females. Their average age was 56.22 ± 19.53 years. The patients were divided into an observation group (using TPU/NS dressing, 41 cases) and a control group (using traditional dressing coated with benzalkonium chloride or iodophor, 57 cases) according to propensity score matching (PSM). All patients agreed to participate in the experiment and signed informed consent. This study has been approved by the hospital ethics committee, and it complies with the Declaration of Helsinki.

Preparation of TPU/NS

TPU membrane (Lubrizol, USA) placed into dopamine (DA) (Sangon, Shanghai, China) solution was soaked at 25°C for 20 h. During this period, membrane color turned from light white into dark brown. Then, the DA-coated film was placed into a 5 mM $AgNO_3$ solution at 25°C for avoiding light for 6 h. At last, ion water was used to wash the sample twice followed by stoving at a temperature of 45°C lasting 4 h to obtain TPU/NS dressings. Scanning electron microscopy (SEM, Crossbeam 340, Zeiss, Germany) was adopted to observe the morphology of original TPU and TPU/NS films and energy-dispersive X-ray spectroscopy (EDS) was used to conduct compositional analysis. ImageJ software was adopted to measure silver nanoparticles' average pore size, porosity, and diameter, and two independent researchers read the data.

Antibacterial Properties of TPU/NS *In Vitro*

S. aureus (ATCC6538, Shanghai Huzheng Biotechnology Co., Ltd, China) and *Escherichia coli* (CICC10662, Shanghai Huzheng Biotechnology Co., Ltd) are common Gram-positive and Gram-negative bacteria in nosocomial infection, respectively, which are used to detect antibacterial properties of TPU/NS dressing. *S. aureus* and *E. coli* were cultured in a 24-well plate with bacterial liquid media containing tryptic soy broth (BD Bacto, Becton, Dickinson and Company, USA; pH 7.3) in a microorganism incubator (51028133, Thermo Fisher, USA) at 37°C and 5% CO_2 according to a previous study (19). The cultured bacteria were adjusted to a concentration of 1×10^6 CFU/ml. The diluents of *S. aureus* and *E. coli* were divided into a blank control group and a TPU/NS group, in which a small number of TPU/NS nanocomposites were added to the TPU/NS group. At the same time, the synthetic TPU/NS solution was diluted into different concentration gradients by the double dilution method, which were added to the Petri dish with bacteria (1×10^6 CFU) for detecting the minimum inhibitory concentration. The activation states of *S. aureus* and *E. coli* were tested by a live/dead bacterial viability kit (AAT-B22411, AAT Bioquest, USA). In this kit, MycoLight 520 solution and propidium iodide (PI) solution were used for viable (green) and nonviable (red) bacteria, respectively.

Therapeutic Method

After fully wound debridement, appropriate fixation methods were adopted for the fracture, and the wound shall be sutured and disinfected. For the wound that could not be sutured in the first stage, the suture or skin grafting shall be performed after the infection was controlled in the second stage. Antibiotics were given half an hour before the operation, which were used three consecutive days after the operation. The additional usage of antibiotics was based on the wound infection. In addition, all patients were given health education about DM, as well as the customize diabetes diet program by the nutrition department. Meanwhile, daily blood glucose monitoring and medication guidance should be implemented. In terms of postoperative wound dressing, the patients were sutured and disinfected routinely on the open wounds. The patients in the control group were treated with traditional dressings coated with benzalkonium chloride or iodophor, while those in the observation group with TPU/NS dressings. During the dressing on the seventh day postoperatively, the exudates from the wounds of the patients should be extracted for bacterial culture, then the wound shall be disinfected with iodophor, and then, the corresponding dressings were used. The outcome indicators were evaluated 2 months after the operation.

Inflammatory Response Test

Before treatment and 1, 3, 7, and 10 days after treatment, two tubes of 5 ml of venous blood were taken from each patient, and one tube was centrifuged at 3,000 rpm to obtain serum. Levels of white blood cell (WBC), neutrophils (NEU%), and erythrocyte sedimentation rate (ESR) were measured by an automatic blood cell analyzer (XN-2000, XISEN Meikang), C-reactive protein (CRP) by the automatic biochemical analyzer (AU-680, Beckman), as well as concentrations of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were detected by an automatic chemiluminescence immunoanalyzer (DXI-800, Beckman). If the above indicators had a downward trend, it was considered an "improved inflammation status." During the dressing on the seventh day postoperatively, the wound secretion was taken for bacterial culture, and the positive rates of bacterial between the two groups were compared.

Evaluation of Clinical Treatment and Adverse Reactions

The clinical recovery of patients is evaluated through the times of dressing, stopping time of wound exudation, wound healing

TABLE 1 | General information table.

Factor	Observation group ($n = 41$)	Control group ($n = 57$)	$\chi 2$	*P*
Gender			0.082	0.775
Male	24 (58.54%)	35 (61.40%)		
Female	17 (41.46%)	22 (38.60%)		
Age (years)			0.674	0.412
≤55	16 (39.02%)	27 (47.37%)		
>55	25 (60.98%)	30 (52.63%)		
BMI (kg/m^2)			2.421	0.120
≤23	13 (31.71%)	27 (47.37%)		
>23	28 (68.29%)	30 (52.63%)		
Gustilo grade			0.917	0.338
II	22 (53.66%)	25 (43.86%)		
III A	19 (46.34%)	32 (56.14%)		
Wound location				
Lateral	17	28		
Medial	13	15		
Bilateral	11	14	0.595	0.743
Limb distribution				
Left	20	32		
Right	21	25	0.519	0.471
Smoking history			1.543	0.214
Yes	20 (48.78%)	35 (61.40%)		
No	21 (51.22%)	22 (38.60%)		
History of alcoholism			0.231	0.631
Yes	8 (19.51%)	9 (15.79%)		
No	33 (80.49%)	48 (48.21%)		
Cultural level			2.211	0.137
High school and above	22 (53.66%)	39 (68.42%)		
Below high school	19 (46.34%)	18 (31.58%)		
Wound area (cm^2)	45.26 ± 5.16	44.77 ± 6.55	0.398	0.691
FBG (mmol/L)	9.82 ± 3.19	9.21 ± 3.02	0.963	0.338
HbA1c (%)	8.19 ± 1.89	8.57 ± 1.71	−1.038	0.302

time, and length of hospital stay. The visual analog scale (VAS) (20) score is used to evaluate the pain degree of patients' wounds. The lower the score, the lower the pain. The adverse reactions of the two groups were recorded, including wound infection, delayed healing, scar hyperplasia, soft tissue necrosis, and fracture pain.

Comparison of Functional Rehabilitation

The functional assessment scale (FIM) (21) was used to evaluate the functional rehabilitation of the two groups of patients, which was divided into self-care function, action, and cognitive function. The higher the score, the better the lower limb function recovery. In terms of life quality, the Orthopedic Quality of Life (SF-36) questionnaire (22) was used to evaluate patients' quality of life. The questionnaire contained some items such as physical function, emotional function, role function, social function, and other dimensions. Each dimension was expressed by 0–100 points; the higher the score, the better the patients' quality of life.

Statistical Methods

SPSS 20.0 (SPSS, Chicago, IL, USA) and GraphPad Prism 8.0 (GraphPad Software, San Diego, California, USA) were used to analyze data and draw the statistical picture. Measurement data presented as mean ± standard deviation (SD) were compared using a *t*-test between two groups, and enumeration data were compared using a χ^2 test. A value of $P < 0.05$ indicated that this difference showed statistical significance.

RESULTS

Comparison of General Information of Both Group Patients

The baseline information of the patients from the observation group ($n = 41$) and the control group ($n = 57$) is shown in **Table 1**. There were no remarkable differences in gender, age, BMI, Gustilo grade, wound location, limb distribution, wound area, FBG, HbA1c, smoking history, history of alcoholism, and cultural level between the two groups (all $P > 0.05$)

Evaluation of Bacteriostasis of TPU/NS Dressing

Due to the exposure of soft tissue and bone, the wound of open fracture is very easy to be complicated with infection. Effectively killing bacteria and reducing viable bacteria were important methods to promote rehabilitation of patients and prevent related complications. In this study, *S. aureus* and *E. coli* were selected to study the antibacterial effect of TPU/NS dressing. We observed the characteristics of TPU/NS by SEM. The results showed that TPU/NS nanoparticles were evenly distributed and well dispersed, with a spherical shape of 95 nm (**Figure 1A**). Meanwhile, TPU/NS dressing could reduce viable (green) bacteria with increased nonviable (red) bacteria (**Figures 1B–I**), and the minimum inhibitory concentration of TPU/NS was 2 μg/ml. The above results show that TPU/NS dressing can effectively use silver ions to achieve excellent antibacterial properties.

Comparison of Serum Inflammatory Reaction and Positive Detection Rate of Wound Bacteria

Inflammatory factors can promote the occurrence of the inflammatory cascade, which is an important indicator of the degree of inflammation. It was found that the TPU/NS dressing could reduce WBC, NEU%, CRP, IL-6, and TNF-α in serum as compared to the control dressing without affecting ESR between both groups (**Figures 2A–F**). In addition, TPU/NS dressing suppressed the positive detection rate of bacteria (4.88% vs. 12.28%) (**Figure 2G**). The above results suggested that TPU/NS dressing can better reduce the level of inflammatory factors to prevent the occurrence of infection.

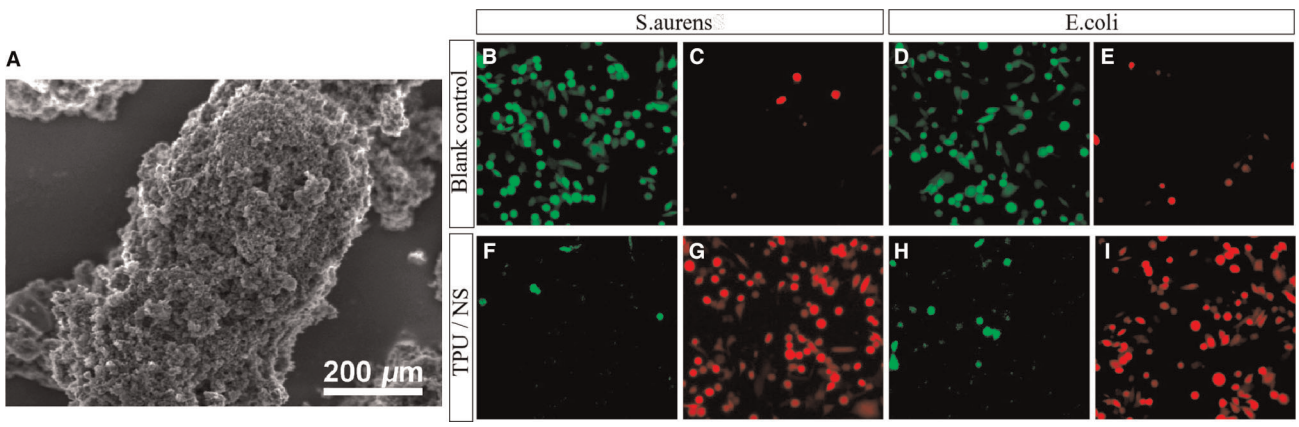

FIGURE 1 | Characterization and antibacterial properties of TPU/NS. (**A**) Scanning electron microscopy image of TPU/NS. (**B,C**) Viable and nonviable staining of cultured *S. aureus* (**B,C**) and *E. coli* (**D,E**) 12 h in the blank control group. (**F–I**) Viable and nonviable staining of cultured *S. aureus* (**F,G**) and *E. coli* (**H,I**) 12 h after adding TPU/NS nanocomposites.

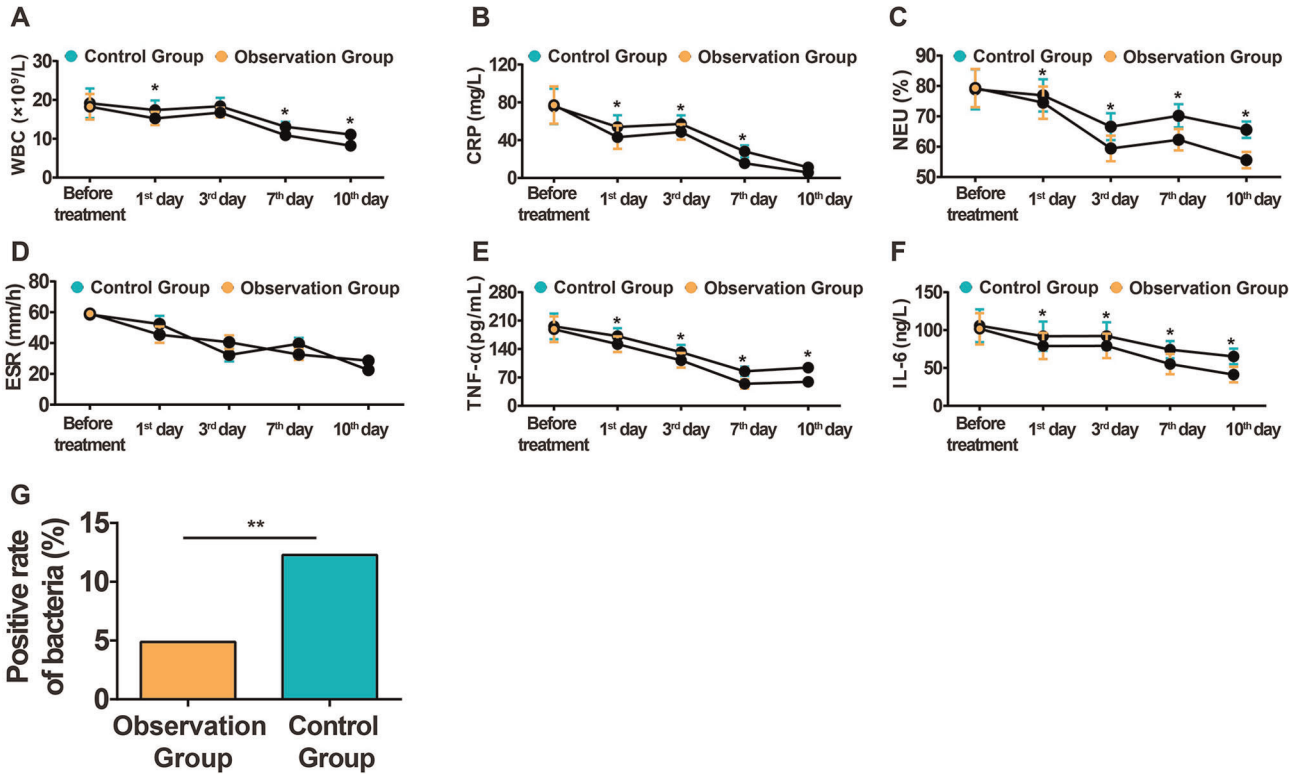

FIGURE 2 | Comparison of inflammatory reaction in both groups. (**A**) Changes in the WBC level in blood. (**B**) Changes in the CRP level in serum. (**C**) Changes in the NEU% level in blood. (**D**) Changes in the ESR level in blood. (**E**) Changes in the TNF-α level in serum. (**F**) Changes in the IL-6 level in serum. (**G**) Bacterial positive detection rate on the 7th day after the operation. $^{*}P < 0.05$, $^{**}P < 0.01$.

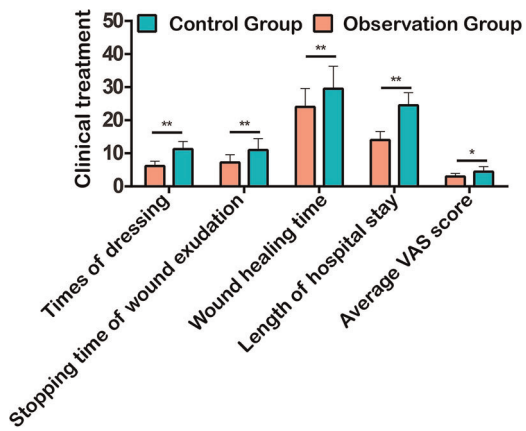

FIGURE 3 | Comparison of clinical treatment in terms of times of dressing, stopping time of wound exudation, wound healing time, hospital stay, and average VAS score. $^{*}P < 0.05$, $^{**}P < 0.01$.

Comparison of Clinical Treatment

The clinical treatment of patients was evaluated from the aspects of the times of dressing, stopping time of wound exudation, wound healing time, hospital stay, and average VAS score. The study showed that the above indexes in the observation group were significantly lower than those in the control group (**Figure 3**), suggesting that the use of TPU/NS dressing effectively promoted patients' rehabilitation and reduced the pain of wounds.

Comparison of Adverse Reactions After Treatment

The incidence of adverse reactions after treatment was evaluated in terms of wound infection, delayed healing, scar hyperplasia, soft tissue necrosis, and fracture pain. The study found that the total incidence of the above adverse reactions in the observation group was significantly lower than that in the control group (17.07% vs. 35.09%, **Table 2**), suggesting that the use of TPU/NS dressing can better inhibit the proliferation of bacteria and promote wound recovery.

Comparison of Functional Rehabilitation and Life Quality

After treatment, the recovery indexes of low limb function in self-care function, cognitive function, and action of patients in the observation group were significantly better than those in the control group (**Figure 4A**), and the physical function, emotional function, role function, social function, and other

TABLE 2 | Comparison of postoperative complications.

Group	Cases	Wound infection	Delayed healing	Scar hyperplasia	Soft tissue necrosis	Pain at the fracture site	Total incidence
Observation group	41	2 (4.88)	2 (4.88)	1 (2.44)	1 (2.44)	1 (2.44)	7 (17.07)
Control group	57	7 (12.28)	5 (8.77)	3 (5.26)	3 (5.26)	2 (3.51)	20 (35.09)
$\chi 2$							3.877
P							0.049

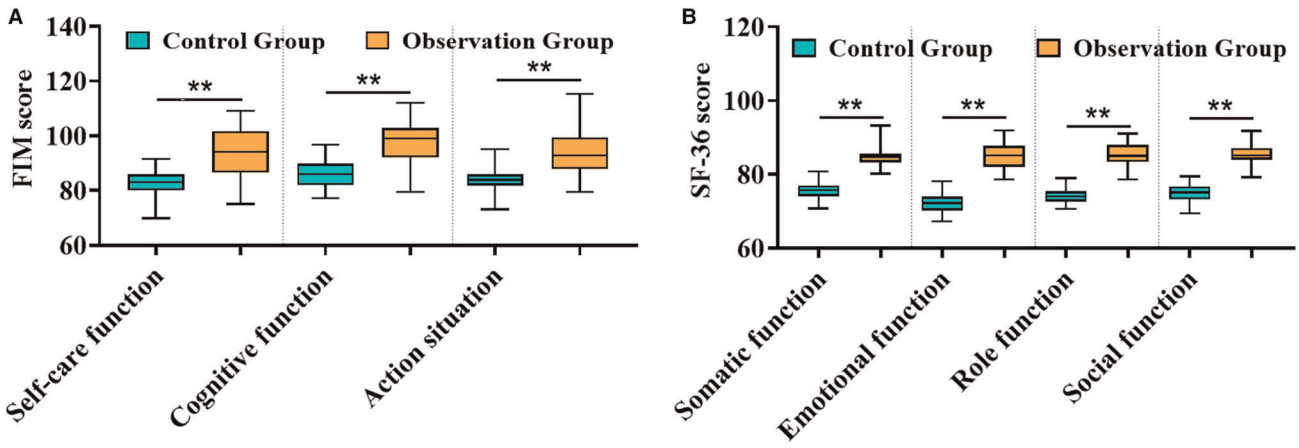

FIGURE 4 | Comparison of rehabilitation between both groups. (**A**) FIM score. (**B**) SF-36 score. $^{**}P < 0.01$.

dimensions of their life quality were remarkably higher than the other (**Figure 4B**), suggesting that TPU/NS dressing is more conducive to wound recovery to better promote the rehabilitation of patients.

DISCUSSION

During the treatment of open fractures, patients often had seriously wound due to high-violence injury, and tension blisters and wound infection are easy to appear in the later stage, resulting in the adverse impact on the recovery of postoperative wounds, the long treatment cycle, as well as poor prognosis (23). In addition, during the treatment, the degree of pain in the wound is also a key factor affecting the rehabilitation effect. Although the pain can promote blood circulation in patients, excessive pain was reported to have an adverse impact on postoperative rehabilitation (24). Therefore, taking effective prevention and treatment for infection after the operation has important clinical significance for postoperative recovery and suppression of complications (25).

With the continuous development of nanomedical technology in the past decade, nanodressings have gradually been applied in clinical practice (26). Bacterial infections have long been a thorny issue in clinical anti-infective treatment, and NS as a new type of antibacterial agent has the advantages of high antibacterial activity and a broad antibacterial spectrum without drug resistance (27). Due to the exposure of soft tissue and bone in the wound of open fracture, it is very easy to be complicated with infection. Effectively killing bacteria and reducing viable bacteria are important methods to promote patients' rehabilitation and prevent related complications. Therefore, NS dressing brings hope to the clinical postoperative anti-infection. The NS dressing using a TPU membrane as a carrier processes pure silver into elemental silver particles with a particle size of about 10 nm and loads them on the TPU membrane. In the antibacterial property experiments, it was found that TPU/NS dressing had a significant antibacterial effect in patients accompanied by the reduced inflammatory reaction, the improved functional rehabilitation, and the alleviated postoperative wound pain. Subsequently, we also tested the positive rate of bacteria in the two groups during the dressing on the seventh day postoperatively. The results showed that the positive rate in the observation group was significantly lower. This also suggests that the application of the nanosilver dressing in open fracture postoperative patients can effectively reduce wound bacteria.

A previous study has pointed out that, unlike the single target effect of antibiotics, NS has a variety of ways to inhibit bacteria (28). For example, it can cause obvious morphological changes in the bacteria by attaching to the surface of bacteria, destroying its cell wall and cell membrane, causing a large

number of substances required for maintaining bacterial metabolism to leak, and even causing bacteria to lyse and die. In addition, it has been pointed out in other literature studies that nanosilver can react with enzymes or proteins containing sulfur groups, thus affecting the metabolism of bacteria and at the same time collapsing proton power, leading to the death of bacteria (29).

We compared the times of dressing, stopping time of wound exudation, length of hospital stay, and wound healing time between the two groups, and the results showed that the clinical treatment of the observation group was better with a lower incidence of complications than that of the control group, suggesting that TPU/NS can effectively promote patients' recovery due to the reduction of the positive rate of bacteria. Recently, studies have pointed out that one of the reasons for the outstanding antibacterial properties of nanosilver is that it has a quantum size effect, meaning that the antibacterial effect of nanosilver is related to its particle size. The smaller the particle diameter, the stronger the antibacterial effect. This is the reason why the antibacterial effect of nanosilver in the clinic is stronger than that of ordinary anionic antibacterial agents (30, 31). Finally, we compared both groups on the quality of life, and the results showed that the observation group was under a remarkably higher quality of life, indicating that optimized TPU/NS dressing after the operation can reduce the psychological and physiological trauma stress response of patients to reduce complications, shorten hospital stay, reduce the risk of readmission, and reoperation rate, thus promoting the recovery of patients as soon as possible.

However, in this study, we did not set up a blank control group using the TPU membrane alone, and prospective observation was lacking, which may offset the results. In addition, the safety of TPU/NS dressings should be evaluated by determining the liver and kidney function in diabetic patients with open fractures of lower extremities, as well as serum deposition because hepatocellular damage and nephropathy were associated with diabetes (32). Furthermore, the wound-healing rate would be assessed in the future to validate our clinical results. The above shortcomings should be improved in the follow-up study.

CONCLUSION

We mixed NS into porous TPU membranes by adopting biomimetic polydopamine and then prepared a kind of wound dressing that has biocompatibility, flexibility, and antibiosis. The whole production process is simple, gentle, and environmentally friendly. TPU/NS dressing has powerful mechanical strength and great flexibility, exhibiting acceptable antibacterial activity against a variety of bacteria. We applied it to the antibacterial treatment of postoperative wounds of DM patients with joint fractures. TPU/NS dressings can lighten the postoperative pain of patients by inhibiting bacterial infection of wounds and promoting postoperative recovery of patients. Therefore, there was a tremendous potential to apply the constructed TPU/NS membrane to open fracture diabetic patients, especially those with soft tissue injury.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Sixth Medical Center of PLA General Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DZ and DCY contributed to the conception and design of the study, and manuscript writing. RFM collected clinical data of patients and prepared software for data analysis. SKN performed data analysis and interpretation. YL made contributions to figures and tables. YZ assisted in the design of the study and participated in manuscript revision. SWZ reviewed and revised the manuscript. All authors read and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Study on Influencing Factors Analysis of Gastric Tube Insertion Length and Construction of Estimation Method

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Background: Influenced by individual differences, the depth of gastric tube placement is often different. Clinically, it is necessary to seek a simple and accurate gastric tube insertion scheme to improve the clinical efficacy of indwelling gastric tube.

Materials and Methods: A total of 100 adult patients undergoing transesophageal manometry *via* nose were included in the study. The *in vivo* length (NCL) of apex-cardia was measured. At the same time, we entered our institutional database, summarized the clinical data of 100 patients, and analyzed the risk factors affecting NCL using stepwise regression analysis.

Results: The NCL length scores of patients with different gender, age, marital status, height, weight, BMI, sitting height, sternum length, hairline-xiphoid process, nose tip-earlobe-xiphoid process and earlobe-xiphoid process were statistically significant ($P < 0.05$). Height, sitting height, gender, BMI and earlobe-xiphoid process were the factors that affected the NCL length score ($P < 0.05$). The prediction equation of the estimation method of gastric tube insertion length was as follows: NCL length score = 39.907 + 2.909× height +0.865× sitting height. Adjust R^2 to 0.506. NCL was positively correlated with height and sitting height. Among them, the correlation with height ($r = 0.711$, $P < 0.001$) and sitting height ($r = 0.397$, $P < 0.001$).

Conclusion: Height, sitting height, gender, BMI and earlobe-xiphoid process were the factors that affected the score of NCL length. There was a significant positive correlation between height, sitting height and NCL length. On this basis, the length of nasogastric tube insertion could be estimated.

Keywords: gastrointestinal decompression, gastric tube insertion, influencing factors, estimation method, insertion length

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INTRODUCTION

Refers to inserting the catheter into the gastrointestinal tract through the nasal cavity or oral cavity, and providing the patients with the necessary food, nutrient solution, water and drugs through the catheter, or performing gastric lavage and gastrointestinal decompression through the catheter, which is a routine nursing operation with wide clinical application (1, 2). Indwelling gastric

tube can not only supply the necessary nutrition for clinical patients, but also achieve the effect of gastrointestinal decompression. Compared with foreign countries, only a small number of studies in China have explored the factors affecting the length of gastric tube placement in adults and its prediction equation through correlation or regression analysis. The existing guidelines also fail to address such issues as the specific length to be extended of gastric tube insertion, and whether it is safe to extend the insertion length. Although the length from the hairline to the xiphoid process or from the earlobe to the xiphoid process is often used as the insertion depth in clinic, the insertion depth is often not the same due to individual differences of patients, so the accuracy of this method has always been questioned (3, 4). Therefore, in this study, the *in vivo* length (NCL) of nasal tip–cardia in adults used as a dependent variable to explore its relationship with other clinical data such as gender, age, height, and weight. At the same time, the prediction equation with optimal stability and accuracy was established based on the above results, in order to provide a theoretical basis for the estimation of the length of gastric tube placement.

MATERIALS AND METHODS

General Information

The convenience sampling method was used to select adult patients who required transesophageal manometry *via* nose or gastroscopy *via* mouth in a 3A hospital in Changsha from March 2020 to February 2022.

Inclusion criteria: (1) Age $\geq$ 18 years old. (2) Conscious, willing to undergo gastroscopy or esophageal manometry, and willing to participate in this study. (3) There is no obvious thoracic deformity, spinal deformity and developmental abnormality. (4) There is no previous operation history of upper digestive tract such as esophagus and stomach. (5) Patients with the course of disease less than three months.

Exclusion criteria: (1) Patients whose esophageal dentate line was found to be vague by gastroscopy. (2) Patients who had obvious vomiting during gastroscopy and failed to complete gastroscopy. (3) Gastroscopy shows esophageal abnormalities, affecting the measurement of esophageal length. (4) esophageal manometry shows severe disorder of esophageal movement. (5) Those who cannot lie flat or sit upright due to scleroderma, neck disease or other reasons.

This study was approved by the Hospital Ethics Committee with the patient's consent and informed consent form signed.

Research Method

The length of gastric tube insertion was the *in vivo* length from the tip of the nose to the cardia. The manometer was placed into the esophagus through the nasal cavity, and the position of the front end of the manometer in the esophagus was determined according to the waveform obtained from the pressure measurement. Read the scale when the front end of the manometer reaches the junction of esophagus and stomach. This distance is the *in vivo* length of nasal tip–cardia, and record as NCL (5).

Clinical data of all patients were collected, including gender, age, marital status, height, weight, BMI of the patients before gastric tube insertion, whether the gastric tube was indwelling for the first time, sitting height, sternal length, diagnosis, chest circumference, waist circumference, hip circumference, xiphoid process-navel length, hairline-xiphoid process, nasal tip-earlobe-xiphoid process, earlobe-xiphoid process and the material of gastric tube.

Statistical Method

SPSS 21.0 is used to establish the database and analyze the data, and the measurement data is described by ($\overline{x} \pm s$). Count data use cases and percentage descriptions, and compare between groups by independent sample *t* test and one-way ANOVA. Pearson correlation analysis was used to analyze the correlation between NCL length score, height and sitting height. The variables with statistically significant differences between groups after *t*-test and Chi-square test were used as independent variables, and stepwise regression linear analysis was carried out, and the estimation equation of gastric tube insertion length was established. All analyses are based on 95% confidence intervals. $P < 0.05$ is statistically significant.

RESULT

General Information

A total of 100 patients were included according to the inclusion and exclusion criteria of research subjects. There 27 females and 73 males. The mean age was (44.27 ± 14.86) years old. There were 55 cases of achalasia of cardia, 7 cases of abdominal pain, 16 cases of Crohn's disease, 9 cases of ulcerative colitis, 8 cases of dysphagia and 5 cases of gastrointestinal bleeding.

Single Factor Analysis of NCL Length Score

As shown in **Table 1**, the scores of NCL length among patients with different gender, age, marital status, height, weight, BMI, sitting height, sternal length, the length from hairline to xiphoid process, the length of nasal tip–earlobe–xiphoid process, and the length from earlobe to xiphoid process were statistically significant ($P < 0.05$). The scores of NCL length among patients with different diagnoses, the first indwelling gastric tube, history of hypertension, chest circumference, waist circumference, hip circumference, and the length from xiphoid process to navel, and gastric tube material were not significant ($P > 0.05$).

Variable Assignment

The length of NCL is always divided into dependent variables, and the items in general data that affect the length of NCL are included in the regression equation as independent variables. Independent variable assignment is shown in **Table 2**.

TABLE 1 | Single factor analysis of NCL length score.

Clinical features	*n*	Constituent ratio (%)	NCL (score)	*t*/*F*	*P*
Gender					
Female	27	27.00	45.57 ± 2.77	3.624	0.001
Male	73	73.00	48.55 ± 3.92		
Age (years)					
≤27	18	18.00	45.68 ± 4.29	2.53	0.045
28–39	23	23.00	49.07 ± 3.56		
40–49	21	21.00	47.26 ± 3.33		
50–59	23	23.00	48.66 ± 4.15		
60–78	15	15.00	47.44 ± 3.24		
Marital status					
Married	82	82.00	48.19 ± 3.64	2.564	0.012
Unmarried	18	18.00	45.68 ± 4.29		
Disease type					
Cardiac achalasia	55	55.00	47.80 ± 3.94	1.05	0.392
Abdominalgia	7	7.00	44.84 ± 2.48		
Crohn's disease	16	16.00	48.79 ± 4.81		
Ulcerative colitis	9	9.00	47.64 ± 3.23		
Dysphagia	8	8.00	48.24 ± 2.58		
Gastrointestinal bleeding	5	5.00	47.10 ± 4.83		
First indwelling gastric tube					
Yes	79	79.00	47.51 ± 3.76	0.329	0.745
No	21	21.00	47.80 ± 2.84		
History of hypertension					
Yes	38	38.00	47.91 ± 3.74	1.400	0.165
No	62	62.00	46.86 ± 3.58		
Height (cm)					
≤160	32	32.00	44.74 ± 2.88	28.53	<0.001
161–170	42	42.00	47.62 ± 3.23		
171–180	22	22.00	51.30 ± 1.99		
181–183	4	4.00	53.45 ± 2.21		
Weight (kg)					
≤50	28	28.00	45.76 ± 2.72	5.66	0.001
51–59	21	21.00	47.10 ± 4.05		
60–69	38	38.00	49.20 ± 3.32		
70–106	13	13.00	48.78 ± 5.25		
BMI (kg/m^2)					
≤25	61	61.00	45.52 ± 3.16	9.569	0.002
>25	39	39.00	51.22 ± 2.45		
Chest measurement (cm)					
≤80	20	20.00	46.57 ± 4.08	1.49	0.223
81–89	43	43.00	48.40 ± 3.44		
90–99	33	33.00	47.36 ± 4.32		
100–112	4	4.00	49.67 ± 1.07		
Waistline (cm)					
≤70	27	27.00	46.57 ± 3.86	1.64	0.185
71–79	31	31.00	48.59 ± 3.49		
80–89	31	31.00	47.55 ± 4.11		
90–112	11	11.00	48.77 ± 3.83		
Hipline (cm)					
≤80	12	12.00	47.70 ± 3.14	1.85	0.143
81–89	39	39.00	46.83 ± 3.87		
90–99	45	45.00	48.28 ± 4.00		
100–115	4	4.00	50.73 ± 2.54		
Sitting height (cm)					
≤80	16	16.00	45.57 ± 3.75	11.78	<0.001
81–89	42	42.00	46.47 ± 4.15		
90–99	28	28.00	50.75 ± 1.91		
100–137	14	14.00	48.04 ± 2.25		
Sternal length (cm)					
≤15	11	11.00	45.72 ± 5.19	3.09	0.031
16–19	44	44.00	47.30 ± 3.60		
20–21	25	25.00	47.85 ± 3.67		
22–28	20	20.00	49.70 ± 3.27		
The length from xiphoid process to navel (cm)					
≤15	23	23.00	47.09 ± 2.88	0.64	0.529
16–20	70	70.00	47.85 ± 3.82		
21–47	7	7.00	48.86 ± 6.77		
The length from hairline to xiphoid process (cm)					
≤45	33	33.00	46.06 ± 3.83	5.72	0.005
46–55	59	59.00	48.39 ± 3.62		
56–59	8	8.00	49.93 ± 3.72		
The length of nasal tip–earlobe–xiphoid process (cm)					
≤50	47	47.00	45.98 ± 3.67	11.45	<0.001
51–55	43	43.00	49.14 ± 3.33		
56–64	10	10.00	50.03 ± 3.50		
The length from earlobe to xiphoid process (cm)					
≤35	40	40.00	45.46 ± 3.73	15.27	<0.001
36–38	38	38.00	48.99 ± 3.30		
39–47	22	22.00	49.74 ± 2.95		
Gastric tube material					
Silica gel	57	57.00	45.17 ± 2.98	1.65	0.197
Fukai gastric tube	31	31.00	46.28 ± 2.41		
Improved gastric tube	12	12.00	45.85 ± 2.69		

Multiple Stepwise Linear Regression Analysis of Influencing Factors of NCL Length Score

As shown in **Table 3**, height, sitting height, sex, BMI and the length from earlobe to xiphoid process are the factors that affect NCL length score ($P < 0.05$). According to the regression principle, an equation is established. At the same time, meaningful variables are screened according to regression analysis. The prediction equation of the gastric tube insertion length estimation method in this study is established as follows: NCL length score = 39.907 + 2.909× height +0.865× sitting height. R^2 is 0.506, and the regression equation can explain 50.6% variation degree of dependent variable.

TABLE 2 | Assignment of influencing factors of NCL length score.

Variable	Assignment
Dependent variable	
NCL	Enter as actual value.
Independent variable	
Gender	Female = 1, Male = 2
Age (years)	≤27 = 1,28–39 = 2,40–49 = 3,50–59 = 4,60–78 = 5
Marital status	Married = 1,Unmarried = 2
Height (cm)	≤160 = 1,161–170 = 2,171–180 = 3,181–183 = 4
Weight (kg)	≤50 = 1,51–59 = 2,60–9 = 3,70–106 = 4
BMI (kg/㎡)	≤25 = 1,>25 = 2
Sitting height (cm)	≤80 = 1,81–9 = 2,90–99 = 3,100–137 = 4
Sternal length (cm)	≤15 = 1,16–19 = 2,20–21 = 3,22–28 = 4
The length from hairline to xiphoid process (cm)	≤45 = 1,46–55 = 2,56–59 = 3
The length of nasal tip–earlobe–xiphoid process (cm)	≤50 = 1,51–55 = 2,56–64 = 3
The length from earlobe to xiphoid process (cm)	≤35 = 1,36–38 = 2,39–47 = 3

TABLE 3 | Multiple stepwise linear regression analysis of influencing factors of NCL length score.

Influencing factor	*B*	*SE*	*β*	*T*	*P*
Constant	39.907	0.911	_	43.782	0.000
Height	2.909	0.339	0.632	8.593	0.000
Sitting height	0.865	0.309	0.206	2.798	0.006
Gender	−1.803	0.675	−0.208	−2.673	0.009
Age	−0.104	−1.719	0.089	−0.175	0.896
Marital status	0.015	0.236	0.814	0.024	0.855
BMI	3.499	0.579	0.444	6.047	0.000
Sternal length	0.003	0.048	0.962	0.005	0.670
The length from hairline to xiphoid process	−0.165	−1.844	0.068	−0.187	0.408
The length of nasal tip–earlobe–xiphoid process	−0.176	−1.309	0.194	−0.134	0.184
The length from earlobe to xiphoid process	0.257	0.089	0.196	2.879	0.005

Correlation Analysis Between Height, Sitting Height and NCL

As shown in **Table 4** and **Figure 1**, NCL was positively correlated with height and sitting height. Among them, the correlation with height ($r = 0.711$, $P < 0.001$) and sitting height ($r = 0.397$, $P < 0.001$).

DISCUSSION

Gastric tube is a common drainage tube after surgery, its clinical effect has been widely recognized. The shape and size of the stomach are affected by such factors as the gastric volume, the stage of food digestion, the intestinal condition, and the body position. Therefore, although there are many studies on the estimation method of the insertion length of gastric tube in China and abroad, their views have not yet been unified. The lengths of gastric tube recommended by different institutes were different, and the common clinical values include 45–55 cm, 55–65 cm, 55–68 cm, and 55–70 cm (6–8). In addition, the commonly used body surface measurement methods for the length of gastric tube in clinic include the length from nasal tip to earlobe to xiphoid process (NEX), the length from nasal tip to earlobe to navel to the midpoint of xiphoid process (NEMU), the length from hairline to xiphoid process (FX), the length from hairline to navel (FU), and the length from hairline to navel to the midpoint of xiphoid process (FMU) (9–12). However, the determination of the above method is mainly based on the clinical experience of physicians and their observation of the treatment status quo, which is greatly affected by individual differences and has a large possibility of operation error.

The study found that if the actual length of gastric tube placement was taken as the dependent variable *Y*, the value of *Y* would not only be affected by such independent variables as height and weight as defined in the study, but also by the instability of its own endpoint. Moreover, the bias of self-endpoint is difficult to control, so it is difficult to establish a relatively stable prediction equation. Therefore, it is difficult to establish a relatively stable prediction equation clinically. Different from the front end of gastric tube, the right side of cardia is wrapped in lesser omentum together with the lower

TABLE 4 | Correlation analysis of height, sitting height and NCL.

Project	NCL	
	r	*P*
Height	0.711	<0.001
Sitting height	0.397	<0.001

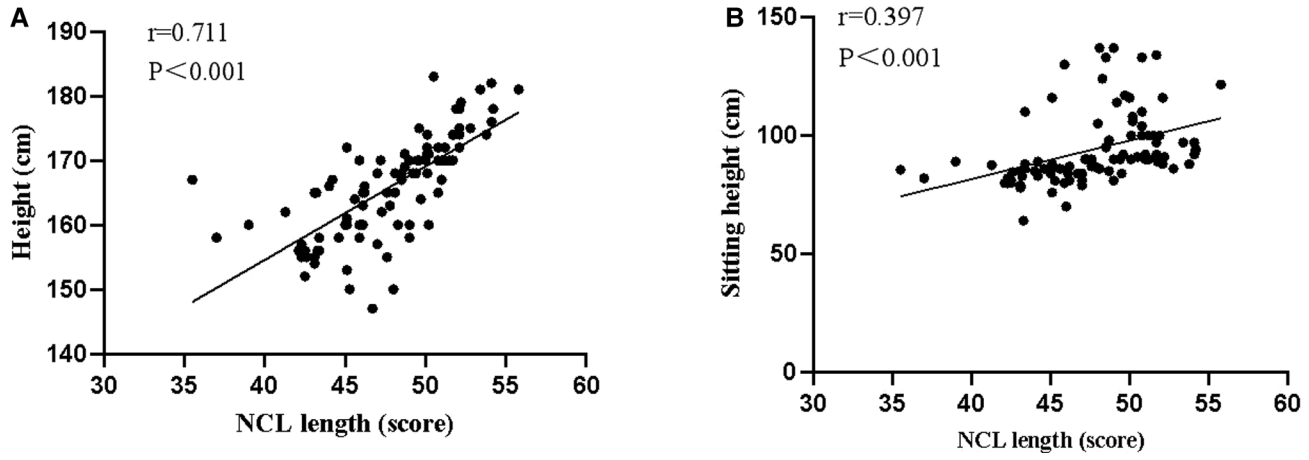

FIGURE 1 | Scatter diagram for correlation analysis of NCL length score with height and sitting height ((**A**) Correlation analysis of NCL length score and height. (**B**) Correlation analysis of NCL length score and sitting height).

end of esophagus, the front and left sides were covered by peritoneum, and the back is diaphragm esophageal ligament Therefore, although the mobility of the stomach is great, the position of the cardia is relatively fixed (13). So when discussing the length of gastric tube insertion, converting the dependent variable *Y* to the *in vivo* length from the nasal tip to the cardia can reduce the bias caused by the movement of the dependent variable's own endpoint and is more conducive to establishing a relatively stable prediction equation. On this basis, NCL was replaced in this study by the *in vivo* length of the nasal tip-cardia.

It has been suggested that the accuracy of the inserted length is closely related to the prognosis of patients, so it is necessary to analyze the factors affecting the inserted length of gastric tube. The results of this study showed that height, sitting height, gender, BMI and the length from the earlobe to the xiphoid process were the factors that affected the NCL length score ($P < 0.05$), and height, sitting height and NCL had a positive correlation. Ellett et al. based on the accuracy of children of similar age to the length of gastric tube insertion by comparing their height (ARHB), the length from tip to earlobe to xiphoid process (NEX), and the length from tip to earlobe to navel (NEMU), and found that the height (ARHB) and the length from tip to earlobe to navel (NEMU) were more accurate than the length from tip to earlobe to xiphoid process (NEX) (14). Malta et al. explored the relationship between the distance from the incisors to the gastroesophageal junction (recorded as EGD), height, the distance from the earlobe to the xiphoid process (EX), and other measured values *in vitro*, and found that height was one of the independent variables with the strongest correlation with EGD (15). Meanwhile, studies have also shown that the height is directly proportional to the length of the gastric tube placement (16), which is similar to the results of this study. The NCL values of patients with different BMI have significant differences. As the height and weight of men are generally higher than those of women, it is believed that there should be differences between men and women in the intubation length (17). Meanwhile, with height and sitting height as independent variables and NCL length as dependent variable, the regression equation was derived: NCL length score = 39.907 + 2.909× height +0.865× sitting height. This further clarified that we could estimate the length of nasogastric tube insertion based on the formula. At the same time, this formula has a certain guiding significance for early calculation of the required length of the catheter for patients, and provides a new reference method for clinical evaluation.

The shortcoming of this study was that the sample size in this study was relatively small, and the formula was not further verified. Therefore, this formula needs to be further corrected. In the future, researchers can conduct multi-center and large sample verification of the correction formula, and achieve individualized nursing operation, thereby improving the therapeutic effect of gastric tube indwelling.

CONCLUSION

In summary, height, sitting height, gender, BMI and the length from earlobe to xiphoid process are the factors affecting NCL. There is a significant positive correlation between height and sitting height and NCL. On this basis, the length of nasogastric tube insertion can be estimated.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Suplementary Material, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by This study was approved by the ethics committee of our hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HZ, HW are the mainly responsible for the writing of the article. XF is mainly responsible for research design. XC is mainly responsible for data analysis. WS is responsible for the guidance of the entire research. The corresponding author is BY, he is responsible for ensuring that the descriptions are accurate and agreed by all authors. All authors contributed to the article and approved the submitted version.

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Correlation Between Serum β2-GPI/oxLDL and the Risk of Cerebral Infarction in Patients with T2DM

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Objective: This study aims to study the correlation between serum β2-glycoprotein I (β2-GPI)/oxidized low-density lipoprotein (oxLDL) and the risk of cerebral infarction in patients with type 2 diabetes (T2DM).

Methods: From January 2019 to March 2021, 56 patients with T2DM combined with cerebral infarction were chosen as a diabetic cerebral infarction (DCI) group, and 60 patients with simple T2DM were chosen as a T2DM group. In addition, 60 healthy volunteers were recruited as a control group. The essential information of each group was collected, and the serum β2-GPI/oxLDL and inflammatory factor levels in each group were compared. The clinical factors that affect the risk of ischemic cerebral infarction in patients with T2DM were analyzed by a logistic model.

Results: Compared with the control group, the level of serum β2-GPI/oxLDL in the T2DM and DCI groups increased significantly, $P < 0.001$. Compared with the T2DM group, the serum β2-GPI/oxLDL level in the DCI group increased significantly, $P < 0.05$. The result of *Pearson's* correlation analysis showed that serum β2-GPI/oxLDL was positively correlated with total cholesterol, triglycerides, fasting blood glucose, 2-h postprandial blood glucose, glycosylated hemoglobin, interleukin-6, and tumor necrosis factor (TNF)-α (all P's < 0.05). Serum TNF-α and β2-GPI/oxLDL were independent risk variates for DCI ($P < 0.05$). Based on the receiver operating characteristic curve analysis, the values of the area under the curve for TNF-α, serum β2-GPI/oxLDL, and the combined diagnosis of DCI were 0.653 (0.552–0.753), 0.680 (0.583–0.777), 0.739 (0.647–0.831), respectively.

Conclusion: In DCI patients, the levels of serum oxLDL/β2-GPI are significantly increased. Serum oxLDL/β2-GPI is an independent risk factor that affects the occurrence of DCI. In addition, the serum β2-GPI/oxLDL level implicates the lipid metabolism and inflammatory status of the internal environment of DCI patients to a certain extent.

Keywords: oxLDL, β2-GPI, cerebral infarction, type 2 diabetes, T2DM

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic disease characterized by progressive insulin resistance and hyperglycemia and is proposed as an independent risk factor for cerebrovascular disease (1–2). T2DM is the most common type of diabetes and is also known as adult-onset diabetes because it occurs mostly in adults. The disease is caused by various causes that lead to insufficient insulin secretion in the body or the body cannot use insulin effectively, resulting in a continuous increase in blood sugar levels, eyes, and other organs. Mild forms of diabetes can be controlled with dietary intervention without medication (3). The largest autopsy study to date of cerebral infarction deceased confirmed a 1.57% increased risk of cerebral infarction associated with T2DM.

At present, cerebral infarction in T2DM is diagnosed mainly by imaging, but the imaging examination has certain limitations. It is of great significance to patients with T2DM if there are suitable serum indicators that accurately predict the risk of cerebral infarction. Low-density lipoprotein is a lipoprotein particle that carries cholesterol into peripheral tissue cells. When low-density lipoprotein, especially oxidized low-density lipoprotein (oxLDL), is in excess, the cholesterol it carries will accumulate on the arterial wall, which is easy to cause arteriosclerosis in the long run. Therefore, LDL is called "bad cholesterol." oxLDL aggravates the inflammatory response and promotes the accumulation of cholesterol in lysosomes as well, eventually leading to cell death (4), which is a key factor in the occurrence of cardiovascular diseases. β2-Glycoprotein I (β2-GPI) activates platelets by interacting with cell surface phospholipids (phosphatidylserine, phosphatidylethanolamine) or platelet membrane receptors and exacerbates the progression of cardiovascular disease (5). oxLDL binds β2-GPI to form an oxLDL/β2-GPI complex, which induces atherosclerosis and the formation of foam cells. Studies have shown that elevated serum β2-GPI/oxLDL is associated with the occurrence of cerebral complications in T2DM patients (6). The purpose of this study was to deeply analyze the role of serum β2-GPI/oxLDL in T2DM complicated with cerebral infarction and to study the effect of serum β2-GPI/oxLDL in predicting cerebral infarction in T2DM patients.

CLINICAL DATA AND METHODS

Clinical Data

From January 2019 to March 2021, a total of 56 patients with T2DM and cerebral infarction admitted to our hospital were included in the diabetic cerebral infarction (DCI) group, which includes 14 patients with cardio-embolism, 25 cases of large artery atherosclerotic, 11 cases of small artery occlusion type, and 6 cases of unknown etiology. There were 27 cases of anterior circulation infarction and 29 cases of posterior circulation infarction. A total of 60 patients only with T2DM were included in the T2DM group, and healthy volunteers without a history of diabetes and cerebral infarction who were age- and sex-matched with the above two groups of patients were included in the control group ($n = 60$). The average age of the DCI group was 65.86 ± 8.74 (43–81 years), with 33 males and 23 females. The average age of the T2DM group was 65.17 ± 10.55 (41–81 years), with 36 males and 24 females. The average age of the control group was 65.18 ± 9.50 (44–82 years), with 34 males and 26 females. Inclusion criteria are as follows: (1) the diagnostic criteria for T2DM conform to the "China Guidelines for the Prevention and Treatment of Type 2 Diabetes (2017 Edition)" (7); (2) the diagnostic criteria for cerebral infarction conform to the "Chinese Guidelines for Diagnosis and Treatment of Cerebral Infarction with Integrated Traditional Chinese and Western Medicine (2017)" (8), and cerebral infarction has occurred within 1 month; (3) 18–85 years old; (4) patients in the T2DM group had no history of cerebral infarction and clinical symptoms and signs of diabetic cerebral infarction; and (5) the physical, electrocardiogram, ultrasound, and biochemical examinations of the volunteers in the control group were all normal. Exclusion criteria are as follows: patients with cerebral hemorrhage on head imaging, gestational diabetes mellitus, diabetic macrovascular (including cardiovascular accident and lower extremity arterial disease) and microvascular (including diabetic nephropathy, diabetic retinopathy, and diabetic neuropathy) complications, type 1 diabetes, infectious disease, chronic liver disease, chronic kidney disease, malignant tumor, or any hereditary disease that affects lipid metabolism. This study was approved by the Ethics Review Board of our institution, and all participants provided written informed consent prior to the study. All methods were performed according to approved guidelines and regulations.

METHODS

Clinical Data Collection

General information about the patient was collected, including age, gender, body mass index (BMI), duration of T2DM, history of cardiovascular disease (history of hypertension, family history of coronary heart disease, history of arrhythmia, family history of hyperlipidemia or diabetes mellitus history), smoking history, drinking history, and biochemical indicators (fasting blood glucose [PBG], 2-h postprandial blood glucose [2-h PG], fasting insulin [Fins], total cholesterol, triglycerides, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], and glycosylated hemoglobin [hemoglobin A1C, HbA1c]).

Serum β2-GPI/oxLDL

The concentration of serum β2-GPI/oxLDL was determined by a sandwich enzyme-linked immunosorbent assay. First, blood samples were collected after 12 h of fasting, centrifuged at 1,500 r/min (radius: 8 cm) for 15 min, and stored at –80 °C. The polyclonal antibody against human β2-GPI was immobilized on a 96-well plate, and the polyclonal antibody against apolipoprotein B was used as the detection antibody. About 500 µl of serum was incubated at room temperature for 2 h, polyethylene glycol was added, and the samples were

incubated overnight (4°C). The sample was centrifuged (10,000 r/min, radius: 8 cm, 20 min), and the obtained precipitate was resuspended in 0.01 mol/L PBS. β2-GPI antibody (2.5 μg/ml) was added to the samples, followed by incubation at 37°C for 2 h and then at 4°C overnight. The diluted samples (1:40) were added to the wells and blocked with 1% gelatin. BSA was added and incubated for 2 h. Standard β2-GPI/ox-LDL complexes were added to the wells and incubated overnight at 4°C to obtain a standard curve. Horseradish peroxidase-labeled goat antirabbit LDL polyclonal antibody was added to the wells, and TMBUS was added after incubation for 3 h (room temperature). The absorbance was read at 450 nm by using a microplate reader, and the serum oxLDL/β2-GPI complex concentration was calculated based on the standard curve.

Serum Inflammatory Factors

An enzyme-linked immunosorbent assay kit (Diaclone, France) was used to detect tumor necrosis factor (TNF)-α and interleukin (IL)-6 in serum, the samples were detected by a Lablifeer/ew 2007, Varioskan LUX multimode microplate reader (CA, USA), and the concentrations of IL-6 and TNF-α in the sample were calculated based on the fitted concentration–absorbance curve. C-reactive protein (CRP) was detected by immuno-turbidimetry using a Hitachi 7020 automatic analyzer (Hitachi Kokusai Electric Inc., Tokyo, Japan).

Statistical Methods

SPSS 20.0 software was used for data analysis; the data were tested for normality first, and the continuous variables conforming to the normal distribution were expressed as $\bar{x} \pm s$). Comparisons between groups were performed using an independent sample *t*-test or one-way ANOVA, and data with skewed normal distribution were expressed as M50 (P25, P75). Comparisons between groups were performed using the Mann–Whitney *U* or the Kruskal–Wallis test. The enumeration data were expressed in the form of cases (percentages), the comparison between groups was performed by the chi-square test, and Pearson's analysis was used to measure the correlation of each index. Logistic model analysis of clinical factors affecting the risk of ischemic cerebral

TABLE 1 | Comparison of clinical data in three groups $\bar{x} \pm s$.

Indexes	T2DM group (*n* = 60)	DCI group (*n* = 56)	Control group (*n* = 60)	*F*/*χ2*/*Z*	*P* value
Age (year, $M_{50}[P_{25},P75]$)	65.17 ± 10.55	65.86 ± 8.74	65.18 ± 9.50	0.096	0.908
Male (cases, %)	36 (60.0)	33 (58.93)	34 (56.67)	0.143	0.931
Smoking history (cases, %)	20 (33.33)	18 (32.14)	21 (35.0)	1.320	0.517
History of alcohol intake (cases, %)	12 (20.0)	11 (19.64)	10 (16.67)	0.262	0.877
BMI (kg/m^2, $\bar{x} \pm s$)	24.05 ± 1.63[a]	24.35 ± 1.63[a]	20.95 ± 1.74	70.460	<0.001
Course of T2DM (cases, %)					
≥10 years	44 (73.33)	34 (60.71)	–	2.094	0.148
<10 years	16 (26.67)	22 (39.29)	–		
History of cardiovascular disease (cases, %)					
coronary heart disease	25 (41.67)	23 (41.07)	–	0.004	0.948
Arrhythmia	31 (51.67)	34 (60.71)	–	0.963	0.327
Hypertension	50 (83.33)	47 (83.93)	–	0.007	0.931
hyperlipidemia	13 (21.67)	11 (19.64)	–	0.072	0.788
Blood index					
Total cholesterol (mmol/L, $\bar{x} \pm s$)	4.54 ± 1.14	4.49 ± 1.18	4.70 ± 1.30	0.494	0.611
Triglycerides (mmol/L, $\bar{x} \pm s$)	1.47 ± 0.41	1.54 ± 0.39	1.40 ± 0.43	1.593	0.206
LDL-C (mmol/L, $M_{50}[P_{25},P75]$)	2.56 (2.01,3.41)[a]	2.71 (1.83,3.35)[a]	2.16 (1.74,2.85)	8.157	0.017
HDL-C (mmol/L, $\bar{x} \pm s$)	1.01 (0.86,1.17)	0.94 (0.82,1.06)[a]	1.02 (0.86,1.22)	4.756	0.093
PBG (mmol/L, $M_{50}[P_{25},P75]$)	8.17 (7.20,9.36)[a]	8.30 (7.25,9.56)[a]	4.83 (4.19,5.60)	112.619	<0.001
2 h PG (mmol/L, $M_{50}[P_{25},P75]$)	15.50 (12.87,18.90)[a]	15.72 (12.59,18.67)[a]	6.23 (5.66,6.81)	117.718	<0.001
HbAlc (%, $M_{50}[P_{25},P75]$)	7.74 (5.77,9.62)[a]	8.30 (6.21,12.75)[a]	5.64 (4.91,6.42)	43.596	<0.001
Fins (mU/L, $M_{50}[P_{25},P75]$)	8.14 (6.63,10.06)[a]	8.23 (6.87,9.76)[a]	5.78 (5.31,6.28)	65.174	<0.001
IL-6 (pg/mL, $M_{50}[P_{25},P75]$)	10.03 (5.05,17.25)[a]	12.65 (6.07,21.80)[a]	4.53 (2.40,11.90)	16.880	<0.001
TNF-α (pg/mL, $M_{50}[P_{25},P75]$)	2.06 (1.01,3.41)	3.65 (1.23,5.14)[ab]	1.36 (0.97,3.14)	14.130	0.001
CRP (mg/L, $M_{50}[P_{25},P75]$)	0.50 (0.50,0.98)[a]	1.40 (0.50,4.55)[ab]	0.60 (0.50,1.20)	19.696	<0.001

BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PBG, fasting blood glucose; 2-h PG, 2-h postprandial blood glucose; HbAlc, glycosylated hemoglobin; Fins, fasting insulin; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; CRP, C-reactive protein.

[a]*P, compared with the control group, P < 0.05.*

[b]*P: compared with the T2DM group, P < 0.05.*

infarction in patients with T2DM was carried out, and the receiver operating characteristic (ROC) curve was used to analyze the diagnostic efficacy of serum β2-GPI/oxLDL for DCI. When $P < 0.05$, the data were statistically different.

RESULTS

Clinical Data Comparison of Three Groups

There were no significant differences in age, gender, smoking history, drinking history, T2DM course, cardiovascular disease history, total cholesterol, triglyceride, and HDL-C among the three groups ($P > 0.05$). Compared with the control group, the BMI, LDL-C, PBG, 2-h PG, HbAlc, Fins, CRP, TNF-α, and IL-6 of the T2DM group and DCI group were significantly increased, with P values less than 0.05. Compared with those in the T2DM group, the TNF-α and CRP levels in the DCI group were significantly increased, and the P values were all less than 0.05, as shown in **Table 1**.

Comparison of Serum β2-GPI/oxLDL Values in Three Groups

The level of serum β2-GPI/oxLDL in the control group, in the T2DM group, and in the DCI group was 0.79 (0.57, 1.03), 1.09 (0.88, 1.28), and 1.34 (1.03, 1.68) mmol/L, respectively. The difference was statistically significant among the three groups ($Z = 53.504$, $P < 0.001$). Compared with that in the control group, the concentration of serum β2-GPI/oxLDL in T2DM and DCI groups increased significantly ($P < 0.001$). Compared with that in the T2DM group, the level of serum β2-GPI/oxLDL in the DCI group was significantly increased ($P < 0.05$), as shown in **Table 2**.

Correlation of Serum β2-GPI/oxLDL With Blood Lipids, Blood Glucose Levels, and Inflammatory Markers

The result of Pearson's correlation analysis showed that serum β2-GPI/oxLDL was positively correlated with total cholesterol, triglyceride, PBG, 2hPG, HbAlc, IL-6, and TNF-α ($P < 0.05$), as shown in **Table 3**.

TABLE 2 | Comparison of clinical data in three groups $\bar{x} \pm s$.

Indexes	T2DM group ($n = 60$)	DCI group ($n = 56$)	Control group ($n = 60$)	Z	P value
β2-GPI/oxLDL	0.79 (0.57, 1.03)[a]	1.09 (0.88, 1.28)[ab]	1.34 (1.03, 1.68)	53.504	<0.001

[a]*P, compared with the control group, P < 0.05.*
[b]*P, compared with the T2DM group, P < 0.05.*

Logistic Model Analysis of Clinical Factors Affecting Cerebral Infarction

Taking cerebral infarction as a dependent variable (occurrence = 1, no occurrence = 0), the basic clinical data were included in the univariate logistic model analysis, and the results showed that HbAlc, serum TNF-α, and β2-GPI/oxLDL were closely related to the occurrence of DCI ($P < 0.05$). The above independent variables were included in the multivariate model analysis, and the results showed that elevated serum TNF-α and β2-GPI/oxLDL levels were independent risk factors for DCI ($P < 0.05$), as shown in **Table 4**.

Diagnostic Efficacy of Serum β2-GPI/oxLDL for DCI

According to the ROC curve analysis, the area under the curve of serum β2-GPI/oxLDL and their combination in the diagnosis of DCI was 0.680 (0.583–0.777), the sensitivity was 0.589, the specificity was 0.750, the cutoff value was 1.256, and the Youden index was 0.339 ($P < 0.05$), as shown in **Figure 1**.

DISCUSSION

Studies have reported that diabetes is an independent risk factor for cerebral infarction (9). The results of this study showed that serum β2-GPI/oxLDL was closely related to the occurrence of cerebral infarction in patients with T2DM. An elevated serum β2-GPI/oxLDL level is an independent risk factor for DCI, and serum β2-GPI/oxLDL is also related to lipids and inflammatory factors in DCI patients. The persistent inflammatory response may be the pathological basis of DCI. In addition, the detection of serum β2-GPI/oxLDL levels is helpful for the diagnosis of clinical DCI.

Cerebral infarction is a common complication of T2DM, with acute onset and high mortality. At present, the diagnosis of DCI mainly relies on examination by imaging, but patients are generally in the attack stage when imaging examinations are performed. Therefore, minimally invasive and accurate biological indicators for the diagnosis of DCI are of great value in patients with T2DM. Hyperglycemia can lead to changes in blood rheology (e.g., reduced red blood cell deformability, increased platelet viscosity, etc.) in patients with T2DM, leading to microcirculation disturbances and a higher risk of stroke (10). In addition, high glucose, high fat, and other risk factors can promote the occurrence of atherosclerosis (AS), which is a complex inflammatory disease and the pathological basis of cardiovascular and cerebrovascular diseases. Hyperglycemia can lead to the production of reactive oxygen species (ROS). Glucose reacts with blood proteins to form glycation end products. It can

TABLE 3 | Correlation of serum β2-GPI/oxLDL concentration with blood lipids, blood sugar, and inflammatory markers.

	Total cholesterol	Triglycerides	LDL-C	HDL-C	PBG	2 h PG	HbAlc	Fins	IL-6	TNF-α	CRP
r	0.176	0.288	0.043	−0.098	0.331	0.273	0.195	0.111	0.207	0.159	0.084
P value	0.020	<0.001	0.570	0.197	<0.001	<0.001	0.010	0.142	0.006	0.035	0.266

TABLE 4 | Univariate and multivariate logistic model analyses of clinical factors affecting cerebral infarction.

Variable	Univariate		Multivariate	
	OR (95%*CI*)	*P*值	*OR* (95%*CI*)	*P* value
Age	0.998 (0.975–1.022)	0.866	–	–
Male	0.957 (0.456–2.008)	0.906	–	–
Smoking history	0.947 (0.436–2.059)	0.891	–	–
History of alcohol intake	0.978 (0.392–2.438)	0.962	–	–
BMI	1.036 (0.834–1.288)	0.748	–	–
T2DM course	0.562 (0.257–1.231)	0.150	–	–
Coronary heart disease	0.976 (0.466–2.044)	0.948	–	–
Arrhythmia	1.446 (0.691–3.023)	0.327	–	–
Hypertension	1.044 (0.390–2.796)	0.931	–	–
Hyperlipidemia	0.884 (0.359–2.176)	0.788	–	–
Total cholesterol	0.962 (0.700–1.321)	0.810	–	–
Triglycerides	1.525 (0.611–3.804)	0.366	–	–
LDL-C	0.890 (0.591–1.339)	0.575	–	–
HDL-C	0.282 (0.053–1.508)	0.139	–	–
PBG	1.013 (0.843–1.217)	0.892	–	–
2-h PG	0.997 (0.930–1.068)	0.929	–	–
HbAlc	1.098 (1.003–1.202)	0.042	1.076 (0.974–1.189)	0.151
Fins	0.980 (0.872–1.102)	0.742	–	–
IL-6	1.025 (0.993–1.058)	0.131	–	–
TNF-α	1.303 (1.090–1.559)	0.004	1.278 (1.047–1.560)	0.016
CRP	1.031 (0.992–1.0741)	0.126	–	–
β2-GPI/oxLDL	4.662 (1.752–12.406)	0.002	5.277 (1.815–15.344)	0.002

BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PBG, fasting blood glucose; 2-h PG, 2-h postprandial blood glucose; HbAlc: glycosylated hemoglobin; Fins: fasting insulin; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α; CRP: C-reactive protein;β2-GPI/oxLDL: β2-glycoprotein I/ oxidized low-density lipoprotein.

also trigger the production of ROS. ROS can trigger a chain reaction leading to increased inflammation, chemical modification of lipoproteins, and reduced nitric oxide utilization, thereby increasing the risk of atherosclerosis in the blood vessels and in the brain (11).

AS is a disease characterized by foam cell formation, lipid accumulation, and inflammation (12). Several studies have demonstrated that oxLDL, endothelial dysfunction, and oxidative stress are the most prominent risk factors for AS (13). oxLDL plays a central role in the initiation and progression of atherosclerosis, as it mediates the promotion of several vascular cells (e.g., neutrophils, monocytes/ macrophages, smooth muscle cells, endothelial cells, and platelets). Inflammatory and pro-regulatory effects (14). The primary mechanism of macrophage formation stems from disturbances in oxLDL uptake and lipid efflux. Under normal circumstances, plasma low-density lipoprotein exists in the blood. Under pathological conditions, LDL-C in the plasma passes through the damaged endothelium and enters the subintima of the blood vessel, where it is oxidized by reactive oxygen species to form oxLDL. oxLDL is toxic to cells and induces inflammatory gene expression that promotes foam cell formation. Pretreatment with ox-LDL can induce downregulation of human cord blood endothelial cell viability or activate cells to secrete chemical factors, cytokines, and inflammatory factors that promote early atherosclerotic plaque formation (15, 16). The rupture of unstable plaques is the direct cause of cerebral infarction, and elevated serum ox-LDL is a risk factor for the formation of carotid atherosclerotic plaques in patients with AS cerebral infarction (17).

β2-GPI is a highly glycosylated plasma protein. β2-GPI can bind to lipoproteins and participate in lipid metabolism. In patients with autoimmune diseases (such as systemic lupus erythematosus), β2-GPI can activate systemic lupus erythematosus—Th17 and Th1 responses in atherosclerotic lesions in patients with antiphospholipid syndrome—and affect the release of inflammatory factors such as IL-17, IL-12, etc., thereby affecting disease progression (18). The increase of anti-β2-GPI antibodies can accelerate the formation of AS plaques in ApoE-/- mice, and β2-GPI can bind to negatively charged oxLDL to form a complex. In patients with antiphospholipid syndrome, the oxLDL/β2-GPI complex was found to be a predictor of heart disease. The occurrence of vascular complications has a favorable effect and is a more

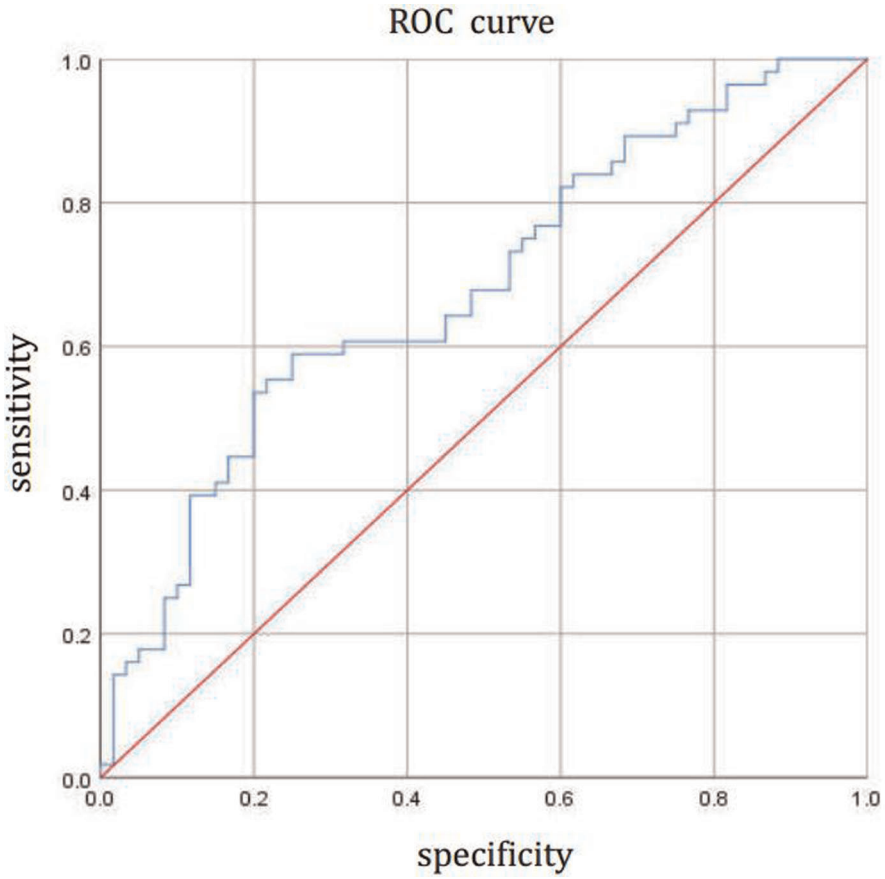

FIGURE 1 | ROC curve of serum β2-GPI/oxLDL in the diagnosis of DCI.

substantial indicator (19). The oxLDL/β2-GPI/anti-β2-GPI antibody complex increases the conversion of macrophages to foam cells, so the oxLDL/β2-GPI/anti-β2-GPI antibody complex increases gradually with the progression of AS disease. Xie et al. (20) also demonstrated that elevated β2-GPI/oxLDL and oxLDL levels were independently associated with diabetic microvascular complications. The results of our study showed that serum TNF-α and IL-6 were significantly increased in DCI, and the serum TNF-α level was an independent risk factor for DCI, which indicated that persistent inflammatory response was closely related to the occurrence of DCI. In addition, serum β2-GPI/oxLDL was significantly increased in DCI patients, and serum β2-GPI/oxLDL was positively correlated with total cholesterol, triglyceride, PBG, 2hPG, HbAlc, IL-6, and TNF-α, indicating that serum β2-GPI/oxLDL can reflect the lipid status and inflammatory status of DCI patients to a certain extent.

In conclusion, serum oxLDL/β2-GPI levels were significantly increased in DCI patients, and serum oxLDL/β2-GPI was an independent risk factor for the occurrence of DCI. In addition, serum β2-GPI/oxLDL levels can also reflect the lipid metabolism status and inflammatory status of DCI patients to a certain extent. Persistent inflammatory response and lipid disturbance may be the pathological basis of DCI. Serum oxLDL/β2-GPI has the potential to become a biomarker for the diagnosis of DCI in T2DM patients and is worthy of clinical promotion.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethics committee of our hospital. The patients/participants provided written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

WK, YL, GL, and YZ are mainly responsible for the writing and research design of the article. GC and BL are mainly responsible

for data analysis. The corresponding author is SK, and she is responsible for ensuring that the descriptions are accurate and agreed upon by all authors. All authors contributed to the article and approved the submitted version.

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Treatment of Elderly Patients with Acute Symptomatic OVCF: A Study of Comparison of Conservative Treatment and Percutaneous Kyphoplasty

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Objective: The present study was designed for the contrastive analysis of conservative and percutaneous kyphoplasty (PKP) on pain severity and recovery of injured vertebrae in elderly patients with acute symptomatic osteoporotic vertebral compression fracture (OVCF).

Methods: A total of 60 elderly patients with acute symptomatic OVCF were divided into two groups according to different treatment protocols, with 30 patients in each group. Patients in the Con group received conservative treatment, while patients in the PKP group received percutaneous kyphoplasty treatment. Clinical evaluation included the visual analogue scale (VAS), the Dallas pain questionnaire, the vertebral body leading edge height, the Cobb angle of injured vertebrae, the MOS item short-form health survey (SF-36), the Barthel index, and the mini-mental state examination (MMSE).

Results: At 3 days, 3 months, and 6 months post-treatment, the score of VAS and the Cobb angle of injured vertebrae in patients of the PKP group were all significantly lower than those in the Con group ($P < 0.05$), while the height of vertebral body leading edge in patients of the PKP group was significantly longer than that in the Con group ($P < 0.05$). At 6 months post-treatment, the scores of the four dimensions of the Dallas pain questionnaire scale in the PKP group were all significantly lower than those in the Con group ($P < 0.05$), while the score of SF-36 (PCS), SF-36 (MCS), and Barthel index in patients of the PKP group were all significantly lower than those in the Con group ($P < 0.05$), and there was no significant difference in the scores of MMSE between these two groups ($P > 0.05$).

Conclusion: Compared with conservative treatment, PKP treatment of elderly patients with acute symptomatic OVCF provides rapid pain relief, restoration of damaged vertebral body height, correction of Cobb's angle, and improved quality of life.

Keywords: OVCF, percutaneous kyphoplasty, pain, comparison of conservative, elderly patients

INTRODUCTION

Osteoporosis is a systemic bone disease in which bone density and bone quality decrease due to various reasons, and the microstructure of bone is destroyed, resulting in increased bone fragility, which is prone to fractures (1, 2). Epidemiological data show that the incidence of osteoporosis in the population over 60 years old in China is about 36%, and the incidence in women is slightly higher than that in men (3, 4). Due to huge population in China, there are about 100 million osteoporosis patients. Fracture is the most common complication of osteoporosis, among which vertebral body compression fracture is the most common, namely, osteoporotic vertebral compression fracture (OVCF) (5). Severe pain and mobility dysfunction are the main clinical manifestations of OVCF patients (6). Therefore, the purpose of OVCF therapy is to relieve the pain symptoms, improve the activity ability of patients, and restore their self-care ability (7).

Currently, there is still no absolutely uniform standard for treating OVCF, and the most widely accepted and clinically implemented methods are mainly minimally invasive surgical schemes and conservative methods (8). The conservative treatment protocol for OVCF is relatively uniform, that is, bed rest, external fixation support, analgesic drug treatment, physical therapy, etc. The disadvantages of conservative treatment of OVCF are obvious, including slow pain relief, long treatment time, and the long-term bed rest easily causes complications such as bedsores, respiratory and urinary tract infections, and constipation (9). Percutaneous kyphoplasty (PKP) is one well-known percutaneous procedure effective in relieving pain caused by acute and subacute vertebral compression fracture (10). However, although OVCF is the most common indication for PKP, provides rapid pain relief, and has an acceptable safety profile when used by skilled physicians, there are still risks of surgery and refractures in elderly patients with OVCF (11). Therefore, the comparative study of the benefits of OVCF patients in different treatment modalities is of great significance to the clinical development of OVCF treatment protocols. In the present study, we compared the effects of conservative and PKP therapy on the recovery of injured vertebral bodies and pain in OVCF patients.

DATA AND METHODS

Selection Criteria

A total of 60 elderly patients with acute symptomatic OVCF were recruited for the present study in Beijing Rehabilitation Hospital from January 2020 to December 2020. Also, all patients were informed about the content of this study and signed informed consent. Beijing Rehabilitation Hospital Ethics Committee is responsible for the ethical review and supervision of this study.

Inclusion criteria are as follows: (1) fracture time lower than 2 weeks, (2) radiographically confirmed osteoporotic vertebral compression fracture, (3) age >60 years, (4) significant back pain but no symptoms of nerve damage, and (5) osteoporosis confirmed by bone densitometry.

Exclusion criteria are as follows: (1) patients with communication disorders, mental disorders, intellectual disabilities, and other reasons who cannot complete the subjective assessment, (2) patients with spinal or skin infections, (3) patients with coagulation disorders, malignant tumors, limb fractures, bone metabolic diseases, or other tissue and organ dysfunction, (4) patients with drug, alcohol, or other drug addiction, (5) incomplete baseline data, and (6) inability to complete a 6-month follow-up after initial treatment.

Treatment Protocol

Patients in the Con group received conservative treatment as follows: rest in bed to reset the fractured vertebral body, exercise the function of the lumbar back muscles, wear a spinal brace to get out of bed for exercise, and walk under the protection of the waist circumference according to the actual situation of the patient. At the same time, antiosteoporosis treatment and drug analgesic treatment were given.

Patients in the PKP group received percutaneous kyphoplasty treatment as follows: pedicle approach, X-ray localization, and local anesthesia. The pedicle was entered along the puncture point under fluoroscopy, the balloon was located at the anterior third-fourth of the vertebral body, the contrast agent was injected under continuous fluoroscopic monitoring, the balloon was slowly expanded, the balloon pressure was observed and the pressure was stopped when appropriate, the contrast agent was withdrawn, and the balloon was withdrawn. At last, the appropriate amount of bone cement was dropped into the vertebral body under fluoroscopic monitoring.

Data Collection and Clinical Evaluation

(1) The baseline data of patients in this study, including gender, age, body mass index (BMI), fracture time, fractured segment, and hospital stay time, were collected.
(2) The visual analogue scale (VAS) scores of the two groups before treatment, 3 days after treatment, 3 months after treatment, and 6 months after treatment were compared. The full score of the scale was 10. A higher score indicated more severe pain (11).
(3) The Dallas pain questionnaire (DPQ) scores before treatment, 3 days after treatment, 3 months after treatment, and 6 months after treatment were compared between the two groups. DPQ included four aspects of daily activity (da), work and entertainment (wl), anxiety and depression (ad), and social interest (SI). A higher score indicated more severe pain (12).
(4) The MOS short-term (SF-36) scores of the health survey before treatment, 3 days after treatment, 3 months after treatment, and 6 months after treatment were compared between the two groups. SF-36 contained 36 questions, covering eight dimensions, including body function, body role, body pain, general health, vitality, social function, emotional role, and mental health, with a maximum score

of 100 points in each dimension. The higher the score in each dimension, the better the state (13).

(5) The scores of the Barthel index (0–20 points) of the two groups before treatment, 3 days after treatment, 3 months after treatment, and 6 months after treatment were compared. The scale included 10 items for evaluating an individual's daily functions, including diet, bathing, appearance, clothing, defecation, urination, self-use of the toilet, transportation ability, activity ability, and going upstairs and downstairs (14). The full score was 100. The higher the score, the stronger the patient's daily living ability.

(6) The mini-mental state examination (MMSE) scores before treatment, 3 days after treatment, 3 months after treatment, and 6 months after treatment in the two groups were compared. MMSE includes six aspects including direction, recording, attention, calculation ability, memory, and language ability, and the score <27 indicated the existence of cognitive dysfunction (15).

Radiographic Evaluation

All patients underwent standing anteroposterior and lateral X-rays before treatment and at 3 days, 3 months, and 6 months post-treatment to determine the vertebral body leading edge height and the Cobb angle of injured vertebrae.

Statistical Analysis

SPSS19.0 software was used for statistical analysis in the present study. Chi-square tests were used to compare the difference between categorical variables. The Kolmogorov–Smirnov test was used to check whether quantitative data conformed to a normal distribution, and data that conformed to a normal distribution were presented as mean ± standard deviation; and unpaired Student's *t*-test was used to compare differences and calculate *P*-values. *P*-values less than 0.05 indicated significant differences.

RESULTS

Baseline Data

Baseline data of patients in two groups are given in **Table 1**. As shown, there was no significantly different between these two groups in the baseline data including gender, age, BMI, fracture time, and fractured segment ($P > 0.05$), while the hospital stay time of patients in the PKP group was significantly longer than that in the Con group ($P < 0.05$).

Pain Severity

Before treatment, the VAS score of patients in the PKP group has no significant difference to patients in the Con group ($P > 0.05$). However, after different treatment methods, the VAS scores of patients in the PKP group were all significantly lower than those in the Con group at 3 days, 3 months, and 6 months post-treatment ($P < 0.05$) (**Figure 1**). At the same time, the scores of the four dimensions of the Dallas pain questionnaire scale in the PKP group were all significantly lower than those in the Con group at 6 months post-treatment ($P < 0.05$) (**Table 2**).

Recovery of Injured Vertebrae

Before treatment, there was no significant difference in the anterior height between Con and PKP groups (1.21 ± 0.12 vs. 1.19 ± 0.11) ($P > 0.05$). However, after treatment with different methods, the heights of the anterior border of vertebral bodies in the PKP group were significantly higher than those in the Con group (1.35 ± 0.24 vs. 1.61 ± 0.23), (1.36 ± 0.23 vs. 1.58 ± 0.21), (1.30 ± 0.25 vs. 1.87 ± 0.22) ($P < 0.05$) 3 days, 3 months, and 6 months after treatment, respectively (**Figure 2**). Similarly, there was no significant difference in the Cobb angle of the injured vertebral body between the Con group and the PKP group (46.58 ± 2.71 vs. 46.71 ± 2.76) ($P > 0.05$). After

TABLE 1 | Baseline data in two groups.

Groups	Con group ($n = 30$)	PKP group ($n = 30$)	t/χ^2	*P*
Male/female (*n*)	13/17	14/16	0.052	0.820
Age (year)	67.03 ± 14.17	67.07 ± 4.03	0.031	0.975
BMI (kg/m^2)	24.78 ± 0.86	24.45 ± 0.58	1.736	0.088
Fracture time (day)	4.57 ± 1.01	4.67 ± 0.76	0.435	0.665
Hospital stay (day)	8.13 ± 0.86	12.97 ± 0.93	20.921	<0.001
Fractured segment (*n*)				
T11	3	4	0.636	0.888
T12	9	7		
L1	11	13		
L2	7	6		

BMI, body mass index.

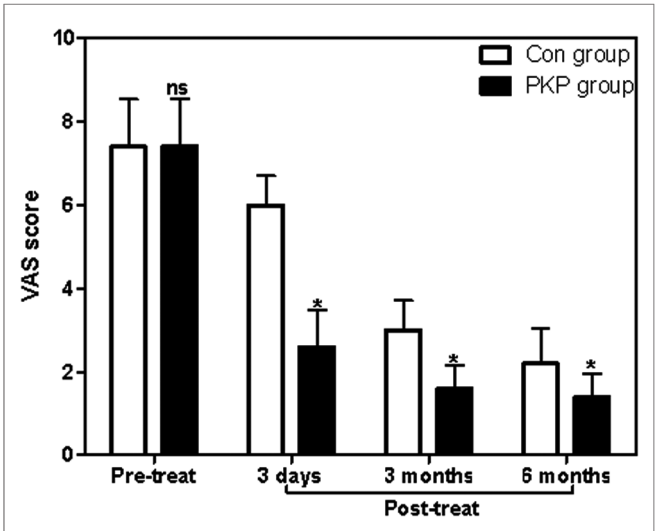

FIGURE 1 | Comparison of VAS scores at different times between two groups. Note: Compared with the Con group, $^{ns}P > 0.05$ and $^{*}P < 0.05$.

TABLE 2 | Comparison of Dallas pain questionnaire at 6 months post-treatment between two groups.

Group	*n*	Daily life	Word and play	Anxiety and depression	Social interest
Con group	30	41.07 ± 3.62	42.57 ± 4.15	33.60 ± 5.13	33.6 ± 5.13
PKP group	30	26.73 ± 4.86	34.90 ± 2.87	16.27 ± 2.79	16.10 ± 3.46
t		12.963	8.324	17.387	15.494
P		<0.001	<0.001	<0.001	<0.001

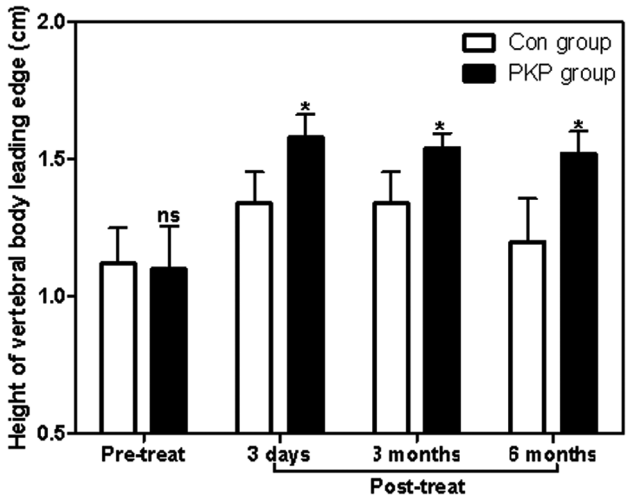

FIGURE 2 | Comparison of the vertebral body leading edge height at different times between two groups. Note: Compared with the Con group, $^{ns}P > 0.05$ and $^{*}P < 0.05$.

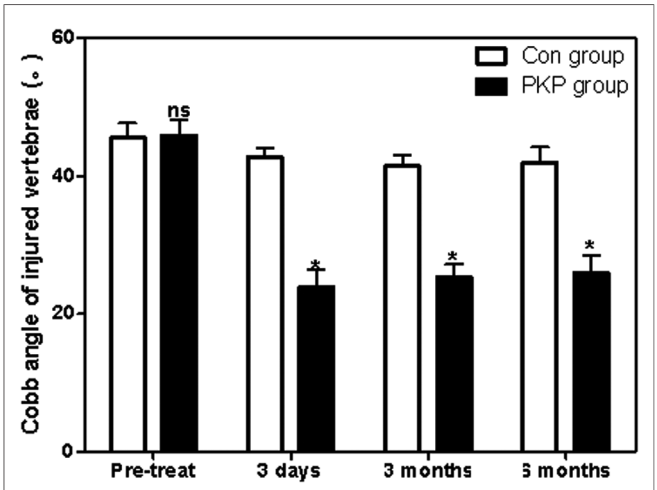

FIGURE 3 | Comparison of the Cobb angle of injured vertebrae at different times between two groups. Note: Compared with the Con group, $^{ns}P > 0.05$ and $^{*}P < 0.05$.

treatment with different methods, the Cobb angles of the injured vertebra in the PKP group were significantly lower than those in the control group ($P < 0.05$) (45.15 ± 2.84 vs. 25.17 ± 3.66), (43.27 ± 2.56 vs 27.33 ± 3.74), (44.28 ± 2.19 vs. 28.41 ± 3.71), 3 days, 3 months, and 6 months after treatment, respectively (**Figures 3**, **4**).

Other Clinical Outcomes

At 6 months post-treatment, the score of SF-36 (PCS), SF-36 (MCS), and Barthel index of patients in the PKP group were all significantly lower than those in the Con group ($P < 0.05$), while there was no significant difference in the scores of MMSE between these two groups ($P > 0.05$) (**Table 3**).

DISCUSSION

Elderly OVCF is one of the most common complications of osteoporosis, and the pathological characteristics of elderly osteoporosis are closely related to systemic functional decline. Surveys have found that the mortality rate of elderly OVCF patients within 5 years is as high as 23%–34% (16). Therefore, it is urgent to find an effective therapeutic scheme in the clinic. It is a specific and prominent symptom of systemic diseases. Conservative treatment and vertebral augmentation techniques are the most common treatment protocols for OVCF patients. Conservative treatment for OVCF such as bed rest, taking calcium and analgesic drugs, and wearing orthopedic braces are all require patients to stay in bed for a long time. However, long-term bed rest can cause dysfunction of the body, which is not only conducive to the recovery of bone volume but also easily accelerates the loss of bone mass, aggravates the pain, and causes muscle atrophy (17). Besides, for elderly OVCF patients, long-term bed rest treatment can also induce other diseases such as pneumonia and deep vein thrombosis, accelerate the deterioration of the disease, and even lead to death (18). Importantly, conservative treatment fails to quickly relieve pain symptoms in OVCF patients, which also aggravates the limitation of conservative treatment. Therefore, surgery is an effective option for OVCF. However, traditional open surgery is traumatic for patients with osteoporosis and prone to internal fixation loosening, which is only applicable to a few patients with symptoms of the spinal cord or nerve compression. In addition, since most OVCF injuries are nonviolent, generally, without symptoms of neurological damage or significant spinal instability, incision surgery and pedicle screw fixation are not required. In addition, due to the characteristics of elderly patients and osteoporosis, pedicle screws are prone to failure. Therefore, the efficacy of traditional open surgery is not significant enough in the clinical treatment of OVCF.

In this study, patients in the PKP group received PKP therapy, and we found that the score of VAS in OVCF patients in the PKP group is significantly lower than that in OVCF patients receiving conservative treatment at 3 days, 3 months, and 6 months post-treatment, while the scores of the four dimensions of the Dallas pain questionnaire scale in the PKP group were all significantly lower than those in OVCF patients receiving conservative treatment at 6 months post-

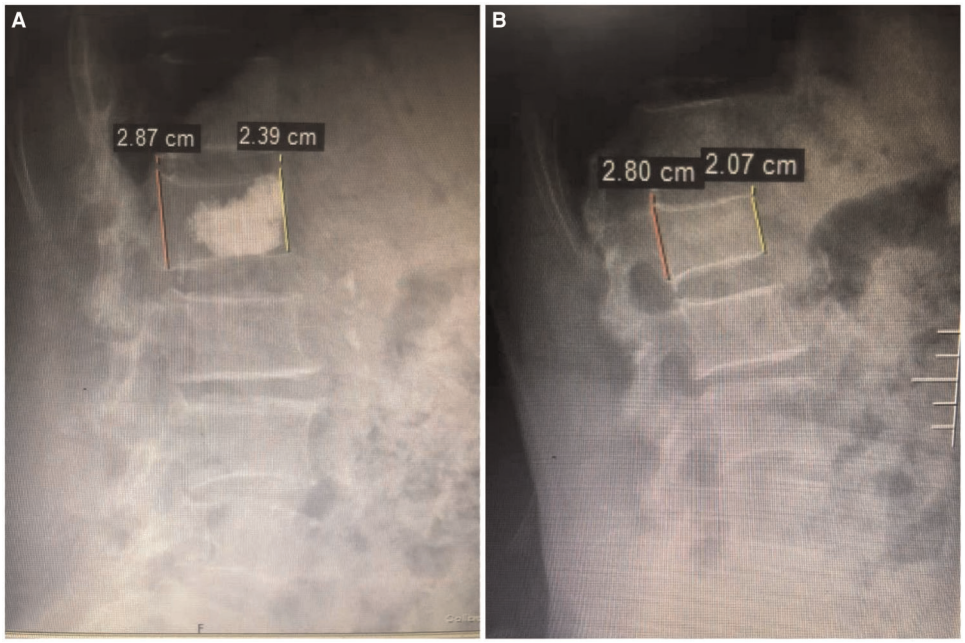

FIGURE 4 | Changes in the height of the anterior vertebral body detected by X-ray before (**A**) and after (**B**) PKP treatment.

TABLE 3 | Comparison of other clinical outcomes at 6 months post-treatment between two groups.

Group	*n*	SF-36 (PCS)	SF-36 (MCS)	Barthel	MMSE
Con group	30	36.27 ± 3.79	58.17 ± 5.95	26.83 ± 6.06	88.00 ± 4.57
PKP group	30	30.60 ± 5.95	47.96 ± 4.89	18.97 ± 4.10	87.50 ± 6.06
t		4.400	7.252	5.888	0.361
P		<0.001	<0.001	<0.001	0.719

SF-36, MOS item short-form health survey; PCS, standardized physical component; MCS, standardized mental component; MMSE, mini-mental state examination.

treatment. These results suggested that PKP treatment relieves pain in OCVF patients faster than conservative treatment. Consistent with previous studies, rapid pain relief is the biggest advantage of PKP over conservative treatment (19). PKP percutaneous balloon vertebroplasty is a microinnovative technique for spine surgery developed on the basis of percutaneous vertebroplasty (PVP) (20). The main protocol for PKP treatment of OVCF is as follows: under the monitoring of imaging equipment, a balloon is inserted and inflated with minimally invasive techniques until the endplate is elevated, the height of the vertebral body is restored satisfactorily, and a cavity is formed in the vertebral body (21). Methyl methacrylate—bone cement—is injected into the vertebral body through the skin and pedicle to fill it, restore the height of the vertebral body, increase the strength of the diseased vertebral body, prevent further collapse and refracture of the vertebral body, correct the kyphosis deformity, relieve pain, and improve physical function so that patients can get out of bed early (22).

In the present, we also found that the Cobb angle of injured vertebrae of OVCF patients in the PKP group is significantly lower than those of OVCF patients receiving conservative treatment, while the heights of the vertebral body leading edge in the PKP group were all significantly lower than those in OVCF patients receiving conservative treatment at 3 days, 3 months, and 6 months post-treatment (23). Therefore, the above results indicated that injured vertebral bodies recovered faster in OVCF patients treated with PKP than those treated with conservative treatment. Furthermore, both pain and vertebral function recovery impact the quality of life and mental status of OVCF patients (24). Although the long-term improvement of pain and functional recovery in acute OVCF patients treated with PKP was not significantly different from conservative treatment in some previous studies, it should be noted that the quality of life and mental status of patients treated with PKP were better than those treated with conservative treatment, which was consistent with conservative treatment. PKP therapy is associated with rapid pain relief and restoration of vertebral function. Consistently, in this study, we found that the scores of SF-36 (PCS), SF-36 (MCS), and Barthel index of patients in the PKP group were all significantly lower than those in the Con group at 6 months post-treatment, which suggested that the quality of life and mental status of patients treated with PKP were better than those treated with conservative treatment. In addition, prolonged hospitalization due to preoperative MRI and bone mineral density testing resulted in a longer average hospitalization in the PKP group than that in the Con group in this study. Patients need to be informed of the operation before the operation to improve the patients' informed degree of the operation.

CONCLUSION

Compared with conservative treatment, PKP treatment of elderly patients with acute symptomatic OVCF provides rapid pain relief, restoration of damaged vertebral body height, correction of Cobb's angle, and improved quality of life. However, the high cost of treatment and the increased risk of postoperative refracture are the disadvantages of PKP treatment for OVCF patients.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethics committee of our hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DY and ZL are mainly responsible for the writing of the article. HW is mainly responsible for research design. RY is mainly responsible for data analysis. FL and YY are responsible for the guidance of the entire research. The corresponding author is FS, and he is responsible for ensuring that the descriptions are accurate and agreed upon by all authors. All authors may have contributed in multiple roles.

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Comparison of PKRP and TUVP in the treatment of high-risk BPH and analysis of postoperative influencing factors

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Objective: This study aims to compare the efficacy of plasma kinetic loop resection of the prostate (PKRP) and transurethral vaporization of the prostate (TUVP) for the treatment of high-risk benign prostatic hyperplasia (BPH), and analyze the influence of the related factors on the operation of BPH.
Methods: A total of 108 high-risk BPH patients diagnosed in our hospital from March 2018 to September 2021 were selected and randomly divided into an observation group and a control group, with 54 cases in each group. The control group was treated with TUVP, and the observation group was treated with PKRP. The international prostate symptom score (IPSS), quality of life (QOL) index, maximum urine flow rate (Qmax), and residual urine volume (RU) were observed before and after treatment. The general information such as age, educational level, residence, and residence status of the patient, as well as clinical information such as surgical method, nocturia frequency, preoperative IPSS score, RU, medical history, and prostate texture, were also recorded. All patients were followed up for 1 month, and complications were recorded.
Results: The IPSS score, QOL score, and RU of patients in the two groups were lower after treatment than those before treatment, and the Qmax was higher than that before treatment ($P < 0.05$). The IPSS score, QOL score, and RU of the observation group were lower than those of the control group, and the Qmax was higher than that of the control group ($P < 0.05$). The incidence of postoperative complications in the observation group was lower than in the control group ($P < 0.05$). Univariate analysis showed that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, medical history, and prostatic texture all could affect the postoperative condition of patients with BPH ($P < 0.05$). Multivariate logistic analysis showed that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, and medical history were the independent influencing factors of the postoperative condition of patients with BPH ($P < 0.05$).
Conclusion: PKRP in the treatment of high-risk BPH patients can effectively reduce the IPSS score, QOL score, and RU and significantly increase Qmax, with fewer complications and a good prognosis. Patients' postoperative recovery was related to their age, surgical method, nocturia frequency, preoperative IPSS score, RU, and medical history. Therefore, choosing PKRP to treat high-risk BPH patients can effectively improve the postoperative urethral functional recovery of patients and reduce the occurrence of complications.

KEYWORDS

high-risk benign prostatic hyperplasia, transurethral plasmakinetic resection of the prostate, transurethral electrovaporization of the prostate, therapeutic effect, influencing factors

Introduction

Benign prostatic hyperplasia (BPH) is a urological disease commonly occurring in middle-aged and elderly men, which manifests as lower urinary tract symptoms caused by enlarged prostate glands and outlet obstruction of the bladder neck, and seriously affects the quality of life of patients (1, 2). High-risk patients with BPH are often accompanied by basic diseases such as hypertension and diabetes. In addition, they are elderly and have poor body resistance, which greatly increases the difficulty of treatment (3, 4). At present, surgical treatment is commonly used in clinical practice. Transurethral resection of the prostate (TURP) is one of the main methods for the clinical treatment of BPH, but due to the inability to completely remove the gland tissue, the gland can still continue to proliferate and lower urinary tract symptoms appear again, which greatly impacts patients (5, 6). Transurethral vaporization of the prostate (TUVP) is an improved resection method based on TURP, which can effectively shorten the operation time and improve the resection quality. However, its effect on the improvement of postoperative urethral symptoms is limited (7, 8). Plasma kinetic loop resection of the prostate (PKRP) is a new type of prostatectomy, which is different from TURP in the working principle. A current does not need to pass through the body, but it can form a local control loop through normal saline to break the molecular bonds in the prostate tissue and thus destroy the tissue to relieve the symptoms of obstruction (9, 10). The purpose of this study was to compare the efficacy of PKRP and TUVP in the treatment of BPH and analyze the effects of relevant factors on the operation of BPH.

Materials and methods

Patients

A total of 108 patients with high-risk BPH diagnosed in our hospital from March 2018 to September 2021 were selected. Inclusion criteria are as follows: all of them met the guidelines for the diagnosis and treatment of benign prostatic hyperplasia (11); there were no contraindications of operation and use of anesthetic drugs; and patients with renal insufficiency did not improve significantly. Exclusion criteria are as follows: acute infection of the urinary system; patients with prostate cancer; patients with bladder stones and other diseases; patients with other additional serious organ diseases; patients with drug allergy; and patients who dropped out during follow-up. A total of 108 high-risk BPH patients were randomly divided into an observation group and a control group, with 54 cases in each group. There was no significant difference in general data between the two groups, as shown in **Table 1**.

Surgical methods

Perioperative risk assessment was conducted before surgery, and surgery was arranged in the absence of absolute contraindication. If a urinary tract infection exists before surgery, empiric antibiotic treatment can be given, and a drug sensitivity test can be performed at the same time. Antibiotic medication can be adjusted according to the drug sensitivity test, urinary tract infection symptoms can be significantly improved, and surgical treatment can be performed later. If the patient has a history of urethral stricture, urethral dilation is feasible.

In both groups, the surgery was performed according to the standard procedures after lumbar anesthesia or continuous epidural anesthesia. The bladder lithotomy position was adopted, and the conventional bladder puncture fistulization was performed under television monitoring. The control group was treated with TUVP: a F26STORZ electrocision mirror (STORZ, Germany) was used, the power of vaporization electrocision was 200–230 W, the power of electrocoagulation was 80 W, and the content of lavage fluid was 5% mannitol. First, the hyperplastic glands were excised at 5–7 o'clock in advance and gradually cut in different regions. Finally, the periphery of the verruca was cut. With the bladder neck and the verruca as the marker points, the cutting depth is as deep as the surgical capsule as far as possible. The prostate fragment tissue was punched out by an Ellik evacuator, and the presence of the fragment residue was carefully examined again. F22 catheter was indwelled and bladder irrigation continued.

The observation group was treated with PKRP (GYRUS, UK). After successful anesthesia (continuous epidural block anesthesia was adopted for all patients), the lithotomy position was taken for the patient. The skin in the operation area was routinely sterilized with high-efficiency iodophor and then covered with a sterile towel. During the operation, the bladder was continuously rinsed, and amedical paraffin cotton ball was used to lubricate the electrocision lens sheath. After the lens sheath with the lens core was inserted, the lens core was extracted (if the external urethral orifice was relatively narrow, the urethral probe was used to expand and then the lens

TABLE 1 Comparison of general data between the two groups.

Group	Age (years)	Course of disease (years)	Preoperative IPSS score (points)
Control group ($n = 54$)	81.05 ± 6.21	4.94 ± 0.75	21.15 ± 2.56
Observation group ($n = 54$)	80.21 ± 6.52	5.08 ± 0.81	22.04 ± 2.75
t	0.679	0.932	1.741
P	0.498	0.354	0.085

sheath was placed). An F26 resectoscope was placed along the sheath to observe the bladder and identify the location of the trigone of the bladder and bilateral ureterostoma, and then, the resectoscope was retreated to the posterior urethra to identify the prostatic hyperplasia and determine the location of the caruncle. The resection point was selected according to the location and degree of BPH. The bleeding was stopped by electric coagulation while the resection was performed. For obvious bilateral lobe hyperplasia, a landmark groove was cut at 6 o'clock to reach the level of the upper margin of Giemu, and the bilateral lobes were cut in sequence. If the hyperplasia of the middle lobe is more obvious, the 5:00 and 7: 00 positions should be marked first, and then the hyperplastic tissues of both lateral lobes and the middle lobe should be successively excised to the level of the upper margin of the Giemu to the depth of the prostatic capsule. Finally, the bladder neck and the prostatic apex were trimmed to ensure that the prostatic part of the urethra was a smooth tunnel. After careful electrocoagulation, hemostasis was performed on the whole wound surface and no active bleeding was detected. The endoscope was retracted. An Eric flusher was used to suck out the resected BPH tissue. An F20 or F22 three-cavity urinary catheter was retained, and the airbag was filled with water. The sterile oil yarn was used to tie a knot at the external orifice of the urethra. After a little traction and pressurization hemostasis were performed, the bladder was continuously rinsed with 0.9% sodium chloride isotonic rinse. And the operation was completed. The prostate tissue resected during the operation was sent for pathological examination for a definite diagnosis. After surgery, patients' consciousness and consciousness were closely monitored, ECG and pulse oxygen were monitored, and vital signs were closely monitored.

Observation indicators

Intraoperative blood loss and hospital stay in the two groups were recorded. The international prostate symptom score (IPSS) (12), quality of life index (QOL) (13), maximum urine flow rate (Qmax), and residual urine volume (RU) were observed before and after treatment. The general information such as age, educational level, residence, and residence status of the patient, as well as clinical information such as surgical method, nocturia frequency, preoperative IPSS score, RU, medical history, and prostate texture, was also recorded. All patients were followed up for 1 month, and complications were recorded.

Statistical methods

SPSS22.0 software was used for processing. The measurement data were expressed by mean ± standard deviation, and *t*-test analysis was used for pairwise comparisons. Count data were expressed by rate, and the chi-square test was used for the comparison between groups. A multivariate logistic regression model was used for multivariate analysis. $P < 0.05$ indicated that the difference was statistically significant.

Results

Comparison of intraoperative blood loss and hospital stay between two groups

The intraoperative blood loss and hospital stay in the observation group were lower than those in the control group ($P < 0.05$), as shown in Table 2.

Comparison of various efficacy indicators between the two groups

The IPSS score, QOL score, and RU of the two groups of patients after treatment were lower than those before treatment, and the Qmax was higher than that before treatment ($P < 0.05$). After the treatment, the IPSS score, QOL score, and RU of the observation group were lower than those of the control group, and the Qmax was higher than that of the control group ($P < 0.05$), as shown in Figure 1.

Postoperative complications in two groups

In the control group, urethral stricture was found in four cases, postoperative hemorrhage in two cases, transient urinary incontinence in two cases, and epididymitis in one case. The complication rate was 16.67% (9/54). In the observation group, there was one case of urethral stricture, one case of transient urinary incontinence, and one case of epididymitis, and the incidence of complications was 5.56% (3/54). There was a significant difference in the incidence of complications between the two groups ($P < 0.05$), as shown in Figure 2.

TABLE 2 Comparison of intraoperative blood loss and hospital stay between two groups.

Group	Intraoperative blood loss (mL)	Hospital stay (d)
Control group	348.52 ± 70.48	7.75 ± 2.58
Observation group	210.54 ± 60.46	6.42 ± 1.98
t	10.919	3.005
P	<0.001	0.003

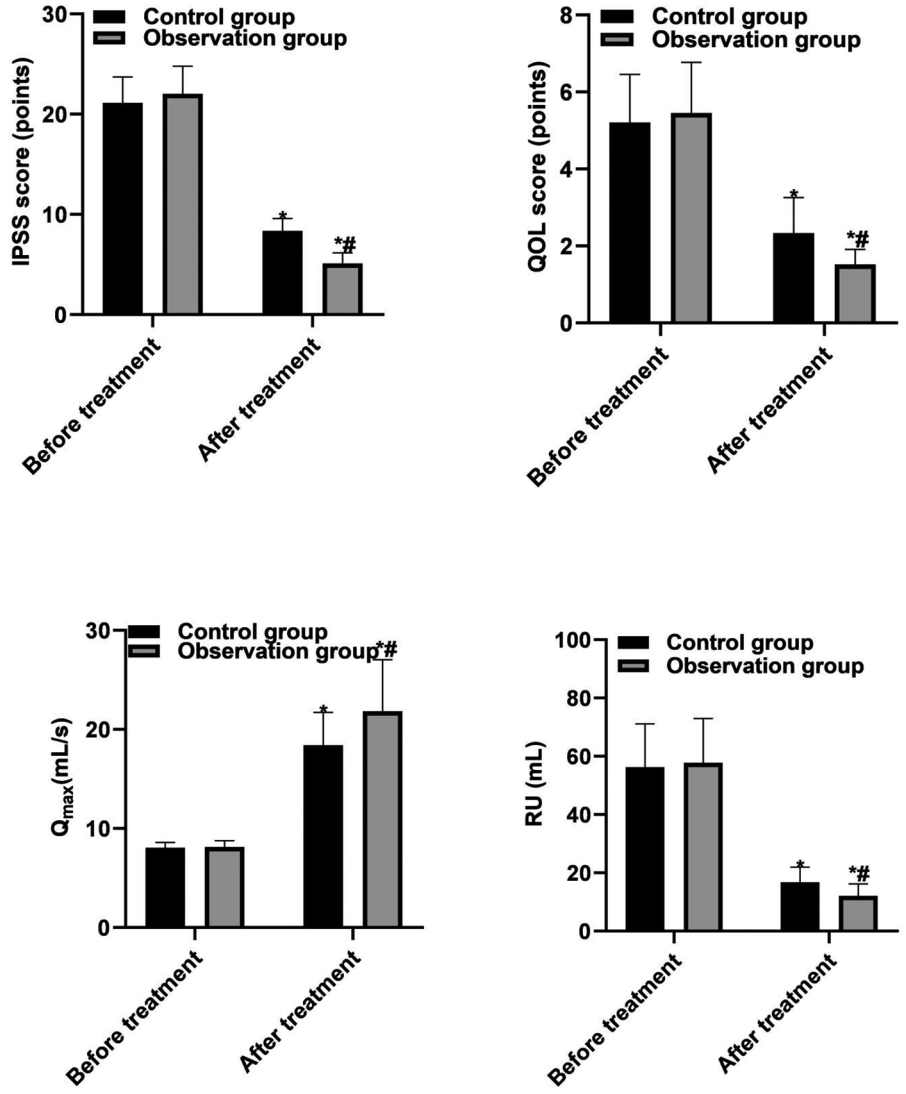

FIGURE 1
Comparison of various efficacy indicators between the two groups. Note: Compared with before treatment, *$P < 0.05$; compared with the control group, #$P < 0.05$.

Single-factor analysis of the postoperative condition (IPSS score) of patients with BPH

Univariate analysis showed that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, medical history, and prostatic texture all could affect the postoperative condition of patients with BPH ($P < 0.05$), as shown in Table 3.

Multifactor analysis of the postoperative condition (IPSS score) of patients with BPH

Multivariate logistic analysis showed that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, and medical history were the independent influencing factors of the postoperative condition of patients with BPH ($P < 0.05$), as shown in Tables 4, 5.

Discussion

Patients with BPH are mainly men over 40 years old. The main symptoms of BPH are enlarged prostate glands and a blocked bladder outlet, causing lower urinary tract symptoms and even possibly leading to renal dysfunction. Especially for high-risk BPH patients, their older age, poorer body function, and more basic diseases increase the difficulty of treatment (14, 15). The treatment of BPH currently mainly includes surgical treatment and nonsurgical treatment. Nonoperative

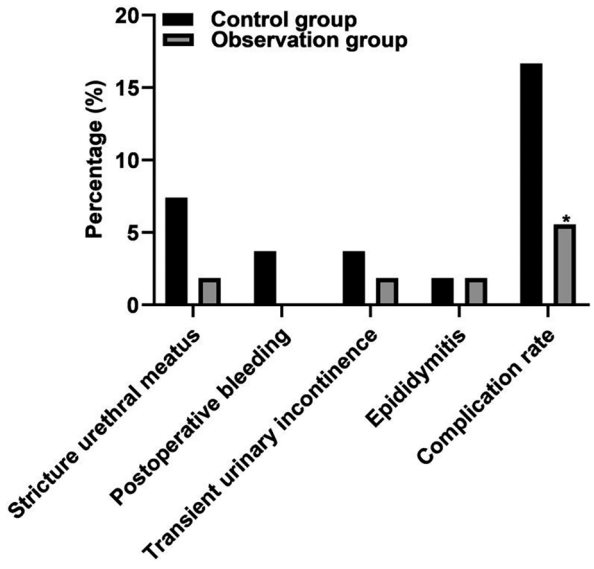

FIGURE 2
Postoperative complications in two groups. Note: Compared with the control group, *$P < 0.05$.

treatment is mainly performed through drugs. Drug treatment is mainly applied to mild lower urinary tract (LUT) symptoms caused by BPH. Most of the LUT symptoms are in the early stage of disease development. LUT symptoms exist but have not yet seriously affected daily life. Such patients can relieve LUT symptoms, delay disease development, inhibit bladder overactivity, promote urination, protect kidney function, prevent and avoid hematuria through drug treatment, and can also be given antibiotics to control urinary system infection and reduce the occurrence of acute urinary retention (16, 17). When the symptoms of LUT are serious, they can seriously affect and interfere with the daily life of patients; Or only have mild LUTs symptoms and have received drug treatment, but the symptoms are not significantly relieved or even worsened, the patient's subjective tolerance is poor, and the patient is seriously troubled; Or repeated hematuria, multiple urinary system infections, urinary retention cannot be alleviated, bladder stones appear, and secondary upper urinary tract hydronephrosis appear (18, 19). TURP is still the gold standard for the treatment of BPH, but it still has certain limitations in practice. High-risk prostatic hyperplasia is considered the relative contraindication for TURP surgery. Most patients can only receive palliative indwelling urinary catheter, cystostomy, and medication, resulting in poor quality of life (20, 21). Therefore, it is extremely important to select effective treatment methods for high-risk BPH patients.

The results of this study showed that intraoperative blood loss and hospital stay in the observation group were lower than those

TABLE 3 Univariate analysis of the postoperative condition (IPSS score) of BPH patients.

Influencing factor		Cases	Postoperative IPSS score (score)	*t*	*P*
Age (years)	70–79	50	5.03 ± 1.86	4.896	0.041
	80–89	58	7.89 ± 2.28		
Degree of education	Junior secondary and below	33	6.55 ± 2.55	1.208	0.462
	High school and above	75	6.75 ± 2.31		
Place of residence	village	58	6.62 ± 2.06	1.606	0.368
	cities and towns	50	6.77 ± 2.44		
Living conditions	live in solitude	32	6.59 ± 2.33	1.385	0.405
	Not living alone	76	6.95 ± 1.59		
Surgical methods	TUVP	54	8.36 ± 1.22	5.472	0.033
	PKRP	54	5.12 ± 1.03		
Number of nocturia (times)	<3	25	5.89 ± 1.92	4.208	0.046
	≥3	83	7.28 ± 2.65		
Preoperative IPSS score (points)	0–10	12	4.08 ± 0.83	8.056	0.001
	11–20	40	7.05 ± 1.22		
	21–30	56	12.52 ± 2.84		
RU (mL)	≥60	70	8.26 ± 2.58	4.586	0.042
	<60	38	5.22 ± 1.77		
Medical history (years)	0–3	23	4.25 ± 0.93	7.589	0.006
	3–5	33	8.18 ± 1.35		
	>5	52	11.98 ± 2.06		
Prostate texture	soft	14	5.06 ± 1.18	6.872	0.012
	middle	67	7.68 ± 2.15		
	hard	27	11.24 ± 2.91		

TABLE 4 Multifactor analysis assignment table.

Factors	Variable	Assignment
Age	X1	70–79 = 0, 80–89 = 1
Surgical methods	X2	TUVP = 0, PKRP = 1
Number of nocturia	X3	<3 = 0, ≥3 = 1
Preoperative IPSS score	X4	0–10 = 0, 11–20 = 1, 21–30 = 2
RU	X5	≥60 = 0, <60 = 1
Medical history	X6	0–3 = 0, 3–5 = 1, >5 = 2
Prostate texture	X7	soft = 0, middle = 1, hard = 2

in the control group, indicating that PKRP could effectively reduce the intraoperative blood loss and hospital stay. The results of this study showed that the IPSS score, QOL score, and RU of patients in the two groups after treatment were lower than those before treatment, and Qmax was higher than that before treatment. The IPSS score, QOL score, and RU of patients in the observation group were lower than those of patients in the control group, and Qmax was higher than that of patients in the control group. One of the reasons was that the working principles of PKRP were different from those of

TABLE 5 Multifactor analysis of the postoperative condition (IPSS score) of patients with BPH.

Influencing factor	B	SE	Walds	*P*	OR	95% CI
Age	0.851	0.533	5.102	0.038	1.533	1.049–1.996
Surgical methods	0.921	0.594	7.025	0.009	1.991	1.405–2.554
Number of nocturia	1.106	0.756	4.693	0.042	1.728	1.372–2.164
Preoperative IPSS score	0.786	0.642	5.955	0.029	2.159	1.298–3.052
RU	1.322	0.495	4.524	0.044	2.385	1.637–2.983
Medical history	0.754	0.518	6.875	0.019	1.958	1.097–3.104
Prostate texture	0.163	0.215	1.833	0.084	1.215	0.896–1.632

TUVP. The working current of PKRP did not need to pass through the body but could directly pass through normal saline to form a local control loop, breaking the molecular bonds in the prostate tissue to destroy the tissue and relieve the symptoms of obstruction, which effectively reduced the tissue damage and improved the symptoms of postoperative urethral stimulation (22, 23). In addition, the research results show that the incidence of postoperative complications in the observation group is significantly lower than that in the control group. Urethral stricture may be caused by a urinary tract infection. The preoperative urinary tract infection is not completely controlled, the preoperative examination and surgical instruments are not disinfected thoroughly, the urethral mucosa is damaged due to lithotripsy and stone removal during the operation for the patients who are accompanied by bladder stones, the postoperative anti-infection treatment and perioperative nursing care were insufficient, and so on. All these aggravate the edema of local tissues, prolong the wound healing time, and finally lead to wound fibrosis and hyperplasia, and then scar healing, the formation of urethral stenosis (24, 25). Urethral stricture may also be caused by preoperative or intraoperative urethral dilatation. When the lens sheath is not sufficiently lubricated, it can also cause damage to the urethral mucosa during the insertion of the lens sheath, and in addition, the long-time compression of the electrotomy lens sheath can lead to ischemia, necrosis, fibrotic hyperplasia, and cicatrix healing of local tissue mucosa, finally forming urethral stricture. Stenosis caused by iatrogenic injury is usually caused by ischemia following uroendoscopic surgery or long-term indwelling catheter. During catheterization, the operator did not act gently enough and the catheter model was thick, hard, and not lubricated enough, thus damaging the urethral wall. Indwelling the postoperative catheter for a long time and long-term compression of the urethral wall lead to local tissue mucosal edema, ischemic necrosis scar healing, and then formation of urethral meatus stenosis (26, 27).

The results of this study show that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, medical history, and prostate texture can all affect the postoperative condition of patients with BPH. Multivariate logistic analysis showed that the patient's age, surgical method, nocturia frequency, preoperative IPSS score, RU, and medical history were the independent influencing factors of the postoperative condition in patients with BPH. The reasons were analyzed as follows: As patients get older, their body immunity weakens and their tolerance to large-scale surgery weakens. Moreover, elderly patients often suffer from chronic diseases such as hypertension, which greatly affects their recovery after surgery. PKRP and TUVP work on different principles. Current does not need to pass through the body, causing little damage to the prostate tissue. Moreover, due to the clear surgical field, the prostate tissue can be excised more accurately, which is conducive to the patient's postoperative urethral recovery. For patients with severe disease and a long history of prostate hyperplasia, it is difficult to resect the prostate tissue during the operation, so it is very easy to affect the curative effect of the operation.

Conclusion

PKRP in the treatment of high-risk BPH patients can effectively reduce the IPSS score, QOL score, and RU and significantly increase Qmax, with fewer complications and a good prognosis. Postoperative recovery was related to the patients' age, nocturia frequency, preoperative IPSS score, RU, and medical history, and the surgical method used. Therefore, selecting PKRP for the treatment of high-risk BPH patients can effectively improve the postoperative urethral functional recovery of patients and reduce the occurrence of complications.

Data availability statement

The original contributions presented in the study are included in the article/Suplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of our Hospital (2018006). The patients/participants provided their written informed consent to participate in this study.

Author contributions

YS, SP, and GL are mainly responsible for the writing and research design of the article. SL and YH are mainly responsible for data analysis. The corresponding author is JY, and he is responsible for ensuring that the descriptions are

accurate and agreed upon by all authors. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Callispheres drug-eluting bead transhepatic artery chemoembolization with oral delivery of sorafenib for the treatment of unresectable liver cancer

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Objective: Liver cancer is a significant contributor to global burden of cancer. Transcatheter arterial chemoembolization (TACE) is the standard of care for patients with unresectable liver cancer, and CalliSpheres, as novel drug-eluting bead (DEB) microspheres, have been found to be associated with a high tumor response rate. However, the outcomes after DEB-TACE treatment are not always satisfactory with tumor recurrence. Herein, we attempt to compare the clinical efficacy and safety of DEB-TACE with sorafenib and conventional TACE in treating advanced liver cancer.
Methods: The study retrospectively reviewed clinical records of 96 patients with liver cancer, among which there were 48 cases receiving DEB-TACE with sorafenib and 48 cases receiving conventional TACE. The physical properties of Callispheres were evaluated in HepG2 cells and a B6/J mouse model.
Results: DEB-TACE with Callispheres were demonstrated to effectively maintain stability and prolong the half-life of epirubicin. Compared with the patients receiving conventional TACE, those receiving DEB-TACE with sorafenib exhibited better patient outcomes with increased survival rate, reduced tumor volume, and declined levels of tumor markers. Additionally, DEB-TACE with Callispheres could effectively protect liver function, as well as reduce the toxic effects of loaded epirubicin, and its combination with sorafenib would not increase the incidence of adverse reactions.
Conclusion: DEB-TACE using CalliSpheres combined with sorafenib could prevent the progression of liver cancer and bring a better prognosis.

KEYWORDS
drug-eluting bead, Callisphere, transarterial chemoembolization, sorafenib, liver cancer

Introduction

According to the WHO/IARC for cancer statistics (year 2020, worldwide, both sexes, all ages) liver cancer had a higher crude rate of incidence (11.6%) and mortality (10.7%) (1). It was accepted as one of the digestive tumors in China with the estimated number of new cases and deaths of 410, 038 and 391, 152 (2). Because the

onset of liver cancer is hidden, and early symptoms are not obvious, patients have often reached the middle and late stage when diagnosed. At this time, liver cancer progresses rapidly, and related complications have often occurred, so patients have already missed the best opportunity for surgical treatment (3). Otherwise, because of the relative shortage of liver donors in China, the vast majority of patients cannot get curative treatment through surgery. At present, for patients with advanced liver cancer, the conventional treatment is mainly radiotherapy and chemotherapy, but due to the more adverse reactions and poor treatment pertinence, the clinical treatment is often not good (4).

The invasive growth of tumor cells is closely related to the supply of blood nutrients, as a result, if the blood supply of liver tumors can be selectively blocked, it will greatly improve the pertinence and clinical efficacy of treatment, and create surgical opportunities for advanced patients (5). Liver blood supply mostly comes from portal vein, and the rest from hepatic artery, on the contrary, the liver cancer blood supply almost all comes from hepatic artery (6). As the different blood supply modes of normal liver tissue and liver cancer, and with the continuous progress of medical technology, transcatheter arterial chemoembolization (TACE) can be implemented in the treatment of hepatocellular carcinoma and has been accepted by more and more clinicians (7). The embolic agent used in conventional TACE (c-TACE) is mainly a mixture of iodized oil and chemotherapeutic drugs. The mixture blocks the target blood vessels through the siphon principle, thus blocking the blood supply of liver cancer, and releases chemotherapeutic drugs around tumor cells at the same time (8). However, excessive iodized oil will cause irreversible damage to the liver, and some scholars have found that iodized oil will be decomposed by tumor cells, and finally degraded by monocyte macrophage system, resulting in the recanalization of tumor blood supply (9). In addition, due to the instability of the mixture, chemotherapeutic drugs are easy to leave the target and enter the peripheral blood circulation, resulting in the decrease of drug concentration at the tumor target and the increase of drug concentration in peripheral blood (10, 11), which aggravates the adverse reactions of drugs. Therefore, the c-TACE scheme needs to be improved to better block the blood supply and stably release chemotherapeutic drugs.

With the continuous progress of medical technology, the improved scheme of drug loaded microspheres for chemoembolization has been proposed. Among them, Callispheres DEB is the latest approved in China (12). Callispheres DEB is mainly synthesized from polyvinyl alcohol and has good biocompatibility with the body. It can choose different diameters according to the different target segments of the blocked hepatic artery, so as to better block the target vessels (13). In addition, Callispheres DEB has good compliance, and its size can be compressed by 50% at most in interventional therapy (14), so that it is not easy to block the microcatheter. When Callispheres DEB reaches the target blood vessel, it can quickly restore the original size and achieve the effect of accurately cutting off the blood supply of the tumor. Moreover, Callispheres DEB cannot be degraded *in vivo*, so that it can permanently cut off the blood supply of the tumor and reduce the number of operations (15). Compared with the traditional unstable mixture, Callispheres DEB have better stability by loading chemotherapy drugs through ion bonds. After reaching the action target, Callispheres DEB can slowly release chemotherapy drugs by exchanging with sodium particles in the blood (16). As a result, it can avoid too many chemotherapy drugs from entering the peripheral blood, on the other hand, it can ensure effective and continuous drug concentration around tumor cells and reduce the dosage of drugs (17), so as to improve the curative effect and reduce the toxic and side effects of chemotherapy drugs.

As a multi kinase inhibitor, sorafenib was the first targeted therapy approved for advanced renal cell carcinoma, transforming treatment, which was reported to effectively reduce angiogenesis, thus reducing blood supply of liver cancer cells with a well characterized tolerability and safety profile (18, 19). However, there are few studies on the treatment of hepatocellular carcinoma with Callispheres DEB TACE combined with sorafenib. This study discusses the therapeutic effect of combined therapy in advanced liver cancer, in order to find a better clinical scheme for patients with advanced liver cancer. A **Supplementary Table S1** showed the full names of abbreviations.

Materials and methods

Callispheres DEB construction

Callispheres DEB (Suzhou Hengrui jialisheng Biotechnology Co., Ltd, Suzhou, China), epirubicin (catalog No. H19990280, Zhejiang Haizheng Pharmaceutical Co., Ltd., 10 mg), sterilized water for injection (catalog No. H41024923, Sinopharm Rongsheng Pharmaceutical Co., Ltd., 2 ml), and iodofol (catalog No. H20143027, Jiangsu Hengrui Pharmaceutical Co., Ltd, 100 ml) were prepared to manufacture drug loaded microspheres used in DEB-TACE. Dissolve the epirubicin with sterile injection water, and the concentration was controlled at 20 mg/ml, then 20-ml syringe was used to extract the dissolved epirubicin for standby. The Callisphere DEB was extracted with 20-ml syringe, and the supernatant was removed after being put for 2 min. Three-way tube was used to connect the syringe with DEB and epirubicin, and epirubicin was injected into the syringe of

drug loaded microspheres. The syringe was then shaked once every 5 min for 6 times, so as to make epirubicin completely loaded on DEB. Finally, the contrast agent iodofol was added according to 1.2 times the volume, and then it was shaken well and let stand for 5 min. At this time, the DEB used by DEB-TACE group was well prepare.

Physicochemical property test of half-time and stability

Callispheres DEB loaded epirubicin, the mixture of iodized oil and epirubicin were administered intraperitoneally in C57BL/6J mouse models with a similar body weight of about 25 g separately ($n = 2$, Shanghai Laboratory Animal Center, Chinese Academy of Sciences, Shanghai, China). The mice were survived during the experiment, and this study was approved by the Ethics Committee of our hospital. Blood samples were taken from the tail vein of the above-injected mice per hour, and epirubicin concentration was detected for the half-time test. The stability of Callispheres DEB was tested by evaluating the diameter alterations in PBS, PBS + 10% serum and PBS+ HepG2 cells, which mimic the blood and tumor environment *in vivo* (20). The sizes of Callispheres DEB were evaluated under scanning electron microscopy (Phenom LE, Phenom Scientific, Netherlands).

Research subject

Patients with liver cancer ($n = 96$) treated in our hospital were enrolled between March 2017 and March 2019. Inclusion criteria: (1) primary liver cancer diagnosed for the first time; (2) liver cancer was diagnosed according to the criteria in *Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma* (21); (3) age range: 18–70 years old with an estimated survival time of more than 3 months; (4) received TACE surgery; (5) Barcelona Clinic Liver Cancer (BCLC) staging classification: Phase B or C (22); (6) Eastern Cooperative Oncology Group performance status (ECOG PS): 0–2 (23). Exclusion criteria: (1) previous history of liver surgery; (2) Child-Pugh C cirrhosis (24); (3) severe coagulation dysfunction; (4) hepatic portal vein occlusion or no collateral circulation; (5) combined with active hepatitis; (6) patients received the any treatments, such as c-TACE, ablation, radiotherapy and chemotherapy. Patients were randomly divided into DEB-TACE group ($n = 48$) and c-TACE group ($n = 48$), and treated with DEB-TACE or c-TACE separately. The general data of the two groups were shown in **Table 1**.

TABLE 1 Baseline data of research subjects.

Baseline information	c-TACE ($n = 48$)	DEB-TACE ($n = 48$)	*P*
Age (year)	50.12 ± 10.23	48.88 ± 10.19	0.553
Gender			
Male	21 (43.75%)	28 (58.33%)	0.196
Female	27 (56.25%)	20 (41.67%)	
BMI (kg/m^2)	24.41 ± 2.36	24.68 ± 2.45	0.584
HCC	41 (85.42%)	44 (91.67%)	0.336
Hepatitis	37 (77.08%)	30 (62.5%)	0.120
Cirrhosis	35 (72.92%)	30 (62.5%)	0.275
Vascular invasion	34 (70.83%)	26 (54.17%)	0.092
Average diameter (cm)	5.12 ± 1.23	4.78 ± 1.12	0.160
BCLC stages			
Phase B	28 (58.33%)	32 (66.67%)	0.399
Phase C	20 (41.67%)	16 (33.33%)	
Child-Pugh Grading			
Grade A	39 (81.25%)	36 (75.00%)	0.459
Grade B	9 (18.75%)	12 (25.00%)	
ECOG score			
0	23 (47.92%)	25 (52.08%)	0.539
1	16 (33.33%)	17 (35.42%)	
2	9 (18.75%)	6 (12.5%)	

TACE interventional therapy process

After disinfection and local anesthesia, the femoral artery was punctured according to Seldinger method (25). Then, the celiac trunk and superior mesenteric artery of the patient were imaged to determine the location of liver tumor and understand its blood supply in detail. Then, the microcatheter was superselective intubated to the blood supply site of liver cancer. In c-TACE group, the mixture of iodized oil (10 ml) and epirubicin (20 mg) was used for chemoembolization (26). In DEB-TACE group, the Callispheres DEB loaded epirubicin (80 mg) (27) was extracted with a 1 ml syringe, and the pulse injection method was used for chemoembolization. The effect of vascular embolization was evaluated by angiography after surgery. When the cancer was completely embolized, the operation was completed. After operation, the puncture point was routinely disinfected, pressurized and bandaged, and symptomatic treatment such as anti-inflammatory, liver protection and pain relief were applied. At the same time, patients in DEB-TACE group were treated with oral medication of 400 mg sorafenib (catalog No. H20160201, Bayer pharmaceutical company, Germany) twice a day (27). Withdrawal criteria: progression or deterioration of the disease, serious adverse reactions, decompensation of liver function (grade C).

Solid tumor efficacy evaluation

The patients were examined by CT/MRI after operation and the survival area of liver tumor was used as the target lesion for efficacy judgment. According to the modified solid tumor efficacy evaluation standard (5), curative effect was divided into complete remission (CR, complete disappearance of target lesion), partial remission (PR, the reduction of target lesion >30%), stable disease (SD, no significant change in target lesion diameter) and progressive disease (PD, the increasing of target lesion >20%), and the objective response rate (ORR) was calculated. ORR = (CR + PR)/total number.

Detection of tumor markers and indicators of liver function

Fasting venous blood (5 ml) obtained from the patients were centrifuged at 3,000 rpm. The supernatant was then stored at −80°C in a medical refrigerator. Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBIL) in serum were detected by automatic biochemical analyzer (BS-280, Mindray, Shenzhen Mairui Biomedical Electronics Co., Ltd, Shenzhen, China). Besides, serum levels of alpha-fetoprotein (AFP), carbohydrate antigen-199 (CA-199) and vitamin K absence of antagonist-II (PIVKA-II) were detected by automatic chemiluminescence immunoanalyzer (DXL-800, Beckman).

Safety evaluation

The adverse reaction was evaluated in terms of gastrointestinal reactions (nausea and vomiting), fatigue, impaired liver function, liver pain, fever and so on, the above adverse reactions were counted.

Follow up

The patients returned to the hospital every 1 month to review liver function, tumor markers and CT/MRI, so as to evaluate the therapeutic effect. Overall survival (OS) and progression free survival (PFS) was defined as duration from the TACE treatment to the death and disease progression, respectively. The follow-up period was 24 months and ended in March 2021.

Statistical analysis

SPSS 22.0 was adopted for statistical analysis. The quantitative data were described by n (%), and χ^2 test was used for inter-group comparison. Besides, the measurement data of normal distribution was described by mean ± SD and t-test was employed for inter-group comparison; While the measurement data of non-normal distribution was described by M (P_{25}, P_{75}), and Mann-Whitney U test was employed for inter-group comparison. Meanwhile, the survival analysis was performed by Kaplan-Meier log-rank survival tests. $P < 0.05$ stands for striking difference.

Results

Physicochemical properties of callispheres DEB

As shown in **Figure 1A**, epirubicin in DEB-TACE group had a longer half-life than that in c-TACE group (10 vs. 2 days). In terms of stability, Callisphere DEB could effectively maintain its stability in serum and liver cancer cells (**Figures 1B,C**), and the electron microscope structure. Furthered showed its stability (**Figure 1D**). As a result, Callisphere DEB could effectively cut off the blood supply of liver cancer cells, thus better inhibit the invasion growth of tumor. In addition, it could reduce the dosage of drugs without affecting the effect.

Clinical remission after TACE surgery

One month after treatment, the ORR of DEB-TACE was higher than that of c-TACE [$P = 0.030$, 95%CI (0.158, 0.924)], suggesting that DEB-TACE could greatly reduce the volume of liver tumors in the short term (**Figure 2A**). At 3rd month after treatment, the ORR of c-TACE decreased, while it further increased in DEB-TACE group [$P = 0.005$, 95%CI (0.117, 0.702)]. Moreover, CR was higher in DEB-TACE than that in c-TACE [25% vs. 8.33%, $P = 0.028$, 95%CI (0.801, 0.919)] (**Figure 2B**). The above results showed that DEB-TACE could better inhibit the invasion and growth of tumor, reduce tumor volume and avoid the further progress of liver cancer.

Changes of serum tumor markers after TACE surgery

One month after treatment, both treatment regimens could reduce the levels of AFP, CA-199, and PIVKA-II, especially in DEB-TACE group (all $P < 0.05$). At 3rd month after treatment, the level of tumor markers in c-TACE group increased without difference when compared with the data at 1 month (all $P > 0.05$), while that in DEB-TACE group continued to decrease (all $P < 0.05$, **Table 2**). The above

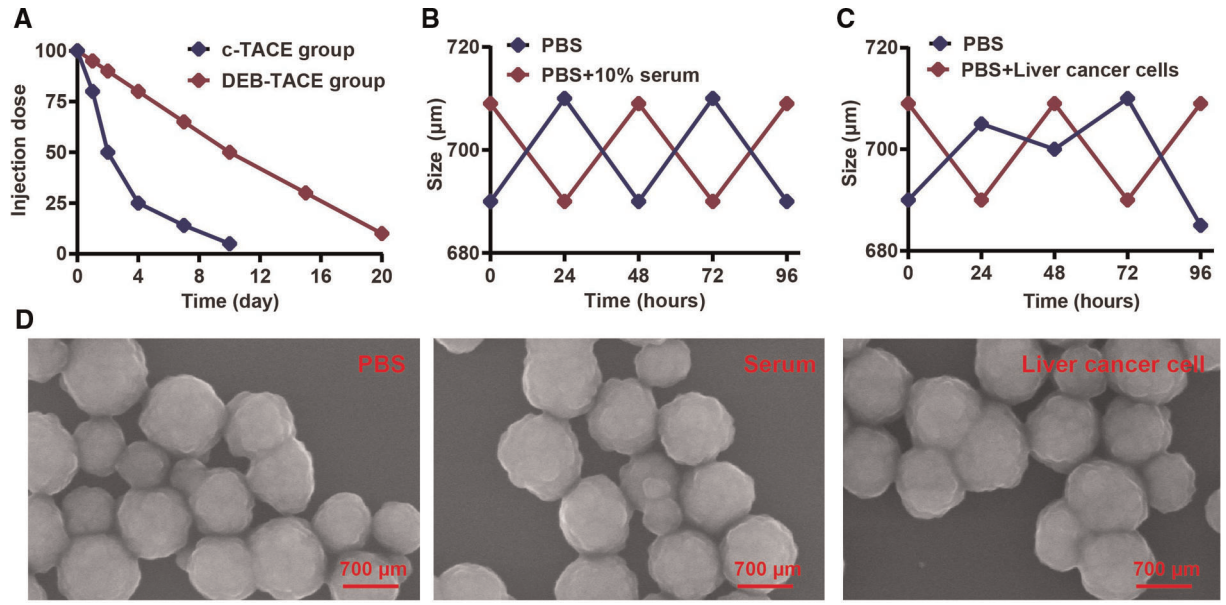

FIGURE 1
Physicochemical property test of callispheres DEB. (A) Half-life period test of Epirubicin in c-TACE and DEB-TACE. (B) Stability test of Callispheres DEB in serum. (C) Stability test of Callispheres DEB in liver cancer cells. (D) Electron microscope structure of Callispheres DEB in PBS, serum and liver cancer cells.

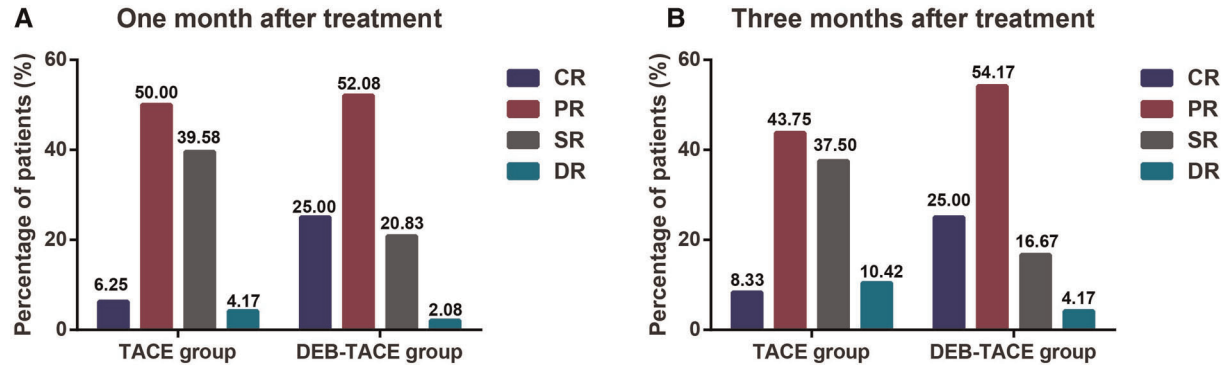

FIGURE 2
The clinical remission after TACE surgery. The ORR (CR + PR) of patients with liver cancer at 1st (A) and 3rd (B) month after treatment.

results showed that DEB-TACE had better clinical efficacy and more lasting antitumor effect.

Changes of liver function after TACE surgery

One week after treatment, the transaminase and TBIL of both groups greatly increased, and the above indexes increased more significantly in c-TACE group (all $P < 0.05$), considering that it was related to the reduction of blood supply and the liver damage of chemotherapeutic drugs. After 1 month, the liver function of the two groups was relieved, and the above indexes decreased significantly, especially in DEB-TACE group (all $P < 0.05$). After 3 months, the above indexes increased again in both groups, especially in c-TACE group, which were greatly higher than those before treatment (all $P < 0.05$, Table 3). The above results suggested that liver function was damaged greater in c-TACE group than that in DEB-TACE group.

TABLE 2 Detection of alpha-fetoprotein (AFP), carbohydrate antigen-199 (CA-199) and vitamin K absence of antagonist-II (PIVKA-II) in serum.

	c-TACE ($n = 48$)	DEB-TACE ($n = 48$)	P
AFP (ng/ml)			
Preoperative	624.10 (25.67–3438.4)	588.34 (19.29–3358.12)	0.217
After 1 month	517.13 (18.45–1123.56)*	381.20 (12.13–965.24)*	<0.001
After 3 months	529.35 (19.23–1214.25)*	334.26 (10.36–856.87)*,**	<0.001
CA-199 (U/L)			
Preoperative	80.10 (9.36–453.42)	83.34 (10.29–512.38)	0.110
After 1 month	53.13 (8.45–215.78)*	41.31 (6.13–165.34)*	<0.001
After 3 months	61.35 (9.13–287.98)*	31.26 (6.23–89.34)*,**	<0.001
PIVKA-II (mAU/ml)			
Preoperative	566.34 (47.66–3664.35)	583.75 (40.67–3721.25)	0.543
After 1 month	473.25 (52.39–3178.27)*	383.25 (124.56–2654.62)*	0.002
After 3 months	467.43 (49.65–2945.63)*	176.87 (31.66–829.64)*,**	<0.001

*Compared with preoperative, $P < 0.05$.
**Compared with 1 month, $P < 0.05$.

TABLE 3 Comparison of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBIL) in serum between c-TACE group and DEB-TACE group.

	c-TACE ($n = 48$)	DEB-TACE ($n = 48$)	P
ALT (U/L)			
Preoperative	80.64 ± 13.03	82.23 ± 12.27	0.540
After 1 week	139.23 ± 23.23*	106.12 ± 19.13*	<0.001
After 1 month	83.02 ± 11.16**	76.59 ± 10.34*,**	0.004
After 3 months	107.58 ± 15.49*,***	83.04 ± 12.71***	<0.001
AST (U/L)			
Preoperative	67.28 ± 10.06	68.14 ± 10.41	0.682
After 1 week	101.24 ± 21.56*	88.12 ± 17.13	0.001
After 1 month	52.23 ± 9.55*,**	45.58 ± 8.13*,**	<0.001
After 3 months	81.19 ± 15.03*,***	65.2 ± 11.42***#	<0.001
TBIL (mol/L)			
Preoperative	50.23 ± 7.53	50.06 ± 7.14	0.910
After 1 week	68.34 ± 11.12*	60.13 ± 10.23*	<0.001
After 1 month	51.46 ± 8.39**	47.15 ± 8.02**	0.012
After 3 months	85.37 ± 16.52*,***	71.11 ± 13.34*,***	<0.001

*Compared with preoperative, $P < 0.05$.
**Compared with 1 week, $P < 0.05$.
***Compared with 1 month, $P < 0.05$.

Incidence of postoperative adverse events after TACE surgery

The incidence of adverse reactions such as gastrointestinal reaction fatigue, liver dysfunction, liver pain and fever were greatly lower in DEB-TACE group when compared to the c-TACE group (Figure 3), suggesting that DEB-TACE could significantly reduce the adverse reactions caused by chemotherapeutic drugs and liver tissue ischemia after embolization.

Survival analysis between DEB-TACE and c-TACE group

After 2 years of follow-up, patients treated with DEB-TACE had higher overall survival rate ($P = 0.007$), and were not easier to relapse and progress ($P = 0.008$) after treatment than those treated with c-TACE (Figure 4). The above results suggested that DEB-TACE could better block the blood supply of liver cancer, inhibit the growth of tumor cells, and effectively avoid tumor recurrence and metastasis.

Discussion

Primary liver cancer is a common malignant tumor, its incidence ranks fourth, and its mortality ranks second among all malignant tumors in China (28). For these patients who are difficult to be treated surgically, radiotherapy and chemotherapy have become common treatment schemes, which, however, could cause systemic injury (29). The emergence of c-TACE treatment scheme provides a new choice for the treatment of these patients, which can superselect the target artery through microcatheter for arterial embolization to make tumor cells ischemic necrosis, and chemotherapeutic drugs can be loaded around the tumor through iodized oil to improve its efficacy (30). However, iodized oil can not completely block blood vessels because of its poor deposition effect, and is easy to be decomposed and absorbed in the later stage. In addition, the stability of the mixture of iodized oil and chemotherapeutic drugs is poor, which makes chemotherapeutic drugs easy to enter the blood circulation, leading to the increase of toxic effects of drugs (30, 31). Therefore, the development of Callispheres DEB

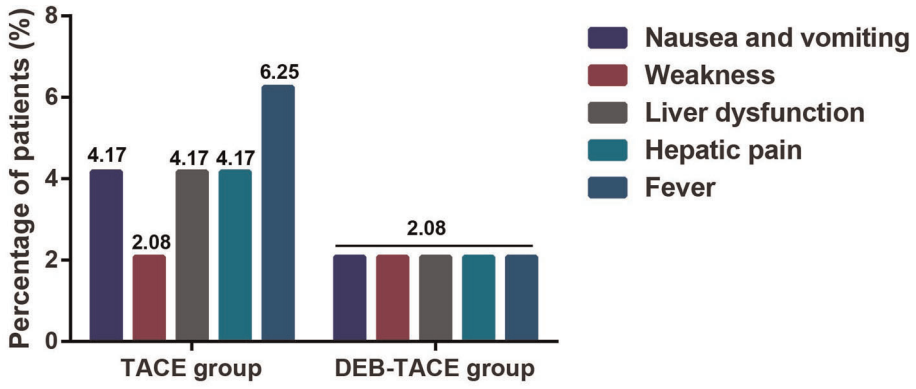

FIGURE 3
The comparison of postoperative adverse reactions in terms of weakness, liver dysfunction, hepatic pain, fever, nausea and vomiting.

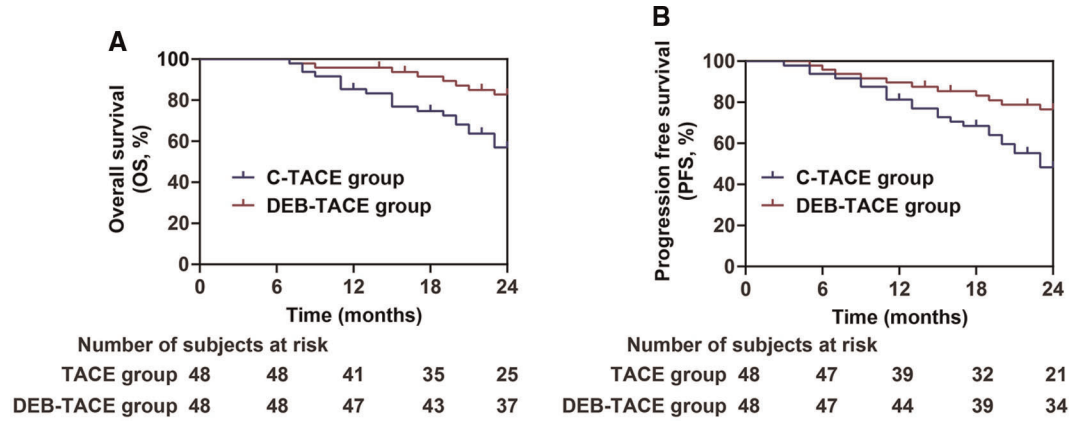

FIGURE 4
Analysis of prognosis of patients in the c-TACE group and DEB-TACE group. (**A**,**B**) Overall survival (**A**) and progression free survival (**B**).

provides a better choice for the therapy of advanced liver cancer.

In our study, the use of Callispheres DEB can help to improve the clinical efficacy, prolong the half-life of chemotherapy drugs. The surface of Callispheres DEB is negatively charged (32). After mixing with chemotherapeutic drugs, the positively charged amino groups in chemotherapeutic drugs can replace sodium ions, and eventually combined stably with hydrogen bond and ion bond forces (33, 34), so as to effectively avoid the loss of chemotherapeutic drugs during transportation. At the same time, after reaching the action target, the chemotherapeutic drugs loaded in Callispheres DEB can be replaced with sodium ions in the blood, so as to continuously release the loaded chemotherapy drugs and maintain the drug concentration around the tumor cells to the greatest extent (35, 36). In addition, Callispheres DEB has non degradability *in vivo*, which helps them to firmly block the target blood vessel after being transported to the target with the blood flow, so as to completely cut off the blood supply of tumor cells (37). In the experiments of physical and chemical properties, it was found that Callispheres DEB could continuously maintain stability in liver cancer cells and significantly prolong the half-life of epirubicin, while iodized oil would be gradually decomposed by liver cancer cells, and epirubicin carried by iodized oil was easier to be metabolized *in vivo*.

After DEB-TACE treatment, the ORR was higher than the c-TACE with lower levels of AFP, CA-199 and PIVKA-II. DEB-TACE has a more thorough embolization effect on blood vessels than c-TACE, and DEB can effectively maintain stability in the blood and continuously release chemotherapeutic drugs. Therefore, DEB-TACE can effectively reduce the tumor volume. Three months after operation, the ORR of c-TACE group decreased compared with that at 1 month after surgery. Similarly, Liu et al. also found that after 3 months of treatment, the ORR of liver cancer patients

treated with DEB-TACE combined with sorafenib were higher (38). The reason may be that the embolization effect of iodized oil is poor, resulting in blood vessel recanalization and collateral circulation. In DEB-TACE group, DEB block blood vessels completely, and the use of sorafenib can effectively reduce the expression of antigenic factors in tumor cells, so as to better inhibit the invasion and growth of the tumor and reduce the level of tumor markers.

The study found that the levels of transaminase and TBIL in both groups increased 1 week after operation, especially in c-TACE group. One month after operation, the liver function indexes in DEB-TACE group basically returned to normal, but those in c-TACE group were still high, and increased again at 3 months after operation. The safety of chemotherapeutic drugs is closely concerned in clinical use, especially its liver toxicity. It is suggested that compared with c-TACE, Callispheres DEB can highly selectively kill liver tumor cells and effectively avoid the damage of normal liver cells.

Relevant studies found that the slow-release of DEB could effectively reduce the extravasation of chemotherapeutic drugs and reduce their concentration in the blood, so as to reduce the occurrence of adverse reactions (39, 40). In our study, after DEB-TACE, the incidence of adverse reactions such as gastrointestinal reaction fatigue, liver dysfunction, liver pain and fever were greatly lower than the c-TACE group. Therefore, DEB-TACE combined with sorafenib is safe in the therapy of advanced liver cancer. Thanks to the fact that DEB-TACE combined with sorafenib can better cut off the blood supply of tumor cells and inhibit the formation of neovascularization in tumor, the survival rate is greatly higher than those in c-TACE group. However, several limitations existed in the current study: (1) other liver function indicators, such as indirect bilirubin and albumin would be determined, which are influence factors affecting the treatment of liver cancer; (2) Further randomized controlled trial with larger sample size is needed to validated our result; (3) The power of sample size should be calculated to avoid conclusion bias.

In conclusion, Callispheres DEB can maintain good stability in the blood, effectively prolong the half-life of the chemotherapy drugs, and reduce their extravasation in the blood. Combined with oral medicine of sorafenib, DEB-TACE could further inhibit the formation of neovascularization in tumor, suppress the level of tumor markers, and reduce the adverse reactions. Therefore, DEB-TACE combined with sorafenib can better inhibit tumor invasion and growth and improve the prognosis of patients with unresectable liver cancer.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by First Hospital of Lanzhou University. The patients/participants provided their written informed consent to participate in this study. The animal study was reviewed and approved by First Hospital of Lanzhou University.

Author contributions

WHW conceived the study and contributed to the writing of initial draft and final manuscript, and supported funding acquisition. FQL assisted in study design and manuscript revision, and was involved in software preparation. PYG collected experimental data and preformed data analysis. BHL contribued to data verification and visualization. SXL participated in data visualization. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.981116/full#supplementary-material.

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The effect of extended continuous nursing strategy applied to patients with mild brain injury on their quality of life and self-efficacy

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Postoperative rehabilitation of craniocerebral injury requires a long process and has many complications. In addition, patients with severe craniocerebral injury are usually accompanied by impaired nervous system function, which will affect the patients' normal life and work in a period of time after surgery. Reasonable rehabilitation nursing plays an active role in restructuring central nervous system function and coordinating muscle and joint activities. Since the rehabilitation of cerebral trauma is a long process, how to ensure the patients to carry out limb and brain function as well as self-care ability and self-care skills according to the rehabilitation exercise plan and intervention measures formulated before discharge has aroused hot debate. This study analyzed the impact of out-of-hospital continuous nursing strategy applied to patients with mild cerebral trauma on their quality of life and self-efficacy level.

KEYWORDS

continuous nursing, brain injury, mild, quality of life, self-efficacy

Introduction

Traumatic brain injury is a common type of surgical system disease in clinical practice. As the brain is a very important organ in the human body, it can dominate the various acts of the body and guide the body to make the corresponding response under the instruction. Once damaged, it will greatly affect the quality of daily life of individuals (1). Patients with mild traumatic brain injury are a relatively special group. On the one hand, there is an individual's self-consciousness, they can feel physical pain and have a certain degree of awareness of their own illness. On the other hand, the lack of self-confidence in the ability to care will further induce individuals to experience negative emotional perceptions such as anxiety and depression (2). So how to effectively connect the nursing during hospitalization and self-care outside the hospital is a major research topic in the field of nursing.

In order to meet the rehabilitation needs of patients after discharge, this study aims to provide a correct self-care channel for the patient's condition management outside the hospital from the perspective of the out-of-hospital continuous nursing strategy,

effectively mobilize the individual's internal subjective initiative, enable the patient to gradually internalize the specific nursing knowledge score, and guide the individual to actively respond to the out-of-hospital condition. All kinds of sudden life events can help individuals master a healthy life philosophy and make the disease develop in a benign direction (3, 4). This intervention program pays more attention to the independent behavior of individuals, and treats the hospitalization and discharge phases of patients as a complete process for management, providing patients with good out-of-hospital care, thereby promoting all-round outcomes of the disease and reducing the long-term sequelae of traumatic brain injury (5, 6). The out-of-hospital continuous nursing strategy puts forward higher requirements for both nurses and patients. The author intends to design a randomized and controlled scientific research idea to further analyze the clinical effect of out-of-hospital continuous nursing strategy applied to patients with mild traumatic brain injury. The research results are now reported as follows:.

Research objects and methods

Research objects

Our hospital admitted and treated 120 patients with mild traumatic brain injury from September 2018 to November 2019. Using the digital table as the basis for grouping, the research subjects of 60 cases who met the inclusion conditions were named as the research group and the control group. Using the digital table as a grouping tool, the subjects who met the inclusion requirements were named as the research group and the control group, with 42 cases in each group.

Inclusion requirements

The patient underwent cranial magnetic resonance and CT examination, combined with his physical symptoms and signs, and was diagnosed with mild traumatic brain injury. diagnostic criteria for the disease; The patient did not have cognitive abnormalities; There are no abnormalities in hearing and vision; have basic verbal communication skills; know the content of this research and sign the consent form; There is no hemolysis and coagulation abnormality; there is no autoimmune system disorder.

Methods

Control group

Routine nursing measures were carried out in this group of patients. Based on the physiological comfort that the patient can perceive on the current body surface, the nurse effectively adjusts the temperature and humidity in the department to ensure that the patient can feel comfortable physically and mentally. Instruct the family to provide the patient with as much food as possible in the meal, high-quality protein, vitamins and low-fat foods. Make the hospital bed clean and fresh; dynamically monitor the patient's current physical symptoms, and notify the doctor in time and take symptomatic treatment once any abnormality is found. And guide individuals to vent their inner fears, anxiety and panic and other negative emotions.

Research group

The patients in this group carried out the out-of-hospital continuous nursing strategy on the basis of the routine nursing measures of the control group. ① Draw up continuous nursing strategies: The responsible nurse as the initiator, integrates the rest of the nurses in the undergraduate room to form a continuous nursing team with a total of 3 members, of which 1 has an intermediate title and the other 3 have a primary title. The responsible nurse as the leader, organizes a joint discussion among all members, using "mild traumatic brain injury" and "continued nursing" as the key words to search and select domestic well-known databases such as "China Knowledge Network", "VIP" and "Wanfang", from which references with high evidence-based levels were selected. All the team members discussed the selected references again, and finally clarified the nursing intervention measures needed for this study. After that, practical skills training was organized for the clear nursing intervention strategy process, and the training time was limited to 8 h. Furthermore, the theoretical cognition and practical skills assessment will be implemented for all team members, and only those who pass both of the assessment objects can enter the next stage of nursing intervention; If one of the assessment results fails, they will need to undergo training again until the assessment results are qualified. ② Pairing patients and their families: Distribute a piece of A4 white paper to the patient, and ask them to list their immediate family members on the A4 white paper, and require that the listed immediate family members live for at least 8 weeks or more. Nurses pair patients with their families and provide them with a relatively private and undisturbed environment for subsequent cognitive interventions. First, the nurse distributed white paper and black pens to both parties, informing both parties in advance that they need to internalize the key points that appeared in this health education. The time for nurses' health education is limited to 20 min, and the content involves the main points of out-of-hospital self-care for mild traumatic brain injury. After finishing the mission, the nurse asked both parties to exchange A4 sheets of recorded points, and asked both parties to retell the important knowledge points understood and internalized this time. Nurses made multi-dimensional corrections for the missing knowledge points and cognitive biases existing on both sides,

thereby strengthening both sides' further cognition of self-care behavior outside the hospital. The whole process of the paired cognitive intervention was recorded by a special person with a mobile phone, and the electronic audio was copied to both parties, and both parties were required to study and strengthen them repeatedly 30 min before going to bed that night. ③ Out-of-hospital real-scenario simulation exercise: Nurses propose specific scripted scenarios based on the situation of cognitive education and common self-care situations that may occur outside the hospital. The scenario requires that the patient's out-of-hospital self-care content be included, such as: "Now, you suddenly feel pain in your brain, what is the first thing you think of?", "What is your current emotional state?", "What measures will you take to deal with it?" etc. Give patients and their families 3 min to immerse themselves in situational awareness and think in combination with the knowledge system they have mastered. In the follow-up role-playing process, the nurses observe the patient's current behavioral performance and mental and emotional state in an all-round way, and then a dedicated person uses a mobile phone to record the whole process. The nurse then decomposes the content of each role-playing situation one by one in the form of video playback, and corrects the cognitive deficits reflected by the patient's behavior, thereby strengthening the individual's internalization and understanding of the relevant knowledge system, so that it can be transformed into own current care behavior. The role-playing time is limited to 10 min. Patients were required to review the recorded specific video 20 min before going to bed that night, and recall according to the nurse's comments, correct their own misunderstandings, so as to continuously consolidate and strengthen the corresponding role-playing situations. ④ Sharing of experience in the symposium: The nurses followed up the patients after discharge, and asked to come to the hospital for a symposium every 2 weeks. During the symposium, each patient was given 2 min to come to the stage to share their experiences and experiences in the past 2 weeks. At the same time, each patient was asked to share their own experiences and insights in text or voice after the symposium way to record, so as to ensure that you can record your own status in real time. The format of each symposium is controlled within 1 h. Afterwards, a WeChat group was established for all patients, and all patients were required to join the group, and everyone was required to share their experiences related to this symposium in text or voice, so as to improve the initiative and enthusiasm of patients.

Observation items

① The patients in the two groups were evaluated by the SF-36 quality of life scale before the intervention and at the 4th weekend after the intervention. The scale contains a total of 7 dimensions, and the score of each dimension is 0–100 score. It indicates that the quality of life level of the corresponding dimension is better (7).

② Both groups of patients received self-efficacy questionnaires before the intervention and at the 4th weekend after the intervention. The questionnaire included 5 dimensions (basic knowledge of the disease, cognition of the hazards of adverse factors, treatment knowledge, self-management knowledge, and complication prevention knowledge). Each dimension is divided into 3 levels, namely poor, good and excellent, and a 3-level scoring method (1 ~ 3 score) is adopted. The higher patient's score means the better the level of self-care (8).

Statistical methods

All the data that met the inclusion criteria were entered into SPSS19.0 software for processing, and the quantitative data were statistically described by the mean and standard deviation, and the t-test was used for comparison between groups; Qualitative data were described by rate, and chi-square test was used for comparison between groups; The rank data were tested by rank sum test. When $P < 0.05$, the difference was statistically significant.

Results

General information

There was no significant difference in the baseline data of the two groups of patients after statistical comparison ($P > 0.05$). As shown in **Table 1**.

Comparison of the quality of life scores of the two groups before and after the intervention

After the intervention, the scores of the SF-36 quality of life scale in the research group were higher than those in the control

TABLE 1 Comparison of baseline data of two groups of patients.

Group	*N*	Gender (male/female, *n*)	Age (year)	Cultural level		
				Primary school	Middle school	College
Research group	60	42/18	41.9 ± 2.7	16	32	12
Control group	60	44/16	42.1 ± 2.8	17	34	9
χ^2/t	—	0.164	0.153		0.519	
P	—	0.685	0.878		0.771	

group, and the difference was statistically significant ($P < 0.05$). As shown in Table 2.

Comparison of self-efficacy levels before and after intervention in the two groups

After intervention, the scores of basic disease knowledge, adverse factor perception, treatment knowledge, self-management knowledge, and complication prevention knowledge in the research group were higher than those in the control group, and the difference was statistically significant ($P < 0.05$). As shown in Table 3.

Discussions

Patients with mild traumatic brain injury are prone to symptoms such as headache, dizziness, and irritability, which significantly reduce the quality of life of patients (8). Due to the long course of the disease, if the patient's personal self-care behavior is not properly managed, under the stimulation of external adverse factors, the patient will be induced to relapse (9). This will not only increase the medical costs, but also increase their physical pain. Since patients usually come to the hospital for treatment in the acute stage, they need to face the distress of discharge after the condition is controlled (10). And after discharge, it also involves the level of personal self-care behavior. If the patient's self-care ability is unreasonable, it will indirectly affect the patient's health status (11). So, improving the self-management ability of patients after discharge is conducive to the overall prognosis and prognosis of their diseases.

In terms of improving the self-management ability of individuals, traditional nursing intervention methods usually adopt the method of health education to let patients understand the theoretical knowledge system of disease occurrence, development, prognosis and outcome (12). However, because the nursing intervention strategy focuses more on the "cramming" instillation of medical knowledge, while ignoring the internal demands of patients at the mental and psychological level, the intervention effect often fails to meet expectations, and it also causes patients to appear after discharge due to past bad behaviors (13). Therefore, under this background, some scholars have proposed a care model based on the concept of continuity (14). This model effectively connects the life and daily care in the hospital and the hospital, starting from the theoretical cognitive level and

TABLE 2 Comparison of quality of life scores between the two groups before and after intervention (score).

Indexes	Before intervention				After intervention			
	Research group ($n = 60$)	Control group ($n = 60$)	t	P	Research group ($n = 60$)	Control group ($n = 60$)	t	P
Physical function	62.4 ± 6.9	62.6 ± 7.0	0.673	>0.05	82.1 ± 10.3	70.4 ± 7.4	13.271	<0.05
Body role	63.6 ± 6.9	64.0 ± 7.0	0.901	>0.05	81.4 ± 10.6	71.5 ± 8.4	9.367	<0.05
Muscle pain	65.2 ± 4.6	65.7 ± 5.0	0.457	>0.05	83.2 ± 8.9	72.7 ± 8.3	7.267	<0.05
General health status	68.7 ± 6.2	69.0 ± 6.3	0.678	>0.05	79.4 ± 8.7	73.1 ± 7.1	9.031	<0.05
Social function	66.4 ± 4.6	66.6 ± 4.8	0.901	>0.05	83.9 ± 9.4	72.6 ± 5.2	15.378	<0.05
Vitality	68.1 ± 5.2	68.3 ± 5.4	1.177	>0.05	84.3 ± 10.6	73.5 ± 5.8	13.278	<0.05
Mental health	62.1 ± 6.0	61.9 ± 5.8	0.453	>0.05	81.1 ± 8.8	71.8 ± 6.9	16.268	<0.05
Emotional role	65.5 ± 5.7	65.7 ± 5.8	0.789	>0.05	82.7 ± 9.6	72.6 ± 7.1	9.013	<0.05

TABLE 3 Comparison of self-efficacy levels before and after intervention in the two groups (score).

Indexes	Before intervention				After intervention			
	Research group ($n = 60$)	Control group ($n = 60$)	t	P	Research group ($n = 60$)	Control group ($n = 60$)	t	P
Basic knowledge of disease	0.8 ± 0.1	0.8 ± 0.1	0.890	>0.05	2.2 ± 0.5	1.3 ± 0.3	13.214	<0.05
Adverse factor risk perception	1.1 ± 0.3	1.0 ± 0.2	1.027	>0.05	2.3 ± 0.6	1.4 ± 0.3	9.367	<0.05
Treatment knowledge	1.2 ± 0.2	1.3 ± 0.3	0.916	>0.05	2.2 ± 0.6	1.3 ± 0.3	10.673	<0.05
self-management knowledge	1.0 ± 0.1	1.1 ± 0.2	0.675	>0.05	2.4 ± 0.4	1.5 ± 0.3	7.367	<0.05
Complication prevention knowledge	1.2 ± 0.2	1.1 ± 0.1	0.589	>0.05	2.4 ± 0.7	1.6 ± 0.4	15.372	<0.05

situational role-playing measures. Strive to let patients have an independent cognition of the disease, and consciously practice the corresponding self-protection behaviors, and achieved considerable clinical results.

The results of this survey showed that the quality of life scores of the patients in the research group after intervention were higher than those in the control group, and the difference was statistically significant ($P < 0.05$). This indicates that the out-of-hospital continuous nursing strategy applied to patients with mild traumatic brain injury can help improve the quality of life of patients in all dimensions. The reasons for this result are closely related to the following factors. ① The determination of intervention plan is the specific presentation of evidence-based medicine model (15). At present, medicine has changed from the traditional empirical medicine to the evidence-based medicine. Therefore, in this study, based on the current internal demands of patients and combined with their specific clinical actual situation, the most cutting-edge theoretical and practical skills were obtained through literature retrieval on databases such as Wanfang, HowNet and VIP, thus guiding clinical practice and enabling patients to obtain the optimal diagnosis and care. On this basis, standardized and standardized training is also carried out for the team members, so that they can master and understand the standardized care mode for patients with traumatic brain injury, and finally improve the management mode of the disease by nurses. ② Patient-family paired cognitive intervention is the premise and guarantee to ensure continuous post-hospital care for patients (16). Only a correct cognitive system can ensure that patients consciously practice correct and scientific behaviors, thereby reducing the incidence of adverse events, avoiding risk factors, and making them face the disease with a more peaceful mind. The traditional cognitive intervention model has not yet started from the patient's subjective level, and more is to provide patients with passive theoretical knowledge points, which cannot ensure that patients can better internalize and absorb relevant knowledge content (17). Under this opportunity, we started from the patients' closest relatives to provide them with appropriate clinical diagnosis and care, so as to ensure the holistic prognosis and outcome of the patient's condition. The patients and their families are organized into teams, so that the patients and their families can learn from each other and make up for the cognitive deficiencies and deficiencies of each other, thereby improving the cognitive level of both sides to the greatest extent in a short time (18). In addition, when the family members also have some understanding of the relevant knowledge content, it provides a guarantee for the construction of an integrated and harmonious atmosphere of the family, and avoids the occurrence of family disputes. In addition, in the process of cognitive intervention, the characteristics of the Ebbinghaus forgetting curve are also introduced. The patient not only has a preliminary understanding of the relevant knowledge score during the study, but also accepts the intervention explained by the two parties after the end. Before going to sleep, recall the content of relevant theoretical knowledge. With the help of the construction of the "recall-memorizing-contemplation" model, it can ensure that they understand the relevant knowledge to the greatest extent. ③ The role-based situational play is based on the patient's mastery of relevant theoretical knowledge (19). After the patient has a comprehensive understanding of the relevant knowledge, behavior management training is required. Effectively avoid and reduce the incidence of adverse events. When the patient thinks about a specific situation, it can make the patient enter into the relevant situation that he may encounter in the future in advance face (20). In addition, when the patient performs specific role-playing, in fact, the relevant theoretical knowledge points that have been mastered before are fully retrieved and put into practice, and finally the internalization and absorption of relevant theoretical knowledge can be achieved. At the same time, nurses use mobile phones to record patients' role-playing situations, guide them, and ask them to observe and learn repeatedly, which can ultimately achieve good behavior management. ④ The sharing of experience in the symposium is a platform that brings patients together, builds a platform between the hospital and patients, and enables patients to communicate with each other. During the communication process, they can re-examine their self-care performance during this period of time, so as to help its architecture system and comprehensive theoretical knowledge system (21). In addition, after the communication is over, the patient is allowed to record the current experience in text and audio, so as to ensure that the patient can further memorize the relevant content. Furthermore, with the help of WeChat Moments, it can provide a 24-hour platform for communication between patients, which is beneficial for both parties to share and exchange relevant theoretical knowledge in real time. Therefore, with the smooth implementation of the above intervention measures, the self-efficacy level of patients can be effectively improved, which is beneficial to the improvement of personal quality of life. Therefore, the results of this survey show that the quality of life of patients in the research group after intervention is higher than that in the control group., the difference was statistically significant ($P < 0.05$).

In conclusion, the out-of-hospital continuous nursing strategy applied to patients with mild traumatic brain injury can improve the self-efficacy level of patients, and can improve their quality of life and nursing satisfaction, which is worthy of further promotion in clinical practice. However, the sample sources of this study are concentrated, the number of samples is small, and it is a single-center study. The follow-up needs large-scale and multi-center research to further demonstrate the research results.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by this study was approved by the ethics committee of our hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

LZ is mainly responsible for the writing, data analysis of the article. YM, JL, MC are mainly responsible for research design. The corresponding author is WZ, and she is responsible for ensuring that the descriptions are accurate and agreed by all authors. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effects of preoperative serum lactate dehydrogenase levels on long-term prognosis in elderly patients with hepatocellular carcinoma undergoing transcatheter arterial chemoembolization

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Hepatic arterial chemoembolization is an effective treatment for primary hepatocellular carcinoma (HCC) and can improve the survival rate of patients. Nevertheless, the long-term prognosis of patients with HCC is not optimistic. In recent years, tumor humoral detection has attracted extensive attention and is expected to become the main examination method for early tumor screening. Studies have found that serum LDH is an indicator with effective potential to predict tumor proliferation and progression, such as pancreatic cancer, esophageal cancer, nasopharyngeal cancer, etc., but the relationship between this indicator and the prognosis of HCC is still unclear. The purpose of this study was to clarify the relationship between serum LDH and the prognosis of patients with HCC, so as to provide an important scientific basis for prognosis judgment of HCC.

KEYWORDS

transcatheter arterial chemoembolization, elderly, hepatocellular carcinoma, lactate dehydrogenase, long-term prognosis

Introduction

Hepatocellular carcinoma (HCC) is abbreviated as liver cancer. As a common malignant tumor, it has a high prevalence in middle-aged men. Although the current treatment technology has been continuously improved, there are still studies reporting that HCC patients recur within 5 years. The rate is as high as 60% or more (1, 2). At present, surgical resection is the preferred method for the treatment of HCC. However, due to the high incidence of postoperative adverse reactions and many surgical contraindications, its clinical application is limited (3, 4). Therefore, the treatment of HCC patients still needs to adopt the form of comprehensive treatment of multiple methods. Among them, an important non-surgical method for the treatment of HCC patients is hepatic arterial chemoembolization (5). Lactate

dehydrogenase (LDH) is a key metabolic enzyme in glycolysis, which can reflect the liver function *in vivo* (6, 7). However, the research on serum LDH level to help diagnose cancer or judge the prognosis is still in the primary stage, especially the correlation research on predicting the prognosis of HCC is few. In this study, 106 elderly patients with HCC who underwent hepatic arterial chemoembolization in our hospital were investigated, and the effect of preoperative serum LDH levels on long-term prognosis was analyzed. The purpose of this study was to explore the value of LDH level in evaluating the long-term prognosis of HCC patients, and then to provide certain schemes and strategies for clinical treatment.

Materials and methods

General information

The random number table method was used to randomly select 106 elderly HCC patients who underwent hepatic arterial chemoembolization in our hospital from January 2011 to December 2013. Among them, 57 patients with preoperative serum LDH level ≤400 U/L were selected as the treatment group, and 49 cases with LDH level higher than 400 U/L were the control group. The content of this study has been reviewed and approved by the Medical Ethics Committee of our hospital, and 106 patients and their families voluntarily signed an informed notice.

Inclusion criteria

According to the imaging examination results, clinical symptoms, pathological tissue biopsy and clinical biochemical treatment comprehensive evaluation, the diagnosis of HCC was made; Patients diagnosed for the first time; The patient's bile duct vessels were not invaded by the tumor; no tumor recurrence was found in the review of tumor markers and imaging 3 months after treatment.

Exclusion criteria

HCC metastasis; Associated with other malignancies; With spontaneous rupture bleeding; with hepatitis C, syphilis, AIDS, etc.; with mental illness.

Treatment methods

In addition to conventional treatments such as anti-tumor and liver protection, both groups were treated with hepatic arterial chemoembolization, and the Seldinger method was used for percutaneous arterial puncture. The catheter was selectively inserted into the blood supply artery of hepatocytes, and angiography was performed to determine the distribution of tumor blood vessels, the blood supply artery of liver tumor and the area of tumor foci. 15 ml of mixed injection of THP, carboplatin, lipiodol emulsion and 5-fluorouracil was perfused into the catheter, and the amount of 1–2 ml could be appropriately increased according to the actual situation of the patient. After completion, the catheter was taken out, and the puncture site was pressed to stop the bleeding, and absolute bed rest ≥2 days. Repeat the treatment every other month for 3–4 times in total, in order to block the blood supply of cancer cells, and then fight against tumor cells.

Detection of serum LDH levels

The same automatic biochemical analyzer (produced by Beckman Coulter, USA, model AU680) was used to analyze the preoperative 7 days and postoperative 1 day, 7 days, 1 month, 6 months, 12 months and 3 years of the two groups. The serum LDH levels of the two groups were detected, and the detection operations of the two groups of patients were carried out by the same laboratory physician in our hospital strictly according to the instructions.

Efficacy evaluation criteria

The clinical efficacy evaluation is divided into markedly effective, effective, general and invalid. (1) markedly effective: the reduction of the tumor focus is 5 cm or more, the alpha-fetoprotein is less than 20 mg/L, and the proliferation activity of the cancer cells disappears completely; (2) Effective: the reduction range of cancer is 3–5 cm, the level of alpha-fetoprotein is 20–150 mg/L, and the proliferation activity of cancer cells disappears; (3) General: The cancer shrinkage range is 1–3 cm, the alpha-fetoprotein level is 150–400 mg/L, and the cancer cells still have proliferation activity; (4) Invalid: Cancer shrinks less than 1 cm, alpha-fetoprotein level is higher than 400 mg/L, and cancer cells are actively proliferating (8).

Statistical methods

The clinically relevant data of the two groups of patients were entered into SPSS 21.0 statistical software for data processing and analysis. The measurement data such as LDH levels at each time point were expressed by ($\bar{x} \pm s$) and t-test was used, while the enumeration data such as the markedly effective rate was used, and the effective rate were expressed

as percentages (%), then the χ^2 test was used, and $P < 0.05$ was considered to be statistically significant.

Results

Comparison of general clinical data of the two groups of patients

There were no significant differences in general data such as sex ratio, age, tumor diameter, tumor number, liver function grading, cytological type, histological differentiation degree and clinical stage between the two groups of patients ($P > 0.05$), which was comparable. As shown in Table 1.

Serum LDH levels of patients in the two groups at various time points after operation

One year after operation, 1 patient in the treatment group was lost to follow-up, and all patients in the control group were followed up. Three years after surgery, 3 patients in the treatment group were lost to follow-up, and 2 patients in the control group were lost to follow-up. One day after operation, there was no significant difference in serum LDH levels between the two groups ($P > 0.05$). At 7 days, 1 month, 6 months, and 12 months after operation, the levels of serum LDH in the two groups were lower than those at 1 day after operation ($P < 0.05$), and the levels in the treatment group were significantly lower than those in the control group ($P < 0.05$). At 3 years after operation, serum LDH levels in both groups were lower than at 1 day after operation (all $P < 0.05$), but there was no statistical significance between the two groups ($P > 0.05$). As shown in Table 2.

Comparison of curative effect of two groups of patients 1 year after operation

The curative effect rate (39.29%) of the treatment group was higher than that of the control group (22.92%) at 1 year after operation ($P < 0.05$), and the general curative effect rate (17.86%) and inefficiency (12.50%) were lower than those of the control group (27.08%)., 20.83%) (both $P < 0.05$). As shown in Table 3.

Comparison of curative effect of serum LDH decreased or increased 3 years after operation

The LDH levels measured at 3 years after surgery were compared with the levels at 1 year after surgery, and it was found that serum LDH levels decreased in 70 patients, while serum LDH levels increased in 41 patients. 3 years after operation, the markedly effective rate (37.14%) and effective rate (41.43%) of patients with decreased serum LDH level were significantly higher than those with increased serum LDH level (19.51%, 29.27%) ($P < 0.05$), the inefficiency (4.29%) was significantly lower than that of those with increased serum LDH level (29.27%) ($P < 0.05$). As shown in Table 4.

TABLE 1 Comparison of general clinical data of the two groups of patients.

Group	Sex ratio (male:female)	Age (year)	Tumor diameter (cm)	The number of tumors (pieces)	Liver function classification (*n*)	
					Child-Pugh A stage	Child-Pugh B stage
Control group ($n = 49$)	31:18	54.75 ± 4.92	2.87 ± 0.86	1.79 ± 0.66	29	20
Test group($n = 57$)	35:22	53.45 ± 4.76	2.76 ± 0.84	1.64 ± 0.75	32	25
χ^2/t	0.96	−0.79	−0.35	−0.47	0.67	
P	0.21	0.25	0.62	0.58	0.43	

Group	Cytological typing (*n*)		Degree of histological differentiation (*n*)			Clinical stage (*n*)		
	Hepatocellular carcinoma	Cholangiocarcinoma	Poorly differentiated	Moderate differentiation	Highly differentiated	Phase I	Phase II	Phase III
Control group ($n = 49$)	40	9	9	39	1	17	31	1
Test group ($n = 57$)	45	12	11	42	4	21	33	3
χ^2	0.74		0.98			0.79		
P	0.38		0.20			0.37		

TABLE 2 Serum LDH levels at each time point after surgery in the two groups of patients ($\bar{x} \pm s$, U/L).

Group	*n*	1 day after surgery	7 d after surgery	1 month after surgery	6 month after surgery	12 month after surgery	3 years after surgery
Control group	47	409.75 ± 28.54	389.75 ± 27.46	333.86 ± 29.54	306.86 ± 24.75	292.75 ± 24.86	257.35 ± 21.54
Test group	54	397.46 ± 23.75	342.85 ± 23.75	299.75 ± 23.75	268.57 ± 23.75	257.86 ± 19.54	244.65 ± 19.43
t		−1.04	−4.86	−4.57	−4.68	−4.35	−2.89
P		0.12	<0.01	<0.01	<0.01	<0.01	0.03

TABLE 3 Comparison of curative effect of two groups of patients at 1 year after operation [*n*(%)].

Group	*n*	Significant effect	Valid	General effect	Invalid
Control group	48	11 (22.92)	14 (29.17)	13 (27.08)	10 (20.83)
Test group	56	22 (39.29)	17 (30.36)	10 (17.86)	7 (12.50)
χ^2		5.56	0.32	4.87	4.37
P		0.02	0.62	0.03	0.04

TABLE 4 Comparison of curative effects of patients with decreased or increased serum LDH 3 years after operation

Group	*n*	Significant effect	Valid	General effect	Invalid
LDH reduce	70	26 (37.14)	29 (41.43)	12 (17.14)	3 (4.29)
LDH raise	41	8 (19.51)	12 (29.27)	9 (21.95)	12 (29.27)
χ^2		7.94	4.92	0.94	12.43
P		<0.01	0.03	0.21	<0.01

Discussions

HCC is one of the third largest tumors of the digestive system, with a high degree of malignancy and rapid disease progression, and its prevalence has been increasing year by year in the past decade (9, 10). The liver plays an important compensatory role in the human body, and at the same time, it usually undergoes changes from hepatitis to cirrhosis before the occurrence of HCC. However, it is difficult to effectively detect early cancer by clinical biochemical indicators. therefore, when liver failure occurs and the corresponding symptoms, most patients have entered the advanced stage of liver cancer. at this time, the best opportunity for treatment has often been lost and the life safety of patients has also received a serious threat (11, 12). After the liver becomes cancerous, cancer cells can spread rapidly in a short period of time, and patients with advanced liver cancer often develop severe jaundice, liver tumors and systemic symptoms (13). Especially in elderly patients, due to their low immune function and poor tolerance, the degree of body failure is relatively severe. At the same time, elderly patients are often complicated by various underlying diseases such as cardiovascular and cerebrovascular diseases, which ultimately lead to higher mortality (14). Transcatheter arterial chemoembolization is an important non-surgical method for the treatment of patients with liver cancer, and its clinical efficacy is ideal, which can effectively prolong the survival time of patients (15). At the same time, it can assist radical resection of liver cancer to play a synergistic role, effectively remove residual cancer cells, thereby effectively enhancing the short-term and long-term efficacy of patients, helping to reduce the disease recurrence rate and improve the prognosis of patients (16).

In this study, we found that the serum LDH levels of patients in the two groups were lower than those in the control group 1 day, 1 month, 6 months, and 12 months after surgery. The results suggested that LDH levels of patients with low preoperative LDH level or high preoperative LDH level could be reduced to a certain extent after hepatic artery chemoembolization, and the reduction amplitude of LDH concentration after operation in patients with low preoperative LDH level was significantly greater than that in patients with high preoperative LDH level. As one of the important enzymes in the process of glycolysis, LDH can exist in the cytoplasm of all tissues and cells of the body, especially in the liver (17). Because the distribution of LDH isozyme has good tissue specificity, it can be used for clinical diagnosis according to its tissue specificity (18). In HCC, because the intensity and speed of metabolism and necrosis of cancer cells are higher than those of normal cells, their cell membrane permeability is prone to change, resulting in the release of more enzymes in cancer cells into serum, which in turn leads to an increase in serum LDH concentration. Studies have reported that the concentration of serum LDH in HCC patients is about 35% higher than that in normal liver, and the positive detection rate of serum LDH for HCC is about 78% (19). It is considered that the detection of serum LDH level is one of the convenient and feasible methods. At the same time, it can not only reflect the metabolism and proliferation of cells, but also reflect the state of glycolysis, anaerobic or malignant lesions when the liver cells become cancerous in the early stage. In addition, changes in LDH serum levels directly or indirectly reflect the strength of

glycolysis, thereby predicting the tumor proliferation and development ability. Therefore, some studies (20) have pointed out that serum LDH is one of the important indicators for evaluating the short-term and long-term efficacy of interventional therapy in patients with HCC.

This study found that the curative effect rate in the treatment group was higher than that in the control group at 1 year after surgery, and the general curative effect rate and inefficiency rate were lower than those in the control group. The results suggest that the high concentration of serum LDH in HCC patients will have a certain impact on the prognosis after interventional therapy. At the same time, this study found that 3 years after surgery, the markedly and effective rates of patients with decreased serum LDH levels were significantly higher than those with increased serum LDH levels, and the inefficiency was significantly lower than those with increased serum LDH levels. The results showed that compared with those with high levels of serum LDH, those with low levels were more helpful to improve the long-term prognosis of elderly HCC patients undergoing hepatic arterial chemoembolization, thereby enhancing their clinical efficacy and prolonging survival time. The reason is that high LDH level may promote tumor occurrence and development by changing the *in vivo* environment and metabolism (21). Therefore, people with high LDH level are more prone to local infiltration, lymph node metastasis, and accelerated cancer progression, affecting the long-term prognosis of elderly HCC.

In conclusion, the detection of preoperative serum LDH level is helpful to evaluate the long-term prognosis of elderly HCC patients undergoing hepatic arterial chemoembolization. The low level of LDH in serum can also reflect the long-term curative effect of the patient, which can provide a certain strategy for selecting a more appropriate and effective program for clinical treatment. However, this study has the following shortcomings: (1) The small sample size included may lead to statistical differences, and it is necessary to further increase the sample size and improve the statistical strength in the future; (2) This study is a retrospective single-center study. There may be some uncontrollable factors or interfering factors in the baseline data of included subjects, and multi-center and prospective studies shall be designed for further verification in the future.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by This study was approved by the ethics committee of our hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

YG is mainly responsible for the writing, data analysis of the article. FG, BD, YL and QX are mainly responsible for research design. The corresponding author is JF, and she is responsible for ensuring that the descriptions are accurate and agreed by all authors. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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