

Bone and Arthroscopy Science

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Bone and Arthroscopy Science

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Bone and Arthroscopy Science is a peer-reviewed articles across a wide spectrum of clinical treatise, basic research, review, frontier of orthopedics, case analysis and comment. This journal is aimed at professionals at all levels engaged in the basic and clinical work of orthopedics. Each issue is guest-edited by an acknowledged expert and focuses on a single topic or controversy.

It mainly reports new viewpoints, new achievements and new technologies in basic and clinical research of bone and joint surgery. The covered topics include, but are not limited to: sports medicine and arthroscopy, prosthetic design, biomechanics, biomaterials, metallurgy, biologic response to arthroplasty materials *in vivo* and *in vitro*.

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Analysis of the Impact of Modified Fuyuan Huoxue Decoction on Inflammatory Factors, Immune Function, and Bone Metabolism Indicators in Patients After Surgery for Limb Fractures

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Abstract: *Objective:* This study aims to analyze the specific effects of modified Fuyuan Huoxue Decoction on inflammatory factor levels, immune function status, and bone metabolism-related indicators in patients after surgery for limb fractures. *Methods:* A total of 100 patients who underwent surgery for limb fractures in the orthopedics department of our hospital from January 2025 to January 2026 were selected and randomly divided into an observation group and a control group, with 50 patients in each group. The control group received only conventional Western medical treatment after surgery, while the observation group received additional intervention with modified Fuyuan Huoxue Decoction on the basis of the same treatment as the control group. Both groups were treated continuously for 4 weeks. Changes in serum inflammatory factors, immune function, and bone metabolism indicators were compared between the two groups before and after treatment. *Results:* After treatment, the reduction in serum interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and C-reactive protein (CRP) levels in the observation group was significantly greater than that in the control group ($P < 0.05$). The percentages of CD3⁺ and CD4⁺ T lymphocytes and the CD4⁺/CD8⁺ ratio increased significantly in both groups ($P < 0.05$), with the observation group showing significantly higher values than the control group ($P < 0.05$). Serum bone gla protein (BGP) and procollagen type I N-terminal propeptide (PINP) levels increased significantly in both groups ($P < 0.05$), while β -C-terminal telopeptide of type I collagen (β -CTX) levels decreased significantly ($P < 0.05$), with the observation group showing significantly greater improvement than the control group ($P < 0.05$). *Conclusion:* Modified Fuyuan Huoxue Decoction can effectively reduce postoperative inflammatory responses, improve immune function, regulate bone metabolism balance, and promote fracture healing in patients with limb fractures, making it worthy of clinical promotion.

Keywords: Modified Fuyuan Huoxue Decoction; Limb fractures; Postoperative; Inflammatory factors; Immune function; Bone metabolism

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1. Introduction

Fractures of the extremities represent one of the most prevalent traumatic conditions in clinical orthopedics, often resulting from direct or indirect violence and frequently accompanied by varying degrees of soft tissue injury ^[1]. Surgical treatment stands as the primary approach for addressing fractures of the extremities, effectively restoring anatomical alignment at the fracture site and limb function. However, the trauma induced by the surgery itself can trigger a robust stress response in the body, leading to the release of a large number of inflammatory factors and the onset of systemic inflammatory response syndrome. This, in turn, suppresses the body's immune function, increasing the risk of postoperative complications such as infection. Furthermore, fracture healing is a complex biological process involving the interaction between osteoblasts and osteoclasts. Postoperative disturbances in bone metabolism directly impact the speed and quality of fracture healing, potentially resulting in delayed union or nonunion. Therefore, effectively mitigating postoperative inflammatory responses, improving immune function, regulating bone metabolism balance, and promoting fracture healing have emerged as hot topics in orthopedic clinical research ^[2,3]. In recent years, the advantages of traditional Chinese medicine in fracture treatment have become increasingly evident. Fuyuan Huoxue Decoction, originating from *Medical Innovations*, is a classic formula renowned for its effects in promoting blood circulation, removing blood stasis, soothing the liver, and dredging the meridians. It is commonly used to treat traumatic injuries with blood stasis obstruction. Modern pharmacological studies have confirmed its anti-inflammatory, analgesic, microcirculation-improving, and tissue-repair-promoting effects ^[4,5]. This study aims to analyze the specific impacts of the modified Fuyuan Huoxue Decoction on inflammatory factor levels, immune function status, and bone metabolism-related indicators in patients following surgery for fractures of the extremities.

2. Materials and methods

2.1. General information

A total of 100 patients who underwent surgery for fractures of the extremities in the orthopedics department of our hospital from January 2025 to January 2026 were included and equally divided into an observation group and a control group, with 50 cases in each group. In the observation group, there were 28 males and 22 females, aged 18–65 years, with a mean age of 42.35 ± 10.26 years. Among them, 38 underwent open reduction and internal fixation, and 12 underwent closed reduction and internal fixation. In the control group, there were 26 males and 24 females, aged 19–64 years, with a mean age of 41.87 ± 9.94 years. Among them, 36 underwent open reduction and internal fixation, and 14 underwent closed reduction and internal fixation. The baseline data of the two groups ($P > 0.05$) suggested comparability between the groups.

Inclusion criteria: (1) Confirmed fractures of the extremities by X-ray or CT; (2) Admission and surgery within 72 hours after injury; (3) Aged 18–65 years; (4) No severe heart, liver, or kidney diseases, no immune dysfunction or blood system diseases; (5) No use of drugs affecting immunity or bone metabolism within 3 months before enrollment.

Exclusion criteria: (1) Pathological or old fractures; (2) Concomitant severe soft tissue injury or vascular nerve injury; (3) Concomitant infectious diseases or malignant tumors.

2.2. Treatment methods

The control group received routine postoperative Western medical treatment: routine anti-infection, analgesia,

and decongestion; immobilization and elevation of the affected limb, guiding patients in early functional exercises; supplementation with calcium and vitamin D; and nutritional support therapy.

The observation group received combined treatment with the modified Fuyuan Huoxue Decoction in addition to the control group's treatment. The basic formula consisted of 15g *Bupleurum*, 12g *Trichosanthes* root, 12g *Angelica sinensis*, 9g *Carthamus tinctorius*, 6g Licorice, 6g *Hirudo* (processed with hot water), 30g *Rhei Radix et Rhizoma* (processed with wine), and 15g *Persicae Semen*. Modifications: For severe pain, add 6g *Olibanum* and 6g *Myrrha*; for significant swelling, add 12g *Lycopus lucidus* and 15g *Leonuri Herba*; for qi and blood deficiency, add 30g *Astragali Radix* and 15g *Codonopsis pilosula*; for liver and kidney deficiency, add 15g *Eucommiae Cortex* and 15g *Dipsaci Radix*. One dose per day, decocted in water to obtain 400ml of juice, taken warmly in the morning and evening, for 4 consecutive weeks of treatment.

2.3. Observation indicators

Fasting venous blood samples (5ml) were collected before treatment and after 4 weeks of treatment, and serum was separated by centrifugation. Inflammatory factors: IL-6 and TNF- α were detected by ELISA, and CRP was detected by immune turbidimetry. Immune function: CD3⁺ and CD4⁺ T lymphocyte percentages were detected by flow cytometry, and the CD4⁺/CD8⁺ ratio was calculated. Bone metabolism indicators: BGP, PINP, and β -CTX were detected by chemiluminescence.

2.4. Statistical methods

Data were processed using SPSS 26.0 software. Continuous variables are presented as mean $\pm$ standard deviation (SD) and compared using *t*-tests; categorical variables are presented as percentages (%) and compared using chi-square tests. A *P*-value less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of inflammatory factor levels before and after treatment between the two groups of patients

After treatment, the levels of the aforementioned indicators in the observation group were significantly lower than those in the control group (*P* < 0.05). See **Table 1** for details.

Table 1. Comparison of inflammatory factor levels (mean $\pm$ SD)

Group	<i>n</i>	IL-6 (pg/ml)		TNF- α (pg/ml)		CRP (mg/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	50	35.62 $\pm$ 8.74	12.35 $\pm$ 3.26	28.45 $\pm$ 6.32	9.67 $\pm$ 2.14	45.26 $\pm$ 10.35	8.42 $\pm$ 2.15
Control group	50	34.89 $\pm$ 8.51	18.72 $\pm$ 4.15	27.98 $\pm$ 6.15	15.23 $\pm$ 3.08	44.78 $\pm$ 10.12	14.69 $\pm$ 3.27
<i>t</i>	-	0.423	8.535	0.377	10.483	0.234	11.329
<i>P</i>	-	0.673	0.000	0.707	0.000	0.815	0.000

3.2. Comparison of immune function indicators before and after treatment between the two groups of patients

After treatment, the aforementioned indicators in the observation group were significantly higher than those in the control group ($P < 0.05$). See **Table 2** for details.

Table 2. Comparison of immune function indicators (mean $\pm$ SD)

Group	<i>n</i>	CD3 ⁺ (%)		CD4 ⁺ (%)		CD4 ⁺ /CD8 ⁺	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	50	58.32 $\pm$ 6.45	68.75 $\pm$ 5.26	32.15 $\pm$ 4.26	40.67 $\pm$ 3.84	1.23 $\pm$ 0.21	1.68 $\pm$ 0.25
Control group	50	57.89 $\pm$ 6.23	63.42 $\pm$ 5.18	31.78 $\pm$ 4.12	35.89 $\pm$ 3.76	1.21 $\pm$ 0.20	1.42 $\pm$ 0.22
<i>t</i>	-	0.339	5.076	0.390	6.289	0.488	5.521
<i>P</i>	-	0.735	<0.001	0.697	<0.001	0.627	<0.001

3.3. Comparison of bone metabolism indicators between the two groups before and after treatment

After treatment, the improvement in the aforementioned indicators in the observation group was significantly better than that in the control group ($P < 0.05$). See **Table 3** for details.

Table 3. Comparison of bone metabolism indicators (mean $\pm$ SD)

Group	<i>n</i>	BGP (ng/ml)		PINP (ng/ml)		β -CTX (ng/ml)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	50	8.76 $\pm$ 2.15	16.32 $\pm$ 3.24	32.45 $\pm$ 6.78	68.72 $\pm$ 10.35	0.87 $\pm$ 0.21	0.42 $\pm$ 0.12
Control group	50	8.59 $\pm$ 2.08	12.45 $\pm$ 2.87	31.89 $\pm$ 6.54	52.36 $\pm$ 9.42	0.85 $\pm$ 0.20	0.63 $\pm$ 0.15
<i>t</i>	-	0.402	6.322	0.420	8.266	0.488	7.730
<i>P</i>	-	0.689	<0.001	0.670	<0.001	0.627	<0.001

4. Discussion

After surgery for extremity fractures, the body experiences a series of pathophysiological changes due to surgical trauma. Firstly, surgical trauma activates the body's inflammatory response system, leading to the activation of inflammatory cells such as monocytes/macrophages and neutrophils. These cells release inflammatory factors such as IL-6, TNF- α , and CRP, which play a role in clearing necrotic tissue and promoting tissue repair. However, excessive release of inflammatory factors can also lead to systemic inflammatory response syndrome, exacerbate tissue damage, and affect fracture healing [6]. Secondly, surgical trauma triggers a stress response in the body, leading to the excitation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system. This results in the massive secretion of hormones such as glucocorticoids and catecholamines, which inhibit the proliferation and differentiation of T lymphocytes, thereby reducing the body's immune function. This increases the risk of postoperative complications such as infections. Moreover, fracture healing is a complex process involving multiple cells and cytokines, and the balance between osteoblasts and osteoclasts is crucial for normal fracture healing. Postoperative factors such as inflammation, stress response, and immobilization can reduce osteoblast activity and increase osteoclast

activity, disrupting bone metabolism balance and leading to greater bone resorption than bone formation, thereby affecting the speed and quality of fracture healing^[7,8].

Traditional Chinese medicine posits that the basic pathogenesis of fractures is “external injury to the limbs leads to internal damage to qi and blood, disrupting the circulation of nutrient and defensive qi and causing disharmony among the internal organs.” After traumatic injury, blood stasis blocks the meridians, impeding the circulation of qi and blood and causing pain. Treatment should focus on promoting blood circulation to remove blood stasis and soothing the liver to unblock the meridians^[9]. Fuyuan Huoxue Decoction, originating from Li Dongyuan’s *Medical Innovations*, is a classic formula for treating traumatic injuries and blood stasis obstruction^[10]. Rhubarb processed with wine is used as the principal drug in a relatively heavy dosage, primarily to eliminate condensed stagnant blood resulting from traumatic injuries and guide the pathogenic factors of blood stasis downward, thereby achieving the effect of eliminating the old and fostering the new. *Angelica sinensis*, peach kernel, and safflower promote blood circulation to remove blood stasis, reduce swelling, and alleviate pain. Leech processed by branding breaks up blood stasis to unblock the meridians and reduces swelling and dissipates masses. Licorice relieves spasms and alleviates pain while harmonizing the actions of the other ingredients and serves as the envoy drug. When combined, these drugs work together to promote blood circulation to remove blood stasis and soothe the liver to unblock the meridians, thereby eliminating blood stasis, generating new blood, unblocking the meridians, and stopping pain.

After treatment, the serum levels of IL-6, TNF- α , and CRP in the observation group were significantly lower than those in the control group, which was related to the anti-inflammatory effects of various drug components in Fuyuan Huoxue Decoction. These components can inhibit the activation of inflammatory signaling pathways such as NF- κ B, reduce the release of inflammatory factors, and alleviate tissue damage caused by inflammatory responses.

The percentages of CD3⁺ and CD4⁺ T lymphocytes and the CD4⁺/CD8⁺ ratio in the observation group were significantly higher than those in the control group ($P < 0.05$). The stress response caused by surgical trauma can lead to a decrease in immune function. However, drug components such as *Bupleurum* and *Angelica sinensis* in Fuyuan Huoxue Decoction have immunomodulatory effects, promoting the proliferation and differentiation of T lymphocytes, enhancing cellular immune function, and reducing the incidence of postoperative complications such as infections.

After treatment, the serum levels of BGP and PINP in the observation group were significantly higher than those in the control group, while the level of β -CTX was significantly lower ($P < 0.05$). This indicates that modified Fuyuan Huoxue Decoction can effectively regulate bone metabolism balance in patients after extremity fracture surgery. BGP is a non-collagenous protein synthesized and secreted by osteoblasts and serves as a specific indicator of osteoblast activity. PINP is a product of type I collagen synthesis and is an important indicator of bone formation. β -CTX is a product of type I collagen degradation and is a specific indicator of bone resorption. Fuyuan Huoxue Decoction can promote the proliferation and differentiation of osteoblasts, enhance osteoblast activity, and promote bone formation while inhibiting osteoclast activity and reducing bone resorption, thereby regulating bone metabolism balance and promoting fracture healing^[11].

5. Conclusion

In summary, the use of modified Fuyuan Huoxue Decoction to treat patients after extremity fracture surgery

can achieve the following effects: reducing the level of inflammatory response in the body, enhancing immune function, and promoting fracture healing. This approach holds significant clinical application value. The results of this study provide a scientific basis for the application of traditional Chinese medicine in the postoperative management of extremity fractures. However, due to the small sample size and short observation period of this study, the long-term efficacy and safety still require further large-sample, multicenter, randomized controlled trials to confirm.

Disclosure statement

The author declares no conflict of interest.

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Clinical Observation on the Efficacy of Hot Wax Therapy Combined with Acupotomy in the Treatment of Stage I Shoulder-Hand Syndrome

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Abstract: *Objective:* To compare the clinical efficacy differences among hot wax therapy, acupotomy therapy, and their combined regimen in treating Stage I shoulder-hand syndrome (SHS). *Methods:* A total of 60 post-stroke SHS Stage I patients admitted to the Rehabilitation Department of Zhungeer Banner Hospital of Traditional Chinese and Mongolian Medicine from December 2024 to December 2025 were selected and randomly assigned to three groups: the hot wax group, the acupotomy group, and the combination group, with 20 patients in each group. The hot wax group received hot wax therapy combined with conventional rehabilitation; the acupotomy group received acupotomy release combined with conventional rehabilitation; and the combination group received both hot wax therapy and acupotomy release along with conventional rehabilitation. The treatment course for all groups was 4 weeks. The Visual Analogue Scale (VAS), Edema Evaluation Score (EES), and Fugl-Meyer Assessment (upper limb motor function) scores were compared among the three groups before treatment, after 2 weeks, and after 4 weeks of treatment. *Results:* After 4 weeks of treatment, all three groups showed significant reductions in VAS and EES scores and significant improvements in Fugl-Meyer upper limb motor function scores compared to before treatment ($P < 0.05$). Inter-group comparisons revealed that the improvement in all outcome measures in the combination group was significantly greater than that in the hot wax group and the acupotomy group after both 2 weeks and 4 weeks of treatment ($P < 0.05$). Furthermore, the acupotomy group demonstrated superior pain relief and edema reduction compared to the hot wax group ($P < 0.05$). *Conclusion:* The combination of hot wax therapy and acupotomy is more effective in alleviating pain and edema, and in promoting the recovery of upper limb motor function and activities of daily living in Stage I SHS patients, compared to either therapy alone or conventional rehabilitation. It represents a safe and effective comprehensive treatment approach.

Keywords: Shoulder-hand syndrome; Acupotomy; Hot wax therapy; Rehabilitation

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1. Introduction

Shoulder-hand syndrome (SHS), also known as complex regional pain syndrome type I, is a common complication after stroke, with an incidence rate as high as 12.5–70.0%^[1]. Stage I (acute stage) is characterized by sudden pain, swelling, increased skin temperature, and limited joint movement in the affected shoulder and hand. If timely and effective intervention is not provided at this stage, it can rapidly progress to stage II (dystrophic stage) and stage III (atrophic stage), leading to hand muscle atrophy, joint contracture deformity, serious damage to upper limb function, and affecting the overall rehabilitation process and quality of life^[2]. At present, clinical treatment for SHS stage I mostly uses comprehensive rehabilitation methods, including good limb positioning, concentric compression wrapping, active and passive joint range of motion training, physical factor therapy (such as transcutaneous electrical nerve stimulation, ultrasound), and drugs. Although these methods have certain efficacy, for some patients, especially those with significant edema and pain, the onset of action is slow and the effect is limited^[3]. Therefore, exploring intervention programs with faster onset and more accurate efficacy is an important issue in rehabilitation clinical practice. Hot wax therapy and acupuncture therapy are both commonly used physical and minimally invasive treatments in the field of pain rehabilitation. Acupotomy therapy is a minimally invasive technology that combines the characteristics of the “needle” of traditional Chinese medicine and the “knife” of Western medicine surgery. It can accurately loosen local adhesions and contracted fascia and soft tissues, effectively reduce intra-tissue pressure, relieve neurovascular compression, quickly relieve pain, and break the vicious cycle of “pain-spasm-ischemia”^[4]. Hot wax therapy utilizes the thermal, mechanical, and chemical effects of molten paraffin. Its large heat capacity and low thermal conductivity allow heat to penetrate into tissues persistently and evenly. It has the effects of significantly improving local blood circulation, promoting lymphatic return, eliminating edema, relieving pain, and softening tissues^[5]. Based on this, this study innovatively combines the “sharp release” of acupuncture with the “deep warming” of hot wax, aiming to exert a synergistic effect and intervene in the core pathological links of SHS stage I. Provide new treatment ideas and a basis for clinical formulation of stepped and precise treatment plans.

2. Clinical data

2.1. General information

Sixty patients with SHS stage I admitted to the rehabilitation department of our hospital from December 2024 to December 2025 were selected. The patients were randomly divided into three groups by the random number table method: hot wax group, acupotomy group, and combination group, with 20 cases in each group. There were no statistically significant differences in baseline data such as gender, age, disease duration, and primary disease type among the three groups of patients ($P > 0.05$), and they were comparable. This study was approved by the hospital Ethics Committee (Approval No.: Z20250009), and all patients signed the informed consent form.

2.2. Diagnostic criteria

Refer to the diagnostic criteria of the *Chinese Guidelines for Early Rehabilitation Treatment of Stroke*^[6]. Has a clear history of cerebrovascular disease; Stage I is characterized by pain and limited movement in the affected shoulder, often accompanied by pain in the ipsilateral finger and wrist joints. The fingers are mostly in a mildly flexed position, and the flexed movement is limited. The pain intensifies during passive flexed

movements. The hands are swollen and the color has changed.

2.3. Inclusion criteria

Meet the above-mentioned diagnostic criteria for SHS stage I; Aged 40 to 75; The first onset of the disease, with a course of less than 6 weeks; Vital signs are stable, consciousness is clear, and the patient can cooperate with treatment and assessment. Sign the informed consent form.

2.4. Exclusion criteria

SHS Stage II or Stage III; There is a fracture in the affected upper limb and chronic diseases in the shoulder in the past, such as gouty arthritis, periartthritis of the shoulder, and shoulder (semi) dislocation, etc. There is severe insufficiency of heart, liver, kidney, and other organ functions or coagulation dysfunction; Have cognitive impairment or mental illness and be unable to cooperate; Allergic to paraffin. Mistakenly included in the group criteria; The treatment was not received in accordance with the procedures stipulated in the research protocol.

2.5. Withdrawal

Patients who withdraw on their own during the treatment period; Adverse reactions related to treatment occur (such as skin burns, allergies, nerve damage, infections, etc.); During the treatment period, if there is a recurrence of stroke, severe cardiovascular and cerebrovascular events or other disease progression, and the trial needs to be discontinued and transferred to emergency treatment; Those who develop other serious diseases during the research process and require priority treatment; Lost contact.

3. Treatment methods

All patients were given corresponding conventional stroke drugs, dietary therapy, care, and conventional rehabilitation treatment based on the primary disease and complications, including good limb positioning, active and passive joint range of motion training of the affected limb, centripetal massage, and health education.

3.1. Hot wax group

The hot wax therapy method uses an intelligent wax therapy machine. Medical paraffin with a melting point of 56°C is selected. The melted wax liquid is poured into an enamel plate to form a wax cake about 2 to 3 cm thick. When it cools to the point where it initially solidifies into a block (surface temperature 45 to 50°C), a small spatula is used to remove the wax block and apply it to the jianyu, jianliao, and ashi points. Then, it is wrapped with plastic sheeting and cotton pads to keep warm for 30 minutes. This is done once a day. Treat for 6 days and rest for 1 day, and continue the treatment for 4 weeks.

3.2. Acupotomy group

Position: For shoulder operations, adopt the upright sitting position; for wrist operations, choose the supine position. Positioning: Shoulder selection points: The doctor holds the affected upper limb to assist the patient in performing passive flexion, extension, abduction, adduction, internal rotation, external rotation, horizontal abduction, and horizontal adduction, etc., to the extent that the patient can tolerate pain. When the patient feels pain, the doctor repeatedly presses around the shoulder of the affected limb and the upper

arm to find the most obvious tender point, or presses on the above areas to find the positive response point (tendon node). Select 2 to 4 points based on the patient's condition and mark them. Wrist point selection: The patient lies supine. At the ulnar edge of the flexor carpi radialis tendon in the transverse crease of the wrist on the distal side of the affected limb, 1–2 points are selected and marked according to the patient's condition. Needle: A disposable small needle knife from Jiangxi Laozongyi Medical Devices Co., LTD. (Gan Medical Device Registration No. 2017220027, specification 0.8 mm × 50 mm) is selected. Local anesthetic drugs: Take a 10 ml disposable sterile syringe to draw a mixed solution of 3 ml of 2% lidocaine injection and 1ml of Zhengqing Fengtongning Injection. Inject approximately 1ml at each application point. Specific operation: Shoulder: The operator should wash and disinfect their hands, wear a medical mask, instruct the patient to take a sitting or semi-reclining position, fully expose the skin, disinfect the operation site with iodophor, wear sterile gloves, and strictly follow the four-step needle insertion procedure of the needle knife to insert the needle, namely, fixed point, fixed direction, pressure, and insertion. The needle knife is inserted along the direction of the tendon and ligament's shape. After getting the breath, it is swung in a longitudinal direction for 3 to 4 cuts. Then, the blade direction is changed to be perpendicular to the muscle fiber direction for cutting. When there is a loose feeling in the hand, the needle knife can be pulled out. After the needle is removed, cover the wound with a band-aid and apply pressure to stop the bleeding for 1 minute. After the needle-knife treatment is completed, manual release should be performed. Slowly flex the shoulder joint forward, abduction, adduction, internal rotation and external rotation 2 to 3 times. The technique should be gentle and passive movement should be within the patient's tolerance range. Wrist: The disinfection method is the same as above. According to the four-step operation procedure of the acupotomy, insert the needle perpendicularly at the inner edge of the flexor carpi radialis tendon at the transverse crease of the wrist on the distal side of the affected wrist. The incision line should be parallel to the direction of the tendon's movement. The insertion depth should be approximately 0.5 cm. When a sense of hollow drop appears under the knife, switch to slow insertion. Make 3–4 longitudinal clear cuts and then swing laterally to separate the adhesions. After the needle is removed, cover the wound with a band-aid and apply pressure to stop the bleeding for 1 minute. After the needle-knife treatment is completed, 5 to 6 times of multi-angle and rotating wrist joint manipulation should be supplemented. Course of treatment: Once a week for 4 consecutive weeks.

3.3. Combination group

On the basis of conventional rehabilitation, the above-mentioned hot wax therapy and acupotomy therapy are combined. Wax therapy is not allowed on the day of acupotomy treatment. The interval should be at least 24 hours. The frequency and parameters of treatment were the same as those of the respective single-use groups.

4. Observation indicators and statistical methods

4.1. Observation indicators

4.1.1. Pain severity

The visual analogue scale (VAS) was adopted for assessment before treatment, at 2 weeks, and 4 weeks after treatment. A 10-cm horizontal straight line was used, with the leftmost end (0 cm) marked as no pain and the rightmost end (10 cm) marked as the worst imaginable pain. Patients placed a single mark on the line according to their overall current painful sensation to indicate pain intensity, and the scale value corresponding to the mark was recorded as the score. Scores ranged from 0 to 10 points; higher scores represented more severe pain.

4.1.2. Degree of edema in the affected hand

Before treatment, 2 weeks after treatment, and 4 weeks after treatment, the scores were 0, 2, 4, and 6 respectively for no edema, edema only limited below the wrist joint (near the metacarpophalangeal joint), edema spreading above the wrist joint, depression at the wrist joint, and edema throughout the upper limb.

4.1.3. Upper limb motor function

Before treatment, 2 weeks after treatment, and 4 weeks after treatment, the Upper Limb Simplified Fugl-Meyer Assessment Scale (FMA-UE) was used for evaluation. This scale contains 33 items in 10 aspects such as reflexes, shoulders, elbows, wrists, and hands. Each item was scored as uncompleted, partially completed, and fully completed with scores of 0, 1, and 2 respectively. The sum of the scores of each item was the total score. The total score ranges from 0 to 66 points. The higher the score, the better the upper limb motor function.

4.2. Statistical methods

Statistical analyses were performed using SPSS 26.0 software. Measurement data were expressed as mean $\pm$ standard deviation (SD). For data satisfying normal distribution and homogeneity of variance, one-way analysis of variance (ANOVA) was used for intergroup comparisons; repeated-measures ANOVA was applied to comparisons at different time points within groups, and the LSD-*t* test was adopted for pairwise comparisons. Enumeration data were presented as case number (percentage [%]), and the χ^2 test was utilized. A $P < 0.05$ was considered statistically significant.

4.3. Safety observation

Adverse reactions occurring during treatment were recorded, including bleeding, hematoma, and infection at acupotomy sites as well as scald induced by hot wax therapy.

5. Results

5.1. Comparison of VAS scores among the three groups before and after treatment

Before treatment, there was no statistically significant difference in VAS scores among the three groups ($P > 0.05$). At each follow-up time point after treatment, the VAS scores of all three groups decreased markedly compared with baseline ($P < 0.01$).

Intergroup comparison: At T1, the VAS scores of the acupotomy group and combination group were significantly lower than those of the hot wax group ($P < 0.05$); the combination group presented slightly lower scores than the acupotomy group without statistical differences ($P > 0.05$). At T2, the combination group had remarkably lower VAS scores versus the hot wax group and acupotomy group (all $P < 0.01$), and the acupotomy group was superior to the hot wax group ($P < 0.05$). These findings indicate that the combined regimen yields superior short- and long-term analgesic effects, and acupotomy exerts faster analgesic onset (see **Table 1**).

5.2. Comparison of affected limb edema scores among the three groups before and after treatment

No intergroup difference in edema scores was detected prior to treatment ($P > 0.05$). Edema scores of all groups were significantly reduced at each post-treatment time point relative to pretreatment ($P < 0.01$).

Intergroup comparison: At T1, edema scores in the acupotomy and combination groups were

significantly lower than the hot wax group ($P < 0.05$), whereas no difference existed between the acupotomy and combination groups. At T2, the combination group achieved significantly lower edema scores than the other two groups (all $P < 0.01$), and the acupotomy group outperformed the hot wax group ($P < 0.05$). It is demonstrated that the combined therapy achieves the optimal detumescence, and acupotomy produces better early detumescence than hot wax therapy (see **Table 1**).

5.3. Comparison of FMA-UE scores among the three groups before and after treatment

Baseline FMA-UE scores were comparable across three groups ($P > 0.05$). All groups obtained statistically elevated FMA-UE scores at each post-treatment time point compared with pretreatment ($P < 0.01$).

Intergroup comparison: No significant between-group difference was observed at T1 ($P > 0.05$). At T2, FMA-UE scores in the combination group were markedly higher than those in the hot wax group and acupotomy group (all $P < 0.01$), with no statistical discrepancy between the latter two groups ($P > 0.05$). The combined treatment possesses prominent long-term benefits in improving upper extremity functional recovery (see **Table 1**).

Table 1. Comparison of VAS scores, affected hand edema scores, and FMA-UE scores among three groups before and after treatment (mean $\pm$ SD, $n = 20$)

Group	Time	VAS (scores)	Degree of edema in the affected hand	FMA-UE
Hot wax	T0	7.3 $\pm$ 1.1	2.3 $\pm$ 0.5	29.5 $\pm$ 5.8
	T1	5.6 $\pm$ 1.0*	1.6 $\pm$ 0.6*	37.8 $\pm$ 6.2*
	T2	3.9 $\pm$ 0.9*	1.0 $\pm$ 0.4*	46.2 $\pm$ 6.5*
Acupotomy	T0	7.5 $\pm$ 1.2	2.4 $\pm$ 0.5	28.8 $\pm$ 6.1
	T1	4.4 $\pm$ 1.1* [△]	1.2 $\pm$ 0.5* [△]	39.2 $\pm$ 5.9*
	T2	3.2 $\pm$ 0.8* ^{△#}	0.8 $\pm$ 0.3* ^{△#}	48.9 $\pm$ 6.0*
Combined treatment	T0	7.4 $\pm$ 1.0	2.3 $\pm$ 0.6	30.1 $\pm$ 5.5
	T1	3.9 $\pm$ 0.9* [△]	1.1 $\pm$ 0.4* [△]	40.5 $\pm$ 5.7*
	T2	2.1 $\pm$ 0.7* ^{△#▲}	0.4 $\pm$ 0.3* ^{△#▲}	55.3 $\pm$ 5.4* ^{△#▲}

Notes: 1. T0: Before treatment; T1: 2 weeks after treatment; T2: 4 weeks after treatment. 2. Compared with T0 in the same group, * $P < 0.01$. 3. Compared with the hot wax group at the same time point, [△] $P < 0.01$. 4. Compared with the acupotomy group at the same time point, [▲] $P < 0.01$. 5. Comparison between T2 of the acupotomy group and T2 of the hot wax group, [#] $P < 0.05$.

5.4. Safety analysis

During the treatment, 2 patients in the observation group developed mild subcutaneous ecchymosis locally after acupotomy, which resolved spontaneously within 3 days without special intervention. One patient complained of a slight burning sensation during the first hot wax therapy due to sensory disturbance, and the symptom did not recur after adjusting the wax temperature. No obvious adverse reactions were reported in the control group. No severe adverse events such as infection, scald, or nerve injury occurred in either group.

6. Discussion

Shoulder-hand syndrome is one of the major disabling complications in patients with ischemic stroke, which severely hinders their early rehabilitation. Without timely intervention, the condition will progress, aggravate disability, and impair patients' activities of daily living. Its core pathogenesis lies in local

vasomotor dysfunction, aseptic inflammation, and obstructed lymphatic drainage caused by hyperactivity of the sympathetic nervous system, further resulting in severe pain, edema, and tissue nutritional imbalance^[7]. Stage I of SHS is the critical period for early intervention. Active treatment can prevent its progression to Stage II and Stage III, while effective clinical regimens remain to be optimized at present^[8].

This study adopted a three-group randomized controlled design to compare the efficacy of hot wax therapy, acupotomy, and their combination in the treatment of stage I SHS. The results showed that all three interventions could effectively relieve pain, reduce edema, and improve upper limb function. The combined group achieved significantly better improvements in all indicators than the two monotherapy groups, verifying the hypothesis of synergistic effects of combined treatment.

Analysis of efficacy trends revealed that at week 2 of treatment (T1), the acupotomy group and the combined group were markedly superior to the hot wax group in alleviating pain (VAS) and reducing edema (EES). It indicates that the mechanical release of acupotomy exerts an immediate effect on rapidly reducing tissue tension and internal pressure, and breaking the vicious cycle in the acute phase. As a pure physical therapy, hot wax therapy relies on the thermal effect to boost circulation and lymphatic drainage, which requires cumulative action and thus takes effect relatively slowly.

At the endpoint of week 4 (T2), the advantages of the combined group became fully evident, with the lowest VAS and EES scores and the highest FMA-UE scores. It suggests that the initial release by acupotomy creates a favorable mechanical environment for tissue repair. On this basis, the continuous warming and dredging effect of hot wax further optimizes local microcirculation and metabolism, and softens tissues. The sequential combination of the two therapies produces continuously amplified therapeutic effects and ultimately promotes the recovery of motor function more effectively.

In terms of mechanism, the pathological basis of stage I SHS includes neurogenic inflammation, excessive sympathetic nerve excitation, and microcirculation disturbance. By releasing lesioned fascia and soft tissues, acupotomy can not only directly reduce the transmission of pain signals but also regulate the tension-strain integrated structure of local soft tissues and modulate the excitability of sympathetic nerve terminals, thereby intervening in vasomotor disorders at the source.

The strong thermal effect of hot wax therapy can sustainably dilate blood vessels, accelerate blood flow, and enhance lymphatic pumping function. It flushes out inflammatory mediators released locally after acupotomy and efficiently removes interstitial fluid, thus consolidating and amplifying the anti-edema effect of acupotomy. The two therapies form a complete therapeutic cycle focusing on structural release and functional improvement respectively.

In terms of safety, the combined treatment does not raise major risks. Acupotomy is performed in strict accordance with aseptic techniques and anatomical principles, with operative sites avoiding major nerves and blood vessels to ensure safety. The temperature of the hot wax is well controlled. Measures such as temperature testing and shortened initial treatment duration effectively prevent scalds in patients with sensory impairment.

This study has several limitations. It is a single-center trial with a relatively small sample size and short follow-up duration, so the long-term efficacy of the combined therapy in preventing the progression of SHS to Stage II could not be observed. Further multi-center, large-sample randomized controlled trials with a follow-up period extended to 3 to 6 months are recommended. Additionally, objective imaging examinations such as ultrasonography and infrared thermography can be applied to further clarify the underlying mechanisms.

7. Conclusion

Combined hot wax therapy and acupotomy is a safe and effective treatment for Stage I SHS, offering superior improvement in pain, edema, upper limb motor function, and daily living activities compared to monotherapy or conventional rehabilitation.

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Disclosure statement

The authors declare no conflict of interest.

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Construction and Validation of a Risk Prediction Model for Perioperative Stroke in Patients with Hip Fracture

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Abstract: *Objective:* To construct a nomogram prediction model for the risk of stroke in patients with hip fractures during the perioperative period. *Methods:* The clinical data of patients with hip fracture surgery admitted to a Class III Grade A hospital from January 2019 to December 2023 were selected ($n = 895$). According to the presence or absence of perioperative stroke, the patients were divided into the case group ($n = 53$) and the control group ($n = 842$). Univariate and multivariate analyses were used to analyze the risk factors of stroke in patients, and a prediction model was constructed. A nomogram was drawn to visualize the logistic regression prediction model, and the ROC curve and decision curve were used to analyze the prediction efficiency of the logistic regression model. *Results:* Age ≥ 60 years, BMI ≥ 24 kg/m², history of hypertension, history of diabetes, history of stroke, general anesthesia, abnormal intraoperative blood pressure, and operation time were included in the final prediction model. The AUC of the validation set was 0.955 (95% CI: 0.923–0.986). The calibration curve showed that the predicted probability fitted the actual incidence well (Hosmer-Lemeshow test $P = 0.005$), and DCA confirmed that the model had a net clinical benefit. *Conclusion:* The risk prediction model constructed in this study can effectively identify patients with a high risk of perioperative stroke after hip fracture surgery, and has good prediction efficiency and clinical practicability, which is convenient for early and accurate prediction of perioperative stroke risk.

Keywords: Hip fracture; Stroke; Risk prediction model

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1. Introduction

Hip fractures are the most lethal type of fracture, and their poor prognosis is closely related to the risk of complications. Studies have shown that perioperative stroke events can increase the risk of death in such patients eightfold ^[1]. Stroke, as a common and serious complication of hip fracture patients, is caused by acute cerebrovascular disease and cerebral blood supply obstacles; according to the mechanism, it can be divided into ischemic and hemorrhagic types, the former is the result of cerebral vascular stenosis or

occlusion, especially the latter non-traumatic parenchymal hemorrhage^[2,3]. Perioperative stroke refers to cerebral infarction caused by ischemic or hemorrhagic cerebrovascular events, which occurs from the operation to 30 days after the operation^[4]. This complication is highly harmful, and its incidence is positively correlated with the age of the patients^[5]. There are significant differences in the risk of type I and type II, among which high-risk surgery can increase the incidence of stroke by about 1.5 times^[6]. Once perioperative stroke occurs, it will significantly prolong the postoperative hospital stay, increase medical costs, and further increase the medical burden of the family and society^[7]. Therefore, this study constructs a risk prediction model for perioperative stroke in elderly patients with hip fractures, so as to provide a theoretical basis for clinical medical staff to identify high-risk groups early.

2. Materials and methods

2.1. Study subjects

Patients with hip fractures admitted to a Class III Grade A hospital from January 2019 to December 2023 were retrospectively collected as the research subjects. Inclusion criteria: (1) Hip fracture was confirmed by CT, MRI and laboratory examination, in accordance with the relevant criteria of *Surgery (9th Edition)*; (2) age ≥ 18 years old; (3) patients met the diagnostic criteria^[8] of cerebral infarction in the 2023 Chinese guidelines for the diagnosis and treatment of acute ischemic stroke, with neurological localization signs, and confirmed by head CT and/or magnetic resonance imaging (MRI). Exclusion criteria: (1) patients with previous history of drug abuse or addiction; (2) patients with severe infectious diseases or central nervous system injury; (3) patients with previous history of mental disorders, liver and kidney dysfunction, acute cerebrovascular accident, nervous system diseases and multiple injuries; (4) pathological fracture: (5) old fracture; (6) incomplete medical records.

2.2. Data collection

The clinical data of patients were collected through the electronic medical record system, including (1) gender, age, height, and weight; (2) Preoperative indicators: patient's past history (hypertension, diabetes, coronary heart disease, previous history of stroke), anemia, atrial fibrillation, carotid artery stenosis, electrolyte disturbance, preoperative acute cerebral infarction, protein level, heart failure, blood lipid, blood glucose, white blood cell count; (3) Intraoperative indicators: anesthesia type, operation time, intraoperative blood pressure, intraoperative blood loss; (4) Postoperative indicators: postoperative blood pressure, anemia, infection and stroke.

2.3. Statistical analysis

SPSS 23.0 statistical software was used to analyze the data. The measurement data in accordance with normal distribution were expressed as mean $\pm$ standard deviation (SD), and the independent sample *t*-test was used. Measurement data with skewed distribution were presented as quartiles, and the rank sum test was used. Count data were described as absolute numbers or percentages and analyzed using the chi-square test. $P < 0.05$ was considered statistically significant. Variables with $P < 0.05$ were included in Logistic regression analysis to screen out independent risk factors related to stroke in patients with hip fractures. R4.1.2 software was used to analyze the independent risk factors, and the rms package was used to construct a nomogram model. The receiver operating characteristic curve (ROC), goodness-of-fit test, and calibration curve were used to evaluate the discrimination and calibration of the model, and the accuracy of the model was calculated. The

Decision Curve package was used to draw the decision analysis curve to evaluate the clinical effectiveness of the model.

3. Results

3.1. General information of the subjects

A total of 895 patients were included in this study, including 350 males (39.1%) and 545 females (60.9%). The mean age was 72.46 ± 14.58 years (range 60–99 years). Postoperative stroke occurred in 22 patients with hip fractures, with an incidence of 2.5%. The incidence was 2.6% in men and 1.5% in women.

3.2. Univariate analysis of perioperative stroke in patients with hip fracture

The 895 patients with hip fractures were divided into stroke occurrence group and non-stroke occurrence group, as shown in **Table 1**.

Table 1. Univariate analysis of the risk of perioperative stroke in patients with hip fracture

Variables	Total (n = 895)	0 (n = 842)	1 (n = 53)	Statistic	P
Gender, n (%)				Squared = 6.41	0.011
1	350 (39.11)	338 (40.14)	12 (22.64)		
2	545 (60.89)	504 (59.86)	41 (77.36)		
Age, n (%)				Squared = 5.02	0.025
1	127 (14.19)	125 (14.85)	2 (3.77)		
2	768 (85.81)	717 (85.15)	51 (96.23)		
BMI, n (%)				Squared = 149.57	<.001
0	191 (21.34)	188 (22.33)	3 (5.66)		
1	526 (58.77)	521 (61.88)	5 (9.43)		
2	178 (19.89)	133 (15.80)	45 (84.91)		
Method of anesthesia, n (%)				Squared = 25.76	<.001
1	511 (57.09)	463 (54.99)	48 (90.57)		
2	384 (42.91)	379 (45.01)	5 (9.43)		
With or without hypertension, n (%)				Squared = 28.33	<.001
0	400 (44.69)	395 (46.91)	5 (9.43)		
1	495 (55.31)	447 (53.09)	48 (90.57)		
Diabetes mellitus, n (%)				Squared = 47.58	<.001
0	641 (71.62)	625 (74.23)	16 (30.19)		
1	254 (28.38)	217 (25.77)	37 (69.81)		
Coronary heart disease, n (%)				Squared = 0.80	0.371
0	718 (80.22)	678 (80.52)	40 (75.47)		
1	177 (19.78)	164 (19.48)	13 (24.53)		
Carotid stenosis, n (%)				Squared = 1.09	0.297
0	860 (96.09)	811 (96.32)	49 (92.45)		
1	35 (3.91)	31 (3.68)	4 (7.55)		
Atrial fibrillation, n (%)				Squared = 0.05	0.826
0	858 (95.87)	808 (95.96)	50 (94.34)		

Variables	Total (n = 895)	0 (n = 842)	1 (n = 53)	Statistic	P
1	37 (4.13)	34 (4.04)	3 (5.66)		
Previous history of stroke, n (%)				Squared = 13.20	<.001
0	307 (34.30)	301 (35.75)	6 (11.32)		
1	588 (65.70)	541 (64.25)	47 (88.68)		
With or without anemia, n (%)				Squared = 2.54	0.111
0	567 (63.35)	528 (62.71)	39 (73.58)		
1	328 (36.65)	314 (37.29)	14 (26.42)		
Presence or absence of electrolyte disorder assignment, n (%)				Squared = 1.10	0.295
0	583 (65.14)	552 (65.56)	31 (58.49)		
1	312 (34.86)	290 (34.44)	22 (41.51)		
Preoperative emergency cerebral infarction, n (%)				-	0.617
0	879 (98.21)	826 (98.10)	53 (100.00)		
1	16 (1.79)	16 (1.90)	0 (0.00)		
Protein level, n (%)				Squared = 2.70	0.100
0	564 (63.02)	525 (62.35)	39 (73.58)		
1	331 (36.98)	317 (37.65)	14 (26.42)		
Heart failure, n (%)				Squared = 0.12	0.733
0	862 (96.31)	810 (96.20)	52 (98.11)		
1	33 (3.69)	32 (3.80)	1 (1.89)		
Blood lipids, n (%)				Squared = 6.03	0.014
0	877 (97.99)	828 (98.34)	49 (92.45)		
1	18 (2.01)	14 (1.66)	4 (7.55)		
Blood glucose, n (%)				-	0.255
0	817 (91.28)	771 (91.57)	46 (86.79)		
1	77 (8.60)	70 (8.31)	7 (13.21)		
2	1 (0.11)	1 (0.12)	0 (0.00)		
Leukocyte count, n (%)				Squared = 7.80	0.020
0	11 (1.23)	9 (1.07)	2 (3.77)		
1	624 (69.72)	581 (69.00)	43 (81.13)		
2	260 (29.05)	252 (29.93)	8 (15.09)		
Operation time, n (%)				Squared = 133.78	<.001
1	787 (87.93)	767 (91.09)	20 (37.74)		
2	108 (12.07)	75 (8.91)	33 (62.26)		
Intraoperative blood pressure, n (%)				Squared = 18.26	<.001
0	369 (41.23)	362 (42.99)	7 (13.21)		
1	526 (58.77)	480 (57.01)	46 (86.79)		
Intraoperative blood loss, n (%)				Squared = 1.62	0.445
0	776 (87.00)	727 (86.65)	49 (92.45)		
1	97 (10.87)	94 (11.20)	3 (5.66)		
2	19 (2.13)	18 (2.15)	1 (1.89)		
Anemia, n (%)				Squared = 0.23	0.632
0	382 (42.78)	361 (42.98)	21 (39.62)		
1	511 (57.22)	479 (57.02)	32 (60.38)		

Variables	Total (n = 895)	0 (n = 842)	1 (n = 53)	Statistic	P
Postoperative blood pressure, n (%)				Squared = 2.04	0.153
1	523 (58.44)	497 (59.03)	26 (49.06)		
2	372 (41.56)	345 (40.97)	27 (50.94)		
Co-infection, n (%)				-	0.491
0	884 (98.77)	832 (98.81)	52 (98.11)		
1	11 (1.23)	10 (1.19)	1 (1.89)		

χ^2 : Chi-square test, -: Fisher exact

3.3. Multivariate analysis of the risk of perioperative stroke in patients with hip fracture

Multivariate logistic regression analysis was used to analyze the risk factors with statistical significance in univariate analysis, and the forward stepwise method and likelihood ratio test were used to exclude the variables with no statistical significance. Independent variables were assigned in the following manner. Stroke: yes = 1, no = 0; Gender: male = 1, female = 0; Age: < 60 years = 1, ≥ 60 years = 2; BMI: thin = 1, normal = 2, obese = 3; Anesthesia method: general anesthesia = 1, local anesthesia = 2; Hypertension: yes = 1, no = 0; Combined with diabetes 1 = yes, 0 = no; Previous stroke history: yes = 1, no = 0; Blood lipids: yes = 1, no = 0; White blood cell count high = 0, low = 1, normal = 2; Operation time: < 3h = 1, ≥ 3 h = 2, intraoperative blood pressure: normal = 0, abnormal = 1. The results are shown in **Table 2**.

Table 2. Multivariate analysis of the risk of perioperative stroke in patients with hip fracture

Variables	Beta	S.E	Z	P	OR	95% CI
Gender	0.49	0.54	0.91	0.360	1.64	[0.57 to 4.70]
Age	0.51	0.92	0.56	0.577	1.67	[0.28 to 10.13]
BMI	2.08	0.71	2.92	0.003	8.04	[1.99–32.53]
Methods of anesthesia	-2.61	0.66	-3.97	<.001	0.07	[0.02–0.27]
Combined hypertension	1.35	0.62	2.16	0.031	3.84	[1.13 to 13.02]
Diabetes mellitus	1.40	0.49	2.84	0.005	4.05	[1.54–10.61]
He had a previous stroke	1.40	0.64	2.21	0.027	4.07	[1.17–14.17]
Blood lipids	2.53	0.88	2.89	0.004	12.60	[2.26–70.29]
White blood cell count	-4.88	1.41	-3.45	<.001	0.01	[0.00 to 0.12]
Duration of surgery	3.65	0.61	6.01	<.001	38.43	[11.69–126.28]
Intraoperative blood pressure	1.33	0.61	2.20	0.027	3.80	[1.16 to 12.43]

3.4. Construction of risk prediction model for perioperative stroke in patients with hip fracture

Through regression analysis of the included nine independent risk factors and their regression coefficients, the prediction model for stroke in patients with hip fracture was constructed by the formula method, and the nomogram for stroke after hip fracture was presented, as shown in **Figure 1**.

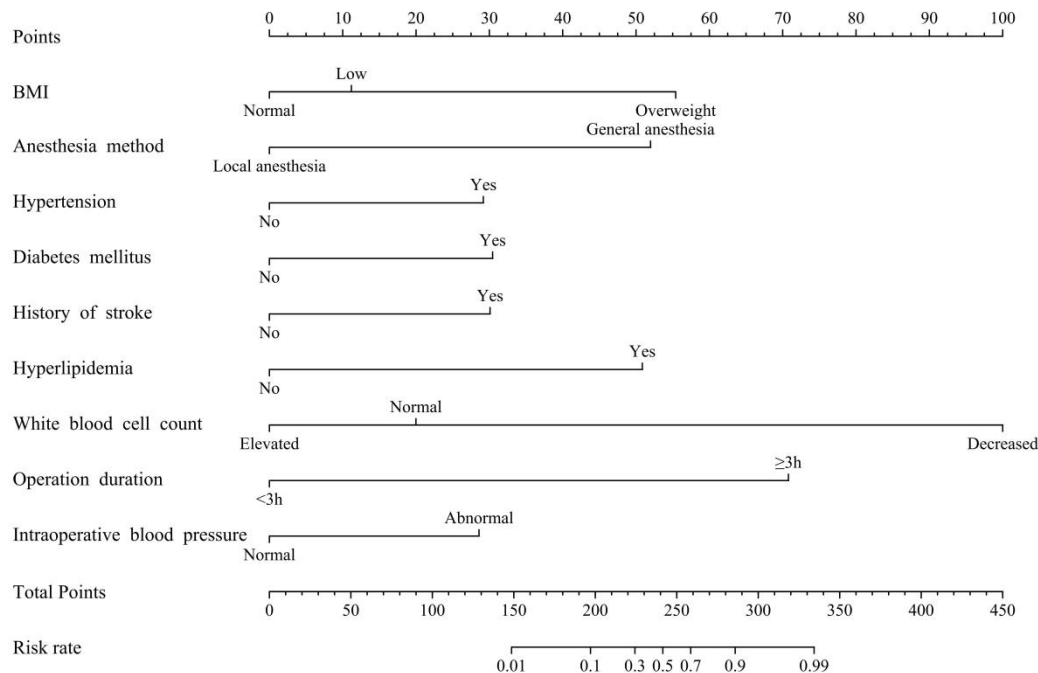


Figure 1. A nomogram model for predicting perioperative stroke in patients with hip fracture

3.5. Validation of the prediction model for perioperative stroke risk in patients with hip fracture

The model was validated by discrimination, calibration, and clinical validity. The results showed that the AUC of postoperative stroke in patients with hip fracture was 0.955 (95% CI: 0.923–0.986). This indicated that the model had good discrimination. See **Figure 1**. Hosmer-Lemeshow test results show $P = 0.009$, which proves that the model predicts well, and the predicted curve is basically consistent with the actual value, as shown in **Figure 2**. The bootstrap method was used to repeat 1,000 times from the original data, and the two-sided test level was 0.05. The results showed that the C-index (95% CI) was better, as shown in **Figure 3**. The DCA decision curve was used to evaluate the clinical effectiveness, and the model curve was closer to the two extreme curves. This model was selected to predict the positive clinical benefit of perioperative stroke in patients with hip fractures, as shown in **Figure 4**. The above results show that the prediction model has preliminary discrimination and calibration ability, but the clinical validity still needs to be further improved.

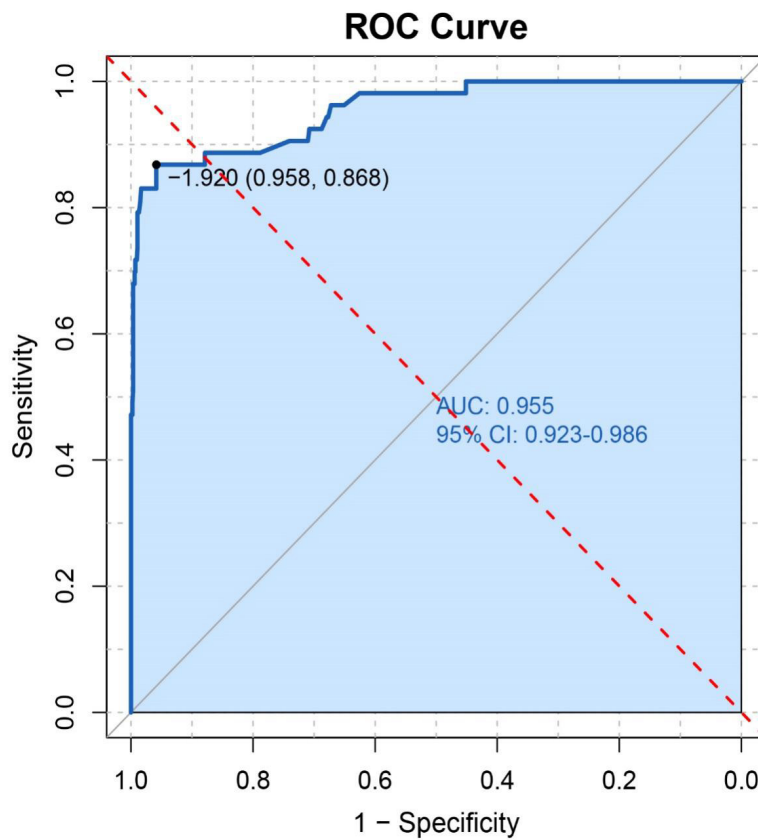


Figure 2. ROC curve for the perioperative stroke risk model in patients with hip fracture

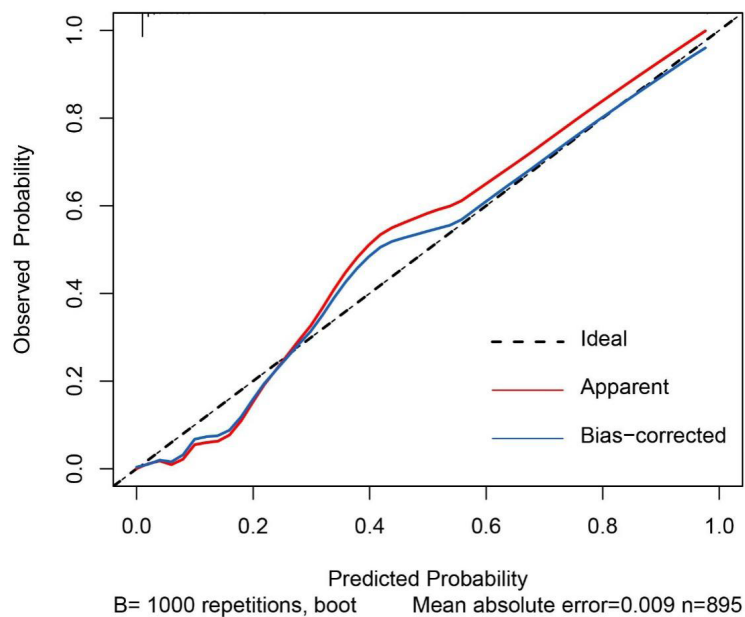


Figure 3. Calibration curve of the perioperative stroke risk model in patients with hip fracture

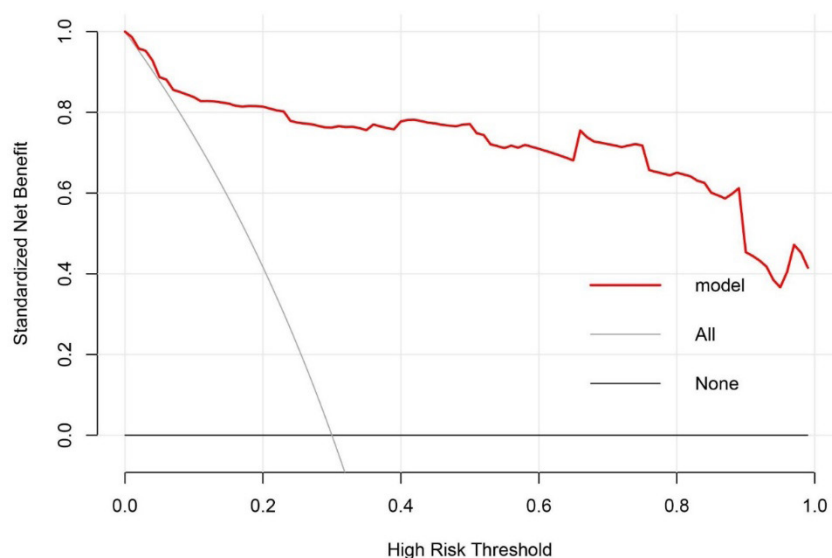


Figure 4. Decision curve analysis of the prediction model perioperative stroke in patients with hip fractures

4. Discussion

4.1. Current status analysis of perioperative stroke in hip fracture patients

Relevant studies have shown that about 5% of stroke patients have hip fractures during the follow-up period after discharge, and the risk of hip fractures is more than 1.5 times higher than that of the same age population^[9]. The risk of falls in this population is significantly higher than that in the elderly general population, and the mechanism may be closely related to the decline of postural control caused by visual pathway disorders and proprioceptive system disorders after stroke. As a typical pathological fracture, a hip fracture is often accompanied by multi-system involvement and biomechanical structure damage of the lower extremities. Its protracted course is easy to induce serious complications such as deep vein thrombosis and pressure injury, which eventually lead to a significant increase in mortality^[9,10].

Based on the previous research on stroke-related risk factors, 11 independent predictors of stroke were screened out by multivariate logistic regression analysis, and a prediction model for perioperative stroke risk of hip fracture was established. The model had good intuitive performance, and internal verification showed that the model had strong predictive ability. It can help medical staff identify the high-risk population of perioperative stroke in hip fracture as early as possible, and take appropriate intervention measures in time to reduce the occurrence of stroke and its complications.

4.2. Risk factors analysis of stroke in patients after hip fracture surgery

4.2.1. Body mass index >24 kg/m²

A BMI >24 kg/m² indicates that the patient is overweight or obese. Studies have shown that body mass index >24 kg/m² is a risk factor^[11] for perioperative cerebrovascular accident. Obesity is the core of metabolic syndrome, often accompanied by insulin resistance, dyslipidemia, chronic inflammatory state, and endothelial dysfunction, which are the basis of atherosclerosis and thrombosis. The stress of surgical trauma and anesthesia can further aggravate this hypercoagulable state and inflammatory response, thus inducing

acute cerebrovascular events. Therefore, structured health education intervention and stepwise weight control strategies should be implemented to reduce the incidence of neurovascular complications.

4.2.2. Methods of anesthesia

This study shows that patients receiving general anesthesia are more likely to have a stroke than those receiving regional anesthesia, which is consistent with the study by Zhou *et al.* ^[3], and may be related to the use of 3 to 4 drugs such as intravenous anesthetics, inhaled anesthetics, and analgesics during general anesthesia. The pharmacological properties of reducing peripheral vascular resistance and cardiac output, and the acidosis caused by hypocapnia and hypoxia caused by hyperventilation will also cause a decrease ^[12] in blood pressure, eventually leading to cerebral hypoperfusion, and leading to the occurrence of central nervous system complications. At the same time, studies ^[13] on anesthesia physiology have pointed out that there are two risk factors in patients with general anesthesia: peripheral vasodilatation and decreased cardiac output. The synergistic effect of the two factors reduces cerebral blood flow to a critical threshold, and the risk factor of cerebrovascular accident increases. Therefore, it is recommended to choose anesthetic drugs with less effect on cerebral blood vessels to maintain the stability of cerebral circulation during the operation.

4.2.3. History of diabetes

This study shows that preoperative diabetic hip fractures are associated with a higher risk of postoperative stroke. Some studies have confirmed that diabetes is an independent predictor of stroke events after hip fracture, and its risk factors are derived from chronic inflammation and abnormal vascular remodeling caused by insulin resistance ^[13,14]. At the same time, the degree of blood glucose variability also plays an important role in accelerating the occurrence of adverse cardiovascular and cerebrovascular events ^[15]. Other studies have shown that hip fracture patients with diabetes mellitus are at high risk of stroke, which may be related to high blood viscosity and hypercoagulable state in diabetic patients^[16]. Therefore, perioperative blood glucose management programs should be implemented for patients with diabetes and hip fracture: (1) Preoperative nutritional intervention should be combined with continuous glucose monitoring to optimize the level of glycosylated hemoglobin, (2) to standardize insulin administration to correct insulin resistance, and (3) to control stress hyperglycemia by adjusting the proportion of dietary fiber and carbohydrate measurement, so as to systematically reduce the risk of postoperative acute cerebrovascular events.

4.2.4. History of hypertension

The results of this study suggest that patients with a history of hypertension are more likely to have a stroke after a hip fracture. This may be related to the increase in the body's blood pressure level, which increases the damage degree of intracranial small arteries, induces cerebral atherosclerosis, causes small artery wall thickening, stenosis, and other lesions, and increases the risk ^[17] of cerebrovascular accident. According to the American Stroke Association ^[18], hypertension can increase the risk of stroke, especially when blood pressure is not well controlled during surgery, which is more likely to cause cerebrovascular problems. The study also found that people with a stroke caused by high blood pressure have more difficulty recovering and are more likely to die ^[19], become disabled, and have a recurrence than those with a stroke caused by other causes. Therefore, patients with hypertension after hip fracture surgery should be focused on monitoring blood pressure changes. According to the patient's age and blood pressure classification, blood pressure should be

controlled within a reasonable range to minimize the risk of stroke in hip fracture patients with a history of hypertension.

4.2.5. History of stroke

The results of this study suggest that patients with a history of stroke are more likely to have a stroke after hip fracture surgery. The study found a 13-fold increased risk of recurrent stroke in patients with a history of stroke. Yu *et al.* ^[20] found that clinical observations showed that patients with previous stroke had a significantly increased risk of a second stroke after undergoing hip fracture surgery. Its pathological mechanism is mainly related to the impairment of cerebrovascular regulation function and old infarction focus after stroke. When there is circulatory fluctuation or metabolic imbalance, the oxygen supply regulation ability of the damaged brain area is limited, which is easy to induce ischemic damage of nerve cells, and then lead to the recurrence of cerebrovascular events. Therefore, for such patients, it is necessary to focus on the implementation of precise hemodynamic management during the perioperative period, and maintain the balance of cerebral oxygen supply and demand to the maximum extent by continuous monitoring of cerebral perfusion pressure and intracranial blood flow, so as to effectively prevent the recurrence of stroke.

4.2.6. Intraoperative blood pressure abnormalities

This study shows that abnormal intraoperative blood pressure is one of the risk factors for postoperative stroke in patients with hip fractures. Intraoperative hypotension is a risk factor ^[21] for perioperative stroke, which may be related to blood volume reduction, electrolyte imbalance, and severe anemia caused by prolonged fasting and water deprivation before surgery. In addition, there may be bone cement implantation reactions, improper management of intraoperative controlled hypotension or large blood loss, and the influence of the depth of anesthesia. If the blood pressure is not maintained effectively and timely, it can lead to long-term hypoperfusion of brain tissue, and then cause ischemia and hypoxia injury. Studies have shown ^[22] that the increase of blood pressure variability during surgery not only disrupts the hemodynamic homeostasis at the capillary level, but also induces capillary hypoperfusion through abnormal shear stress of vascular endothelium, which in turn leads to tissue oxygenation disorder. Therefore, medical staff should strengthen the management of intraoperative blood pressure, control blood pressure before surgery, and do a good job of preoperative psychological care for patients to avoid increasing the risk of stroke.

4.2.7. White blood cell count

This study found that postoperative white blood cell count abnormality was an independent predictor of postoperative stroke in patients with hip fractures. This result is consistent with the study by Yao *et al.* ^[23], who confirmed that increased white blood cell count was a significant risk factor for perioperative stroke through a retrospective analysis of 361 elderly patients with hip fractures. Most of the patients with hip fractures are very elderly, often accompanied by a variety of underlying diseases. An elevated white blood cell count may be a response to an occult or undetected infection (e.g., urinary tract infection, respiratory tract infection, pressure sores, etc.), which itself is an important risk factor for stroke. On the other hand, leukopenia may indicate the presence of malnutrition, extreme immunosuppression, or more serious underlying disease states, which may reduce the patient's ability to cope with surgical trauma and stress, and the risk of organ dysfunction (including cerebrovascular events) is correspondingly increased. Therefore,

nursing staff should improve the awareness of the risk of stroke, identify high-risk patients with abnormal white blood cells early, and establish targeted nursing programs.

4.2.8. High blood lipids

The results of this study found that preoperative dyslipidemia is an important risk factor for perioperative stroke, which is basically consistent with the prospective study of Ni *et al.* ^[24]. In 169 hip fracture patients, the incidence of dyslipidemia and perioperative cerebrovascular events was 2.3 times higher than that in the normal group. Related studies have shown that hyperlipidemia promotes atherosclerosis and arterial stenosis, which increases the risk ^[25] of stroke. This may be related to high LDL-C level, which leads to microcirculation disorders in the cerebral perfusion area by promoting the formation of atherosclerotic plaque and increasing platelet aggregation. While low HDL-C weakens the vascular endothelial repair ability and anti-inflammatory function, it synergistically aggravates the risk of perioperative cerebral ischemia. Therefore, nurses should comprehensively evaluate the blood lipid status and medication history of patients before surgery. It is necessary to focus on the importance of continuous use of statins to maintain the stability of blood lipids and prevent the risk of stroke, and urge patients to take medication regularly until the day of surgery.

4.2.9. Operation time

This study confirmed that prolonged operation time is an independent risk factor for perioperative stroke in patients with hip fractures. The prolonged operation time directly reflects the increased surgical traumatic stress. This may be related to the complex operation, the difficulties encountered during the operation, and more bleeding and fluid transfer, which will aggravate the physiological stress response of the patient. This strong stress state will lead to the massive release of stress hormones such as catecholamines and cortisol, which will cause blood pressure fluctuation and heart rate increase, and increase the cardiac load, which may induce arrhythmias such as atrial fibrillation, or lead to the unstable rupture of the original atherosclerotic plaque, and ultimately greatly increase the risk ^[26] of perioperative ischemic stroke. In addition, prolonged anesthesia itself will challenge the stability of the circulatory system, increase the probability of hypotension events, and cause cerebral hypoperfusion. Therefore, clinical medical staff should implement the whole process of patients from preoperative to postoperative, more targeted monitoring and intervention, and ultimately play a key role in improving the prognosis of patients.

5. Conclusion

This study focused on the high risk of perioperative stroke in patients with hip fractures, and successfully constructed and validated a nomogram model for predicting the risk of this complication. The results show that the nomogram model can more accurately identify patients with a high risk of stroke during the perioperative period of hip fracture, and provides an important quantitative reference tool for clinical medical staff in preoperative evaluation, early warning, formulation of personalized nursing intervention plans, and optimal allocation of medical resources. Although the prediction model constructed in this study shows good performance in the sample of a single center, there may be a certain bias in the results due to the limited sample. Future studies can further conduct multi-center and prospective validation, and explore the clinical application effect of the model and its practical value in improving the prognosis of patients.

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Disclosure statement

The authors declare no conflict of interest.

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Research on the Application of Enhanced Recovery After Surgery (ERAS) Concept Combined with Wiltse Approach TLIF in Elderly Patients with Lumbar Spinal Stenosis

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Abstract: *Objective:* To evaluate the clinical efficacy and safety of the enhanced recovery after surgery (ERAS) concept combined with the Wiltse intermuscular approach transforaminal lumbar interbody fusion (TLIF) in the treatment of elderly patients with lumbar spinal stenosis. *Methods:* A prospective study was conducted on 63 elderly patients with lumbar degenerative diseases and lumbar spinal stenosis admitted to our hospital from February 2021 to June 2022, aged ≥ 60 years. Patients were randomly divided into an ERAS group (32 cases) and a control group (31 cases) using a random number table method. The ERAS group received standardized perioperative management based on the ERAS concept and underwent TLIF via the Wiltse intermuscular approach, while the control group received conventional perioperative management and underwent TLIF via the traditional posterior median approach. Perioperative indicators such as general patient information, length of hospital stay, operative time, intraoperative blood loss, and postoperative complications were compared between the two groups. Pain in the affected limb was assessed using the visual analogue scale (VAS) before surgery and on postoperative days 1, 3, and at 1 month and 3 months. Functional status was evaluated using the Oswestry disability index (ODI) before surgery and at 1, 3, and 6 months postoperatively. The overall therapeutic effect was evaluated according to the modified MacNab criteria at the last follow-up. *Results:* There were no statistically significant differences in general patient information between the two groups ($P > 0.05$). Compared with the control group, the ERAS group had significantly reduced intraoperative blood loss and postoperative hospital stay ($P < 0.05$). There were no statistically significant differences in operative time, preoperative VAS score for pain in the affected limb, or preoperative ODI score between the two groups ($P > 0.05$). The VAS scores in the ERAS group were significantly lower than those in the control group on postoperative days 1, 3, and at 1 month and 3 months ($P < 0.05$), with no significant difference between the two groups at 3 months postoperatively ($P > 0.05$). The ODI scores in the ERAS group were significantly better than those in the control group at 1, 3, and 6 months postoperatively ($P < 0.05$). At the last follow-up, according to the modified MacNab criteria, the ERAS group had 29 excellent cases, 2 good cases, and 1 fair case, with an excellent and good rate of 96.9%; the control group had 26 excellent cases, 2 good cases, and 3 fair cases, with an excellent and good rate of 90.3%. There were 4 postoperative complications in the ERAS group

and 9 in the control group, with no postoperative readmissions or deaths within 30 days postoperatively in either group. *Conclusion:* The application of the ERAS concept combined with the Wiltse approach TLIF in elderly patients with lumbar spinal stenosis can reduce blood loss and complications, alleviate early postoperative pain, accelerate functional recovery, and shorten hospital stay while ensuring surgical safety, which is of great clinical significance.

Keywords: Enhanced recovery after surgery concept; Lumbar spinal stenosis; Elderly; Interbody fusion cage; Spinal fusion surgery

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1. Introduction

Enhanced recovery after surgery (ERAS) is a comprehensive set of perioperative optimization strategies proposed based on evidence-based medicine. Through multidisciplinary collaboration, targeted interventions are implemented at every stage—before, during, and after surgery—to reduce the body's stress response, minimize complications and readmission rates, shorten hospital stays, and thereby enhance patient satisfaction. The ERAS model has garnered substantial evidence-based support in fields such as general surgery and joint replacement^[1,2]. In recent years, it has also been gradually applied in spinal surgery^[3], demonstrating favorable outcomes. However, prospective studies specifically targeting elderly patients with lumbar spinal stenosis remain limited. From a surgical approach perspective, the Wiltse intermuscular approach is a method that accesses the lamina and facet joint regions through the natural muscle gap between the multifidus and longissimus muscles along the lumbar back. This approach reduces paraspinal muscle dissection and retraction, preserving as much of the posterior column muscle-ligament complex as possible, thereby alleviating postoperative low back pain and reducing the risks of muscle atrophy and scar adhesion. When combined with the transforaminal lumbar interbody fusion (TLIF) technique, it is considered a less invasive variant compared to the traditional posterior midline approach TLIF. If further complemented by systematic ERAS management, it holds promise for amplifying the minimally invasive effects in elderly patients.

Based on a summary of previous evidence-based research on ERAS and spinal surgery, this study constructed a set of ERAS perioperative management procedures specifically tailored for elderly patients with lumbar spinal stenosis. These procedures were compared prospectively with traditional management approaches, utilizing the Wiltse intermuscular approach TLIF and the traditional posterior midline approach TLIF as surgical methods. By comparing perioperative indicators, pain and functional recovery, and the incidence of complications, the safety and efficacy of this comprehensive strategy were evaluated, providing a reference for the standardized diagnosis and treatment of the ERAS model in elderly patients.

2. Materials and methods

2.1. Study subjects

This study was a prospective controlled trial that included 63 elderly patients with lumbar degenerative diseases accompanied by lumbar spinal stenosis admitted to our hospital from February 2021 to June 2022. All patients met the surgical indications and had imaging-confirmed lumbar spinal stenosis at the responsible

levels.

Inclusion criteria: (1) Age ≥ 60 years; (2) Diagnosed with lumbar degenerative diseases accompanied by lumbar spinal stenosis requiring surgical decompression and fusion, including lumbar spondylolisthesis, lumbar spinal stenosis, and lumbar disc herniation with stenosis; (3) Number of responsible levels ≤ 2 ; (4) No severe cognitive impairment, able to cooperate with follow-up and functional assessment.

Exclusion criteria: (1) Spinal lesions and deformities caused by non-degenerative etiologies such as spinal infections, trauma, tumors, and ankylosing spondylitis; (2) Previous history of lumbar surgery; (3) Severe complications during the perioperative period requiring transfer to another department for treatment; (4) Number of responsible levels > 2 ; (5) Severe coagulopathy or systemic conditions intolerant to anesthesia and surgery.

2.2. Grouping and surgical methods

Prospective randomization was used to divide patients who met the inclusion criteria and completed follow-up into an ERAS group (32 cases) and a control group (31 cases) according to a random number table. All surgeries were performed by the same spinal surgery team under general anesthesia, with consistent anesthesia methods and basic perioperative anti-infective and internal medicine management principles.

The ERAS group underwent TLIF via the Wiltse intermuscular approach. Based on the location of the responsible intervertebral space, small incisions of approximately 4–5 cm were made about 2–3 cm laterally from the spinous process on both sides. After incising the lumbar back fascia, blunt dissection was performed along the natural muscle gap between the multifidus and longissimus muscles to expose the spinous process crest, where pedicle screws were inserted. On the decompression side, the multifidus muscle was moderately separated outward to expose the lamina, followed by decompression of the spinal canal and intervertebral foramen, as well as discectomy. A fusion cage was implanted and fixed, and connecting rods were installed and tightened. The wound was irrigated, a drainage tube was placed, and the layers were sutured sequentially.

The control group underwent TLIF via the traditional posterior midline approach. Patients were placed in the prone position, and a longitudinal incision was made along the posterior midline. The paraspinal muscles were stripped subperiosteally from the spinous processes to the roots of the transverse processes on both sides, exposing the laminae, facet joints, and transverse processes. Pedicle screws were inserted at the responsible levels, followed by decompression of the spinal canal and intervertebral foramen, resection of the diseased intervertebral disc, implantation of an appropriately sized interbody fusion cage, installation and tightening of connecting rods, routine irrigation, and layered suture. A drainage tube was placed at the incision site.

2.3. ERAS perioperative management procedures

The ERAS group implemented systematic ERAS management based on the aforementioned surgical approach, with the procedures outlined in **Table 1**.

Table 1. ERAS process management measures

Time	Item	ERAS group	Control group
Preoperative	Preoperative education	From pre-hospitalization, use multimedia videos, spinal anatomy models, etc., to explain to patients and family members the condition, surgical approach, possible complications, postoperative functional exercises, etc. Systematic re-education is given 1 day before surgery.	Education given 1 day before surgery, explaining the condition, surgical approach, possible complications.
	Psychological assessment	A psychiatrist performs psychological assessment and intervention after admission.	None
	Preemptive, multimodal analgesia	Perform VAS score after admission; give regular daily oral NSAIDs.	None
	Preoperative fasting time	Fluid fasting time: 2h before surgery, with oral clear fluids allowed before that (total < 400 ml); Food fasting time: 6h before surgery.	Fast from food 12h before surgery, fluids 4h before surgery.
	Preoperative nutritional support	Use nutritional risk screening to assess nutritional status; provide high-protein diet during perioperative period.	Regular diet
Intraoperative	Temperature management	Maintain room temperature at 20-24°C; cover exposed areas with blankets promptly after disinfection and surgery; use a forced-air warmer during surgery; warm irrigation fluid to ~37°C; use a fluid warming device for intravenous fluids.	Surgery performed at 20-24°C.
	Surgical approach	Unilateral Wiltse approach TLIF surgery.	Traditional posterior midline approach TLIF surgery.
	Bleeding management	Give a bolus of tranexamic acid 10-20 mg/kg before incision to reduce intraoperative blood loss.	None
	Incision management	Mix ropivacaine and lidocaine before closure; inject around the incision at multiple points using a 5 mL syringe needle.	Routine suture closure of the incision.
Postoperative	Early feeding	After full recovery from anesthesia, encourage water intake; give room-temperature liquid food orally 2-4h after surgery. After 3-4h from the first feeding, increase frequency and amount according to gastrointestinal tolerance.	Feed after the patient has passed flatus.
	Tube management	Remove urinary catheter after recovery from anesthesia. Male patients with high risk factors for urinary retention may have the catheter removed on the morning of postoperative day 2. Remove the incision drain when output is <50 mL.	Remove urinary catheter on postoperative day 2; remove incision drain when output is <50 mL.
	Early rehabilitation activities	After recovery from anesthesia, begin toe flexion/extension, ankle pump, quadriceps isometric contraction, and straight leg raise exercises. After physical strength recovers, ambulate with the assistance of professional rehabilitation personnel.	After removal of urinary catheter and drain, gradually begin bed exercises under guidance.

2.4. Observation indicators and evaluation methods

Perioperative clinical indicators included: gender, age, operation time, intraoperative blood loss, postoperative hospital stay, types and incidence of postoperative complications, as well as postoperative readmission and mortality within 30 days.

Pain assessment was conducted using the Visual Analog Scale (VAS) (0-10 points), with the degree of pain in the affected limb recorded before surgery and on postoperative days 1, 3, and at 1 month and 3 months. Functional assessment was performed using the Oswestry Disability Index (ODI) to evaluate the

degree of lumbar-related dysfunction before surgery and at 1 month, 3 months, and 6 months postoperatively. At the final follow-up, overall efficacy was evaluated according to the modified MacNab criteria, categorized into four grades: excellent, good, fair, and poor, with the excellent and good rates calculated.

2.5. Statistical analysis

Statistical analysis was performed using SPSS 27.0 software. Continuous data that followed a normal distribution and had homogeneous variances were expressed as mean $\pm$ standard deviation (SD). Comparisons between groups were made using repeated measures analysis of variance. Non-normally distributed data were analyzed using the Mann-Whitney U test. Categorical data were compared using the χ^2 test or Fisher's exact test. A P -value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general data

The ERAS group consisted of 32 patients, including 12 males and 20 females, with an average age of 65.13 ± 4.30 years. The control group consisted of 31 patients, including 16 males and 15 females, with an average age of 66.55 ± 3.82 years. There were no statistically significant differences between the two groups in terms of gender composition, age, operation time, preoperative VAS pain scores for the affected limb, and ODI scores ($P > 0.05$, **Table 2**).

Table 2. Comparison of general data and perioperative data between the two groups

Group	Number of cases	Male/Female (n/n)	Age (years)	Preoperative VAS score of affected limb	Preoperative ODI score
ERAS group	32	12/20	65.13 ± 4.30	7.81 ± 1.03	78.16 ± 9.88
Control group	31	16/15	66.55 ± 3.82	8.16 ± 1.13	78.39 ± 9.92
$\chi^2/t/Z$ value		1.270	2.932	-1.282	-1.349
P value		0.260	0.170	0.205	0.183

3.2. Perioperative clinical indicators

Compared with the control group, the ERAS group demonstrated a significant reduction in intraoperative blood loss and a shorter postoperative hospital stay, with statistically significant differences ($P < 0.001$, **Table 3**). In terms of operative time, the ERAS group was slightly longer, but the difference was not statistically significant ($P > 0.05$, **Table 3**). Regarding postoperative complications, there were 4 cases in the ERAS group and 9 cases in the control group, indicating a significantly lower complication rate in the ERAS group. Neither group experienced readmission or death within 30 days postoperatively.

There was no statistically significant difference in preoperative VAS scores between the two groups ($P = 0.205$, **Table 2**). The VAS scores for pain in the affected limb in the ERAS group showed a gradual decrease on postoperative days 1, 3, and at 1 and 3 months ($P < 0.001$, **Table 4**), with a consistent trend of improvement, suggesting superior early and mid-term pain control with ERAS management combined with the Wiltse approach.

There was no statistically significant difference in preoperative ODI scores between the two groups ($P = 0.183$, **Table 2**). Postoperative assessments at 1, 3, and 6 months showed significant improvement in ODI scores over time in both groups, with the ERAS group consistently outperforming the control group, with

statistically significant differences ($P < 0.001$, **Table 5**). This suggests that ERAS management combined with the Wiltse approach TLIF facilitates accelerated postoperative functional recovery.

This study employed modified MacNab criteria for efficacy evaluation and recorded complications. At the last follow-up, the ERAS group had 39 excellent cases, 2 good cases, and 1 fair case, with an excellent and good rate of 95.3%; the control group had 35 excellent cases, 2 good cases, and 3 fair cases, with an excellent and good rate of 87.5%. Both groups showed good overall efficacy, with the ERAS group slightly outperforming the control group, as shown in **Table 6**.

In terms of postoperative complications, there were 4 cases in the ERAS group, including pulmonary infection and urinary tract infection, while there were 9 cases in the control group, with a statistically significant difference in complication rates. Neither group experienced severe complications requiring readmission or resulting in death within 30 days postoperatively.

Table 3. Comparison of hospital stay, operative time, and blood loss between the two groups

Group	Number of cases	Hospital stay (days)	Operation time (min)	Intraoperative blood loss (ml)
ERAS group	32	12.00 ± 1.63	77.78 ± 11.54	120.63 ± 9.31
Control group	31	17.00 ± 1.61	74.19 ± 8.77	203.23 ± 51.29
$\chi^2/t/Z$ value		-12.251	1.393	-8.826
P value		<0.001	0.169	<0.001

Table 4. Comparison results of VAS scores for pain in the affected limb at different time points between the ERAS group and the control group (mean ± SD, points)

Group	n	Preoperative	Postoperative day 1	Postoperative day 3	Postoperative month 1	Postoperative month 3
ERAS group	32	7.81 ± 1.03	2.31 ± 0.69	1.56 ± 0.67	1.38 ± 0.49	1.28 ± 0.46
Control group	31	8.16 ± 1.13	2.81 ± 0.83	2.06 ± 0.63	1.71 ± 0.64	1.32 ± 0.54
F value			$F_{\text{time}} = 1168.907, F_{\text{group}} = 8.858, F_{\text{interaction}} = 1.292$			
P value			$P_{\text{time}} < 0.001, P_{\text{group}} = 0.004, P_{\text{interaction}} = 0.278$			

Note: Comparison was made using multivariate analysis of variance. Compared with the preoperative values within the same group, $*P < 0.05$.

Table 5. Comparison results of ODI scores at different time points between the ERAS group and the control group (mean ± SD, points)

Group	n	Preoperative	Postoperative 1 month	Postoperative 3 months	Postoperative 6 months
ERAS group	32	78.16 ± 9.88	22.75 ± 4.54	15.19 ± 2.97	6.87 ± 1.34
Control group	31	78.39 ± 9.93	30.77 ± 5.55	20.03 ± 3.05	11.61 ± 1.86
F value			$F_{\text{time}} = 1735.992, F_{\text{group}} = 41.112, F_{\text{interaction}} = 4.628$		
P value			$P_{\text{time}} < 0.001, P_{\text{group}} < 0.001, P_{\text{interaction}} = 0.035$		

Note: Comparison was conducted using multivariate analysis of variance. Compared with the preoperative values within the same group, $*P < 0.05$.

Table 6. Comparison of clinical efficacy evaluated by modified MacNab criteria between the ERAS group and the control group (cases)

Group	Excellent	Good	Fair	Poor	Excellent-good rate (%)
ERAS group	29	2	1	0	96.9
Control group	26	2	3	0	90.3

Note: The excellent and good rate was calculated as (Excellent + Good) / Total number of cases $\times$ 100%. Comparison between the two groups was conducted using Fisher's exact test, with $P = 0.355$ (two-tailed).

4. Discussion

The study results indicate that, among elderly patients with lumbar spinal stenosis, perioperative management based on the ERAS concept combined with the Wiltse intermuscular approach for TLIF significantly reduces intraoperative blood loss and shortens hospital stays compared to traditional perioperative management combined with the posterior midline approach for TLIF. This approach also lowers the incidence of complications, improves early postoperative pain and mid-term functional recovery, and achieves a higher excellent and good rate according to the MacNab criteria at the last follow-up. These findings suggest that combining surgical trauma control with comprehensive perioperative optimization offers significant clinical advantages in the surgical treatment of elderly patients with lumbar spinal stenosis.

Traditional posterior approaches often lead to denervation and ischemic changes in the paraspinal muscles, whereas the Wiltse approach^[4] preserves the innervation and blood supply of some muscles, reducing the occurrence of chronic postoperative low back pain. The preservation of the paraspinal muscles and posterior ligamentous complex via the Wiltse approach may influence the postoperative recovery process through multiple mechanisms^[5]. First, reducing muscle dissection and retraction can decrease local inflammatory responses and ischemia-reperfusion injury, creating favorable conditions for early postoperative mobilization. Second, maintaining the integrity of the muscle-ligament complex may help preserve spinal dynamic stability, thereby alleviating early postoperative mechanical pain. This hypothesis aligns with the improvement in early postoperative VAS scores observed in our study patients, but further validation through imaging and biomechanical studies is needed. Research has shown^[6] that the Wiltse approach preserves approximately 70% of paraspinal muscle function, which may be a key reason for faster postoperative recovery.

Notably, the accelerated functional recovery observed in the ERAS group in this study suggests that reduced surgical trauma may alter the kinetics of postoperative recovery. Traditional views^[7] hold that postoperative recovery in elderly patients is primarily limited by underlying diseases and physiological reserves. However, our study results indicate that these limitations can be partially overcome by optimizing surgical techniques and perioperative management. This finding has significant implications for geriatric spine surgery, suggesting that elderly patients should not be simply regarded as a "high-risk group" with lowered treatment goals. Instead, their prognosis can be improved through technological innovation and management optimization. In terms of complication prevention, our study results support the concept of "prevention is better than treatment." The lower complication rate in the ERAS group may be related to multiple factors: multimodal analgesia in the ERAS protocol (e.g., local infiltration anesthesia, NSAIDs) reduces the need for opioids, thereby decreasing the risk of postoperative delirium, ileus, and other complications; early mobilization reduces pulmonary complications; and nutritional support promotes

wound healing and improves immune function. Reduced intraoperative blood loss lowers the need for blood transfusions and associated risks; these factors collectively create a virtuous cycle, particularly beneficial for elderly patients with limited physiological reserves.

However, several aspects of this study's design require cautious interpretation. First, combining the surgical approach with perioperative strategies as a single intervention makes it impossible to distinguish their individual contributions. Second, a 6-month follow-up period is clearly insufficient for evaluating long-term outcomes such as fusion rates and adjacent segment degeneration. Third, the lack of objective muscle function assessments and inflammatory marker measurements limits the interpretation of underlying mechanisms. Future studies will adopt a multicenter design, extend follow-up periods, and incorporate more objective indicators to comprehensively evaluate the value of this comprehensive intervention. From a clinical practice perspective, our study results suggest that combining minimally invasive surgical techniques with the ERAS concept may yield superior clinical outcomes compared to traditional methods for elderly patients with lumbar spinal stenosis.

5. Conclusion

In summary, this study provides new insights into the treatment of elderly patients with lumbar spinal stenosis, but the relevant conclusions require further validation in larger, more rigorously designed studies. Future research directions should include comparing the benefits of different technical combinations, evaluating long-term functional outcomes, conducting cost-effectiveness analyses, and optimizing individualized protocols guided by biomarkers.

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The authors declare no conflict of interest.

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Analysis of the Efficacy of 3M Physical Therapy in Adolescent Female Patients with Hallux Valgus

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Abstract: *Objective:* To observe the clinical efficacy of safe and non-invasive 3M physical therapy on adolescent female patients with hallux valgus. *Methods:* From January 2024 to September 2025, 58 female hallux valgus patients aged 12–18 who received treatment at our hospital were selected and randomly divided into a treatment group and a control group, with 29 patients in each group. The treatment group received 3M physical therapy (including manual therapy, exercise therapy, and physical factor therapy); the control group received foot and toe function health education, requiring patients to improve their shoe-wearing and walking posture. After 8 weeks, hallux valgus angle (HVA), intermetatarsal angle (IMA), hallux valgus score American Orthopaedic Foot and Ankle Society (AO-FAS), and VAS scores were measured to evaluate rehabilitation effectiveness. *Results:* After 8 weeks, the VAS score in the control group was significantly lower compared to before treatment ($P < 0.05$); in the treatment group, HVA, IMA, and AO-FAS were significantly improved after 8 weeks compared to before treatment ($P < 0.05$), and the VAS score was decreased ($P < 0.01$); after 8 weeks of treatment, compared with the control group, HVA, IMA, and AO-FAS in the treatment group were significantly improved ($P < 0.05$), and the VAS score was decreased ($P < 0.01$). *Conclusion:* The application of 3M physical therapy in the treatment of adolescent female patients with hallux valgus can achieve significant therapeutic effects, significantly improve the hallux valgus angle, intermetatarsal angle, and pain, enhance the hallux valgus score level, and is suitable for the clinical rehabilitation treatment of adolescent female patients with hallux valgus.

Keywords: Hallux valgus; 3M physical therapy; Metatarsal

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1. Introduction

Hallux valgus is a common foot deformity primarily characterized by hallux valgus and subluxation or complete dislocation of the first metatarsophalangeal joint, with clinical manifestations including forefoot

pain, deformity, difficulty in wearing shoes, and functional impairment ^[1]. In clinical diagnosis, hallux valgus can be confirmed if the hallux valgus angle (HVA) exceeds 15° ^[2]. The incidence of this condition is significantly higher in females than in males, with a ratio of 15:1 for females to males ^[2]. Due to the deformity of the toes, pain, walking dysfunction, and abnormal gait, patients often experience significant physical and psychological stress. With the improvement of living standards and enhanced aesthetic awareness, an increasing number of adolescent females and their parents are actively seeking intervention due to the impact of hallux valgus on foot aesthetics and pain, a phenomenon that has garnered increasing attention in recent years. Although hallux valgus is not life-threatening, its impact on patients' daily quality of life cannot be overlooked. Currently, conservative clinical treatments for hallux valgus primarily focus on health education and orthotic appliances. However, health education content is often abstract, lacking systematic, quantitative training prescriptions and clear precautions, making it difficult for patients to effectively implement. Additionally, during the wearing of orthotic appliances, adolescent patients often experience poor compliance and significant discomfort, leading to suboptimal treatment outcomes and difficulty in achieving sustained improvement in deformities. Therefore, exploring a non-surgical therapy that is more operable, comprehensive, and acceptable to patients holds significant clinical importance.

3M physical therapy is a comprehensive rehabilitation intervention that integrates manual therapy, movement therapy, and modality therapy ^[3], aiming to correct hallux valgus deformities from both structural remodeling and functional reconstruction perspectives of the foot. This method has demonstrated favorable outcomes in the rehabilitation treatment of musculoskeletal system diseases. Currently, domestic clinical research on its application in hallux valgus treatment remains limited, particularly with insufficient evidence of its efficacy in adolescent females. Based on this, this study systematically evaluates the clinical efficacy of 3M physical therapy in improving hallux valgus in adolescent females, aiming to provide a scientific basis for clinical rehabilitation practice and lay the foundation for subsequent related research.

2. Materials and methods

2.1. Study subjects

A total of 58 adolescent females with hallux valgus who visited our hospital from January 2024 to September 2025 were selected as study subjects. They were randomly divided into a treatment group and a control group using a random number table method, with 29 cases in each group. The treatment group ranged in age from 12 to 18 years, with an average age of 13.83 ± 1.583 ; the control group ranged in age from 12 to 18 years, with an average age of 13.93 ± 1.668 . There were no statistically significant differences in general information between the two groups ($P > 0.05$), indicating comparability and compliance with study requirements. All patients and their guardians thoroughly read and signed informed consent forms, voluntarily agreeing to receive treatment.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Female patients with a disease duration of less than 3 years and aged between 12 and 18 years; (2) $HVA \geq 15^\circ$, intermetatarsal angle (IMA) $\geq 9^\circ$, Chippaux-Smirak index (CSI) $> 45\%$, with the dominant foot included for observation; (3) Patients experiencing pain on the medial side of the toes but not affecting normal walking; (4) Patients and their guardians have no intention of undergoing surgery.

Exclusion criteria: (1) Individuals with leg length discrepancy, limping, or leg injuries that prevent

completion of the experiment; (2) Thumb deformities caused by fractures or other violent factors; (3) Hallux valgus deformities caused by other diseases such as clubfoot or foot hemangioma; (4) Patients with consciousness or comprehension disorders that prevent cooperation with treatment.

Exclusion and dropout criteria: (1) Failure to complete the full course of treatment as required due to subjective willingness or objective conditions; (2) Inability to tolerate treatment after the trial or the occurrence of adverse reactions during treatment; (3) Early withdrawal due to poor compliance or dissatisfaction with treatment outcomes, or loss of contact during follow-up (loss to follow-up).

2.3. Research methods

Both groups of patients maintained normal living environments, diets, and rest routines during the treatment period. The control group received health education on hallux valgus, with the following specific content:

- (1) Patients were instructed to avoid prolonged local pressure on the toes during the trial period, and dance students (e.g., ballet) should cease relevant training.
- (2) Avoid wearing pointed-toe shoes, high heels, overly tight canvas shoes, and flip-flops.
- (3) Body weight should be controlled within the normal body mass index (BMI) range (18.5–23.9 kg/m²). For adolescent female patients who are overweight (24.0–27.9 kg/m²) or obese (≥ 28 kg/m²), they should be instructed to control their diet, engage in reasonable exercise, and be recommended aerobic exercises such as swimming.

The treatment group adopted 3M physical therapy on the basis of health education. For physical factor therapy, a low-frequency neuromuscular electrical stimulation therapy device (model: RH-SJSS-A) from Henan Ruihe Medical Equipment Co., Ltd. was used to provide electrical stimulation treatment to the abductor hallucis and peroneus longus muscles of patients. Manual therapy involved plucking and pressing the toe joints and adductor hallucis muscles, followed by the application of structural techniques to adjust the skin direction of the patients' lower limbs. Patients were placed in a prone position to release the quadriceps femoris, adjust the bone alignment of the feet, and reposition the talus. Exercise therapy involved comprehensive training of the intrinsic and extrinsic foot muscles: (1) Resistance training for ankle and toe flexion using elastic bands, including toe flexion and extension, ankle flexion and extension, and lateral ankle movements; (2) Training patients to use their hallux valgus toes to pick up objects such as small bamboo sticks, towels, and socks to exercise the functions of the extensor hallucis brevis and longus, abductor hallucis, flexor digitorum longus and brevis, dorsal interossei, and plantar fascia of the affected foot; (3) Modified TSO exercise training, which involved myofascial release along the direction of the peroneus longus muscle, followed by lifting all toes while keeping the metatarsal heads and heels on the floor. The little toe was placed on the ground first, then the big toe was pressed inward and downward, and finally, the fourth, third, and second toes were sequentially placed on the ground. Each exercise training session consisted of three sets of movements, with each set lasting for 3 minutes and a 1-minute rest between sets.

Both groups received treatment for 8 weeks.

2.4. Efficacy evaluation

The HVA, IMA, American Orthopaedic Foot and Ankle Society (AO-FAS) score, and pain level were compared between the control group and the treatment group before treatment and after 8 weeks of treatment.

AO-FAS score: It is an internationally recognized tool for evaluating foot and ankle function, encompassing three major dimensions: pain, function, and alignment, with a total score of 100 points. A

higher score indicates better function.

Pain level: The visual analogue scale (VAS) was used to assess patients' pain. It is a clinical assessment tool that quantifies pain intensity using a linear scale approximately 10 centimeters long, with "0 points" (painless) and "10 points" (excruciating pain) marked at both ends. Patients were asked to mark the corresponding position on the scale based on their subjective pain perception, and physicians measured the value at the marked point to obtain the pain score.

HVA: Measured using an anteroposterior radiograph of the foot, with a normal range of $\leq 15^\circ$. It represents the angle between the longitudinal axis of the first metatarsal bone and the longitudinal axis of the proximal phalanx, reflecting the degree of outward deviation of the big toe.

IMA: The angle between the longitudinal axes of the first and second metatarsal bones, with a normal range of $\leq 9^\circ$. An increased angle suggests metatarsus adductus.

2.5. Statistical analysis

All data were processed using SPSS 25.0 statistical software. Measurement data were expressed as mean $\pm$ standard deviation (SD). A normal distribution test was performed on the data. If the data conformed to a normal distribution, they were expressed as mean $\pm$ SD and analyzed using a *t*-test. If the data did not conform to a normal distribution, they were expressed as median and quartile points and analyzed using a rank-sum test. A *P*-value < 0.05 was considered statistically significant, and a *P*-value < 0.01 was considered highly statistically significant.

3. Results

There were no statistically significant differences in HVA, IMA, and AO-FAS scores between the control group before and after treatment ($P > 0.05$), while the VAS score significantly decreased after 8 weeks of treatment ($P < 0.05$). In the treatment group, after 8 weeks of treatment, HVA and IMA significantly decreased, the AO-FAS score increased ($P < 0.05$), and the VAS score significantly decreased ($P < 0.01$). There were no statistically significant differences in various indicators between the two groups before treatment ($P > 0.05$). After 8 weeks of treatment, the improvement in HVA, IMA, and AO-FAS scores in the treatment group was superior to that in the control group ($P < 0.05$), and the decrease in the VAS score was more significant ($P < 0.01$). See **Table 1**.

Table 1. Comparison of HVA, IMA, AO-FAS scores, and VAS scores in patients before and after treatment (mean $\pm$ SD)

Indicator	Before treatment	Before treatment	After 8 weeks	After 8 weeks
	Control group (<i>n</i> = 29)	Treatment group (<i>n</i> = 29)	Control group (<i>n</i> = 29)	Treatment group (<i>n</i> = 29)
HVA (degrees)	21.47 $\pm$ 4.44	21.98 $\pm$ 2.70	21.34 $\pm$ 4.56	16.94 $\pm$ 2.80 [△]
IMA angle (degrees)	11.23 $\pm$ 2.37	11.42 $\pm$ 1.13	11.17 $\pm$ 4.38	9.22 $\pm$ 3.24 [△]
AOFAS (points)	62.56 $\pm$ 9.79	64.89 $\pm$ 10.30	63.67 $\pm$ 9.78	79.22 $\pm$ 7.12 [△]
VAS score (points)	5.44 $\pm$ 1.42	5.33 $\pm$ 1.58	4.89 $\pm$ 1.27 [△]	1.78 $\pm$ 1.20 ^{•▲}

Note: ○ indicates a comparison within each group before and after the experiment, with $P < 0.05$; ● indicates a comparison within each group before and after the experiment, with $P < 0.01$; △ indicates a comparison between the control group and the treatment group, with $P < 0.05$; ▲ indicates a comparison between the control group and the treatment group, with $P < 0.01$.

4. Discussion

The coordinated contraction of the intrinsic and extrinsic foot muscles is crucial for maintaining the dynamic stability of the foot arch. The tibialis anterior and tibialis posterior muscles maintain the height of the medial foot arch through traction, while the flexor digitorum longus, flexor hallucis longus, and intrinsic foot muscles work together to counteract the downward pressure and posterior tilt of the talus, preventing arch collapse^[4-6]. When wearing inappropriate footwear for extended periods or having abnormal gait patterns, abnormal anterior displacement of plantar pressure can occur, leading to compensatory tension in the adductor hallucis and flexor hallucis brevis muscles, which in turn pulls the big toe outward, forming hallux valgus deformity. The skeletal and soft tissues of adolescents exhibit strong plasticity and respond better to physical stimuli than adults, providing a favorable physiological basis for conservative correction. However, research on non-surgical interventions for adolescent hallux valgus is relatively limited, with traditional conservative treatments focusing on passive measures such as health education and orthotic wear, lacking a systematic treatment regimen that actively corrects foot biomechanical imbalances. Therefore, exploring the efficacy of 3M physical therapy for treating adolescent hallux valgus holds significant clinical importance.

The results of this study show that after 8 weeks of 3M physical therapy intervention, the HVA and IMA significantly decreased, the AO-FAS score increased, and the VAS pain score significantly decreased ($P < 0.01$) in the treatment group of adolescent female patients with hallux valgus, while the control group only showed improvement in the VAS score ($P < 0.05$), with no significant changes in other indicators. After treatment, all indicators in the treatment group were significantly better than those in the control group ($P < 0.05$ or $P < 0.01$), indicating that 3M physical therapy has a definite corrective and analgesic effects on mild hallux valgus in adolescents. Compared to previous studies, the breakthrough of this study lies in: for the first time, integrating physical factor therapy, manual therapy, and exercise therapy into a systematic 3M physical therapy intervention regimen, focusing on adolescent females, a high-risk population. Firstly, physical factor therapy employs low-frequency electrical stimulation technology, precisely targeting the abductor hallucis and peroneus longus muscles. Electrical stimulation induces rhythmic muscle contractions, enhancing neuromuscular recruitment efficiency and improving muscle active contraction ability, thereby improving the dynamic motor function of hallux valgus^[7]. Secondly, manual therapy focuses on the abductor hallucis muscle—the only intrinsic muscle on the medial side of the foot that directly counteracts hallux valgus deformity—effectively adjusting the positional relationship between the navicular bone and the first metatarsal bone, restoring the normal alignment and mechanical axis of the first metatarsophalangeal joint, and reducing abnormal stress at the medial bony prominence^[8]. Finally, exercise therapy includes toe curling exercises, short foot exercises, and Tensor Fasciae Latae Strengthening Orthosis (TSO) exercises. Toe curling exercises activate the intrinsic plantar muscle group, short foot exercises emphasize actively shortening the foot arch length while keeping the heel and metatarsal heads grounded, and TSO exercises strengthen the eccentric and concentric control abilities of the intrinsic foot muscles through specific postures

and loads. These exercises work together to maximize the activation of the abductor hallucis muscle's active stability function^[9]. The synergistic effect of the above 3M physical therapy can rebuild the balance between the intrinsic and extrinsic foot muscle groups, improve foot arch support, and thereby delay or partially correct deformity progression from a biomechanical perspective. The clinical guidance value of this study lies in: for mild hallux valgus patients with immature skeletons, a comprehensive conservative treatment regimen combining active muscle group training with passive manual therapy and physical factors should be prioritized, rather than passive deformity correction or premature consideration of surgical intervention. It is particularly emphasized that adolescent skeletons are not yet fully mature, and the epiphyseal plate still has growth potential, with the plasticity of foot soft tissues being superior to that of adults. Therefore, 3M physical therapy can leverage this physiological characteristic to guide the normal development of foot structure, holding significant early intervention value. Compared to previous studies, most conservative treatments only focus on a single aspect, such as using night splints or silicone toe separators alone, which can temporarily relieve symptoms but fail to fundamentally correct muscle imbalances and joint alignment abnormalities. This study systematically integrates three modules of comprehensive treatment, significantly improving the stability and sustainability of therapeutic effects.

5. Conclusion

This study holds definite clinical guidance value: specifically, in clinical practice, it is recommended to intervene 3–4 times a week, for 40–60 minutes each session, with 8 consecutive weeks as one course of treatment, while guiding patients to perform home exercise training (such as 20 short foot exercises and 50 toe curling exercises daily, holding each for 20 seconds)^[10], and regularly re-measuring HVA, IMA, and functional scores. Of course, this study also has certain limitations, such as a relatively limited sample size and a follow-up period of only 8 weeks, with long-term efficacy and recurrence rates requiring longer-term tracking and observation. Future research can further explore the exercise prescription-effect relationship of 3M physical therapy and utilize objective means such as three-dimensional gait analysis and plantar pressure testing to deeply reveal its biomechanical regulatory mechanisms. In conclusion, 3M physical therapy provides a safe, effective, and sustainable innovative strategy for the conservative treatment of hallux valgus in adolescent females, worthy of promotion and application in clinical rehabilitation.

Disclosure statement

The authors declare no conflict of interest.

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Expanding Therapeutic Potential and Mechanisms of SIRT3 in Bone-Related Diseases through Mitochondrial Function Regulation

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Abstract: As a representative degenerative joint disease, the pathological mechanism of osteoarthritis has increasingly highlighted the critical role of SIRT3 protein in various bone-related disorders. Beyond its significant impact on osteoarthritis, mitochondrial dysfunction is closely linked to the pathogenesis of multiple bone diseases, including osteoporosis, osteonecrosis, bone erosion in rheumatoid arthritis, abnormal fracture healing, and bone tumors. This review systematically explores how SIRT3 regulates mitochondrial function, thereby influencing metabolic processes, apoptosis, autophagy, and senescence in various bone-related cells such as osteoblasts, osteoclasts, osteocytes, and chondrocytes. By conducting cross-disease comparative analysis, we reveal the central role of the SIRT3-mitochondrial function axis in maintaining skeletal homeostasis, providing important theoretical basis and research directions for the future development of broad-spectrum skeletal protection strategies targeting SIRT3.

Keywords: Sirtuin 3; Mitochondria; Osteoporosis; Osteonecrosis; Rheumatoid arthritis

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1. Introduction

Currently, Chinese manufacturing enterprises are experiencing a slowdown in growth and face issues such as the need for further optimization of their internal human capital structures. To address this situation, tax incentive measures such as additional deductions for R&D expenses can be implemented. By reviewing relevant domestic and international literature, a majority of scholars, such as Ma ^[1], argue that the policy of additional deductions for R&D expenses is a special provision established by the government aimed at

encouraging companies to increase their investment in R&D and support technological innovation. Studies by Guceril *et al.* ^[2] indicate that when companies benefit from tax reduction incentives, their investment behavior is significantly stimulated.

Bone and joint diseases represent a significant global health concern affecting individuals across all age groups, characterized by remarkable diversity and complexity. These conditions encompass both degenerative disorders such as osteoarthritis, as well as metabolic bone diseases (e.g., osteoporosis), inflammatory bone diseases (e.g., rheumatoid arthritis), traumatic bone injuries (including fractures and their complications), and various benign and malignant bone tumors. Although the etiologies and clinical manifestations of these diseases vary, recent studies suggest they may share certain common underlying pathophysiological mechanisms. Growing evidence indicates that mitochondrial dysfunction constitutes a pivotal shared biological basis, involving multiple aspects including abnormal energy supply, disruption of redox homeostasis, and disturbances in cellular metabolic regulation ^[1-4].

As a deacetylase primarily localized within mitochondria, SIRT3 is regarded as a core regulatory factor essential for maintaining cellular homeostasis. It plays a pivotal role in regulating cellular energy metabolism, enhancing cellular antioxidant stress resistance, and modulating the processes of apoptosis and autophagy ^[5-7]. Currently, researchers have preliminarily elucidated the protective mechanisms of SIRT3 in the progression of osteoarthritis, such as delaying disease progression by reducing chondrocyte apoptosis and inhibiting inflammatory responses ^[8]. However, for other types of bone and joint diseases, the specific functional mechanisms, expression changes, and potential therapeutic value of SIRT3 remain inadequately systematically summarized or thoroughly investigated.

Therefore, this article aims to provide a comprehensive review of the latest research advancements on SIRT3 in various bone-related diseases, analyze its expression patterns and biological functions under different pathological conditions, and further investigate whether it could serve as a common therapeutic target across diverse bone disorders, thereby offering theoretical support and novel research insights for future precision treatment strategies for bone and joint diseases.

2. The multicellular regulatory role of SIRT3 in bone homeostasis

Bone tissue, as a complex structure composed of various cell types, primarily includes osteoblasts, osteoclasts, osteocytes, and chondrocytes. Each of these cells performs distinct physiological functions and collectively maintains bone homeostasis. This homeostasis is sustained through a dynamic functional equilibrium among these cells; dysfunction in any cell type can lead to bone metabolic disorders. Studies have demonstrated that SIRT3, as a key deacetylase, exerts profound effects on the survival, differentiation processes, and functional performance of these critical cells in bone tissue by regulating mitochondrial function ^[9]. Specifically, SIRT3 plays a pivotal regulatory role in the biological activities of osteocytes by optimizing mitochondrial energy metabolism, antioxidant capacity, and apoptosis pathways.

2.1. Osteoblasts

As a key class of deacetylases, SIRT3 plays a pivotal role in the regulation of osteoblast function. It significantly enhances mitochondrial oxidative phosphorylation, improves energy metabolism efficiency, thereby robustly promoting ATP synthesis and supply, providing ample energetic support for the mineralization function of osteoblasts ^[10,11]. Meanwhile, SIRT3 also mitigates cellular damage caused by

oxidative stress by inhibiting the excessive accumulation of reactive oxygen species (ROS), significantly reducing the apoptosis rate of osteoblasts, thereby effectively promoting bone formation and maintaining skeletal homeostasis ^[12].

2.2. Osteoclasts

SIRT3 may significantly influence the differentiation process and bone resorption activity of osteoclasts by regulating mitochondrial energy metabolism and oxidative stress pathways ^[13,14]. However, there remains considerable controversy regarding its specific mechanisms of action. Different studies indicate that it may exert diametrically opposed regulatory effects under varying conditions, demonstrating complex bidirectional regulatory characteristics ^[15].

2.3. Osteocyte

As essential mechanoreceptors within bone tissue, osteocytes play a pivotal role in sensing mechanical stimuli and regulating bone metabolism. The mitochondrial function of osteocytes is critical for maintaining their normal survival and signaling capacity, involving multiple aspects such as energy metabolism, calcium ion homeostasis, and oxidative stress regulation. Studies have demonstrated that SIRT3 may effectively delay the aging process of osteocytes by modulating mitochondrial dynamic equilibrium and autophagic activity ^[16]. Specifically, SIRT3 promotes a dynamic balance between mitochondrial fusion and fission, enhances the capacity of mitochondria to clear damaged organelles through autophagy, thereby improving mitochondrial function and reducing oxidative damage, ultimately contributing to the maintenance of osteocyte homeostasis and physiological functions ^[17].

2.4. Chondrocytes

Multiple studies have conclusively demonstrated that the OA (osteoarthritis) model reveals the significant protective effects of SIRT3 protein on chondrocytes, which effectively delays the progression of cartilage degeneration through multiple mechanisms including reduction of oxidative stress and inhibition of inflammatory responses ^[18]. Furthermore, given its pivotal regulatory role in cartilage metabolism, SIRT3 may also play significant biological functions in various other cartilage-related disorders, such as the repair of cartilage tissue damage and the initiation and progression of chondromas, demonstrating broad potential research value and application prospects ^[8].

3. Expansion of the mechanism of action of SIRT3 in common bone-related diseases

3.1. Osteoporosis

Osteoporosis is a chronic metabolic bone disease characterized primarily by a significant reduction in bone mass and degeneration of bone tissue microstructure, with its core pathogenesis stemming from a functional imbalance between osteoblasts and osteoclasts. SIRT3 may play a crucial regulatory role in this process through multiple molecular pathways ^[19]. On one hand, SIRT3 enhances the mitochondrial bioenergetic metabolic efficiency of osteoblasts, promotes bone matrix synthesis and mineralization processes, thereby significantly improving bone formation capacity ^[20,21]. On the other hand, it can inhibit excessive differentiation and bone resorption activity of osteoclasts by regulating glucose metabolism and

reactive oxygen species levels within them, thereby preventing accelerated bone loss ^[22]. Furthermore, SIRT3 specifically activates the critical SIRT3-FOXO3a signaling axis, enhancing the antioxidant defense mechanisms of various cells in bone tissue, effectively eliminating excess free radicals, and reducing osteocyte apoptosis induced by oxidative stress ^[23]. The aforementioned multiple mechanisms work synergistically and collectively to regulate the dynamic balance of bone metabolism from both the promotion of bone formation and the inhibition of bone resorption, ultimately contributing to slowing or even reversing the progression of osteoporosis.

3.2. Osteonecrosis

Bone necrosis, as a severe skeletal disorder, is typically closely associated with multiple factors such as ischemia and prolonged use of hormonal medications. In the early stages of the disease, a pivotal pathological event is the onset of mitochondrial dysfunction, which directly impairs the normal metabolism and function of osteocytes. SIRT3 is believed to play a significant protective role in combating bone necrosis ^[24]. Its mechanisms of action primarily include the following aspects: First, SIRT3 effectively maintains the stability of mitochondrial membrane potential, thereby inhibiting the apoptosis process mediated by the mitochondrial pathway ^[25]. Secondly, it significantly enhances the activity of mitochondrial autophagy, promoting the timely clearance of damaged or dysfunctional mitochondria and preventing their accumulation from causing further cellular damage ^[26]. Furthermore, SIRT3 can enhance ATP production efficiency by optimizing energy metabolism pathways ^[27], thereby enabling osteocytes to better adapt to adverse microenvironments such as hypoxia and improving their survival capacity under stress conditions.

3.3. Rheumatoid arthritis bone erosion

Rheumatoid arthritis is a chronic autoimmune disease characterized primarily by persistent synovitis and progressive bone erosion. Recent studies have revealed that the mitochondrial-associated protein SIRT3 may play a significant regulatory role in the pathogenesis and progression of this disease through multiple mechanisms ^[28]. SIRT3 may maintain cellular energy metabolic homeostasis by inhibiting mitochondrial functional impairment in chondrocytes and osteoblasts within the inflammatory microenvironment, thereby delaying the deterioration of joint structure ^[29]. Additionally, SIRT3 can regulate the mitochondrial metabolic status of various immune cells, including macrophages, influencing their polarization and function, thereby modulating the progression of inflammatory responses ^[30]. Furthermore, SIRT3 can also inhibit the activation of NF-κB through the SIRT3-NF-κB signaling pathway ^[31]. It reduces the release of downstream inflammatory factors, ultimately mitigating the extent of inflammatory bone destruction. These mechanisms collectively demonstrate the multifaceted protective role of SIRT3 in the pathological process of rheumatoid arthritis.

3.4. Fracture healing

Fracture healing is a complex biological process involving multiple interconnected stages such as inflammation, repair, and remodeling, which requires substantial energy expenditure. During this process, SIRT3 may exert positive effects through various mechanisms: for instance, by promoting the proliferation and differentiation of osteoblasts and chondroblasts, accelerating intracartilaginous ossification, and effectively improving mitochondrial function, thereby providing critical support for callus formation and

mineralization^[32]. These effects contribute to enhancing the efficiency and quality of fracture healing, highlighting the potential significance of SIRT3 in bone metabolism regulation^[33].

4. The cross-disease potential and challenges of SIRT3-targeted therapy

Based on the aforementioned mechanisms, SIRT3 agonists, lifestyle interventions, and gene therapy strategies not only hold promise as novel therapeutic approaches for osteoarthritis (OA) but may also be extended to various other bone-related disorders. For instance, SIRT3 agonists such as resveratrol and quercetin may exert protective effects in conditions like osteoporosis and osteonecrosis by regulating mitochondrial function, inhibiting oxidative stress, and suppressing inflammatory responses^[34,35]. Meanwhile, non-pharmacological interventions such as moderate exercise and scientifically guided caloric restriction have been demonstrated to exert positive effects on various skeletal disorders—including reduced bone mass and bone microstructural degeneration—by activating the SIRT3 pathway and regulating bone metabolic balance^[9,36]. Furthermore, with continuous advancements in gene editing and vector technologies, SIRT3 gene therapy strategies utilizing lentiviruses or AAV vectors have demonstrated precise and highly effective therapeutic potential in localized bone disorders such as osteonecrosis, delayed fracture healing, and bone defect repair^[37].

However, this field still faces numerous scientific and technological challenges. Firstly, the precise mechanisms of action of SIRT3 in different types of osteocytes (such as osteoblasts, osteoclasts, and bone cells) remain incompletely understood, and its biological effects may exhibit cell-specificity^[9]. Secondly, while systemic administration of SIRT3 agonists has demonstrated metabolic improvement effects in animal models, their long-term impacts on systemic energy metabolism, insulin sensitivity, and other organ functions require careful evaluation. Finally, targeted delivery systems for various skeletal disorders—including tissue-specific promoters, nanocarriers, and localized sustained-release technologies—still require further optimization to enhance therapeutic precision and safety.

5. Conclusion and prospects

As a core regulatory factor governing mitochondrial function, SIRT3 not only plays a pivotal role in osteoarthritis but also demonstrates significant potential in the treatment of various bone-related disorders such as osteoporosis, osteonecrosis, and bone tumors^[9]. It exerts regulatory effects through multiple biological mechanisms, including modulating cellular energy metabolism processes, enhancing antioxidant defense capacity, inhibiting abnormal apoptosis, and promoting protective autophagy, thereby maintaining homeostatic balance within bone tissue.

These mechanisms suggest that SIRT3 holds significant promise as a shared therapeutic target for multiple bone disorders. Future research should focus on several key directions:

First, it is essential to elucidate the cell-specific mechanisms of SIRT3 in different types of bone diseases and clarify its distinct regulatory networks in osteoblasts (which form new bone), osteoclasts (which resorb bone), and chondrocytes (which maintain cartilage). Uncovering these cell-type-specific roles will facilitate the development of more targeted therapeutic interventions.

Second, it is essential to develop advanced drug delivery systems that specifically target bone tissue to improve therapeutic precision and reduce systemic side effects. Current challenges include off-target effects

and limited bioavailability in bone microenvironments, which could be addressed by nanoparticle-based carriers or bone-homing peptide conjugates that selectively accumulate in skeletal tissues.

Third, it is essential to actively advance preclinical animal studies using disease-relevant models (such as ovariectomized mice for osteoporosis) and subsequent translational clinical research to systematically verify the actual therapeutic efficacy and safety of SIRT3 agonists. Rigorous study design and standardized outcome assessment will be critical for successful clinical translation.

In-depth investigation of the SIRT3-mitochondrial function axis not only improves our understanding of the shared pathophysiological mechanisms underlying multiple bone disorders, but also provides critical scientific evidence and research directions for developing novel “one-target, multiple-disease” therapeutic strategies that target the same molecular target. This approach has the potential to treat osteoporosis, osteoarthritis, and bone fractures through a unified mechanism, reducing the need for polypharmacy.

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Disclosure statement

The authors declare no conflict of interest.

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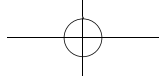
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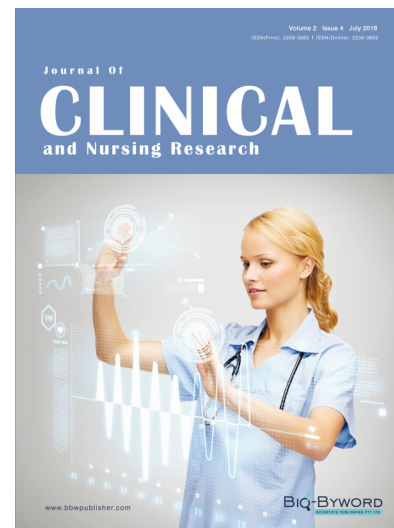
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