

Clinical Orthopaedics

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Clinical Orthopaedics

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Clinical Orthopaedics (CO) is an international academic journal dedicated to advancing the theory and practice of orthopaedic surgery and musculoskeletal medicine. The journal serves as a comprehensive platform for clinicians, researchers, and allied health professionals to disseminate cutting-edge research, innovative surgical techniques, and evidence-based clinical practices across all subspecialties of orthopaedics, including but not limited to joint reconstruction, trauma, sports medicine, spine surgery, paediatric orthopaedics, orthopaedic oncology, and foot and ankle disorders. The journal welcomes submissions from the global orthopaedic community and is dedicated to fostering academic exchange and professional development among orthopaedic surgeons and researchers worldwide.

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Neutrophil-to-Lymphocyte Ratio and Monocyte-to-Lymphocyte Ratio as Early Predictive Biomarkers of Surgical Site Infection Following Open Extremity Fractures: A Retrospective Cohort Study

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Abstract: *Objective:* To investigate the association between postoperative neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) and the development of surgical site infection (SSI) in patients with open extremity fractures, and to evaluate their utility for early risk stratification and optimization of antimicrobial stewardship. *Methods:* We conducted a retrospective cohort study involving 115 adult patients with open extremity fractures admitted to Yuhang District First People's Hospital between January 2023 and December 2025. Patients were categorized into an infection group (n = 22, 19.1%) and a non-infection group (n = 93) based on the occurrence of SSI within 30 days postoperatively, per Centers for Disease Control and Prevention (CDC) and AO Foundation criteria. Baseline demographics, Gustilo-Anderson classification, injury-to-surgery interval, preoperative and serial postoperative (days 1, 3, and 7) complete blood count parameters (used to compute NLR and MLR), operative details, and clinical outcomes were extracted from electronic medical records. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of SSI. Receiver operating characteristic (ROC) curve analysis was used to assess discriminatory performance, including area under the curve (AUC), optimal cut-off values (determined by Youden index), sensitivity, and specificity. *Results:* The infection group exhibited a significantly higher proportion of Gustilo-Anderson type III injuries (50.0% vs. 20.4%, $P < 0.01$) and longer injury-to-surgery intervals (>6 hours: 45.5% vs. 24.7%, $P = 0.042$). Median NLR [8.12 (5.85–11.45)] and MLR [1.08 (0.82–1.45)] measured during postoperative days 1–3 were markedly elevated relative to the non-infection group [4.25 (3.10–5.76) and 0.67 (0.51–0.89), respectively; both $P < 0.001$]. Multivariate logistic regression confirmed that postoperative NLR (adjusted odds ratio [aOR] = 1.26, 95% CI: 1.12–1.41, $P < 0.001$) and MLR (aOR = 2.08, 95% CI: 1.42–3.05, $P < 0.001$) were independent predictors of SSI. ROC analysis demonstrated that NLR achieved an AUC of 0.805 (cut-off: 6.72;

sensitivity: 76.5%; specificity: 77.4%), MLR an AUC of 0.778 (cut-off: 0.90), and their combination yielded superior discrimination (AUC = 0.859; sensitivity: 82.1%; specificity: 80.6%). Patients in the infection group experienced significantly prolonged hospitalization [16.5 (11–22) vs. 8.5 (6–11) days, $P < 0.001$] and higher reoperation rates (31.8% vs. 5.4%, $P < 0.01$). *Conclusion:* Early postoperative elevation of NLR and MLR constitutes a simple, cost-effective, and clinically actionable inflammatory signature predictive of SSI following open extremity fractures. Serial monitoring of these ratios may facilitate timely risk stratification, guide intensified antimicrobial and wound management strategies, and support personalized postoperative surveillance.

Keywords: Open fracture; Surgical site infection; Neutrophil-to-lymphocyte ratio; Monocyte-to-lymphocyte ratio; Inflammatory biomarker; Retrospective cohort study

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1. Introduction

Open extremity fractures represent high-acuity orthopedic emergencies associated with substantial soft-tissue disruption^[1], bacterial contamination, and compromised local perfusion—factors collectively contributing to an elevated risk of surgical site infection (SSI) compared with closed fractures. Epidemiological data indicate SSI incidence escalates with Gustilo-Anderson severity^[2]: approximately 0–5% for type I, 2.4–9.7% for type II, and up to 13.8–52% for type III injuries—with subtypes IIIB and IIIC carrying the highest morbidity, including osteomyelitis, nonunion, chronic pain, and limb loss. Such complications impose considerable clinical burden and escalate healthcare expenditures.

Although conventional systemic inflammatory markers—including white blood cell count (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin (PCT)—are routinely employed in postoperative surveillance, their clinical utility is constrained by limited specificity and sensitivity^[3]. These parameters are susceptible to confounding influences such as surgical stress, comorbidities (e.g., diabetes, chronic kidney disease), and antimicrobial therapy, thereby reducing reliability for dynamic infection assessment. Moreover, repeated measurement of certain biomarkers (e.g., PCT) entails relatively high cost and limited accessibility in resource-constrained settings.

In contrast, composite hematologic indices derived from routine complete blood counts—namely, the neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR)—have emerged as promising alternatives^[4,5]. Their calculation requires only automated differential leukocyte counts, rendering them inexpensive, widely available, and amenable to serial monitoring. Biologically, NLR reflects the imbalance between innate neutrophil-driven inflammation and adaptive lymphocyte-mediated immunity: neutrophils rapidly infiltrate infected tissues, releasing proteases, reactive oxygen species, and neutrophil extracellular traps (NETs), whereas lymphopenia impairs antigen-specific immune responses. MLR captures the interplay between monocyte recruitment—subsequently differentiating into pro-inflammatory M1 or reparative M2 macrophages—and lymphocyte homeostasis. Accumulating evidence supports the prognostic value of NLR and MLR across diverse clinical contexts, including oncology, cardiovascular disease, spinal surgery, and musculoskeletal infections^[6–8].

Emerging literature further suggests relevance in open fracture management^[9]. Nevertheless, existing evidence remains fragmented—predominantly derived from small, single-institution cohorts, static time-

point assessments, or fracture-specific subsets. Rigorous, systematic evaluation of “dynamic” NLR and MLR trajectories during the critical early postoperative window (days 1–7) and their robust association with objectively defined SSI is notably lacking. Consequently, the strength of current evidence limits clinical translation.

To address this gap, we conducted a comprehensive retrospective cohort study of 115 patients with open extremity fractures. This investigation systematically characterizes the temporal evolution of NLR and MLR following definitive surgical intervention, rigorously evaluates their independent association with CDC/AO-defined SSI, and quantifies their predictive performance using contemporary statistical methodology. Our aim is to establish a pragmatic, low-cost risk stratification framework to inform early, targeted antimicrobial escalation, optimized wound care protocols (e.g., vacuum-assisted closure adjustments), and individualized follow-up—thereby enhancing preventive precision. Furthermore, we examine potential effect modification by key clinical variables to inform future prospective validation and multi-center implementation.

2. Materials and methods

2.1. Study design and patient selection

This retrospective cohort study included 115 consecutive adult patients (≥ 18 years) diagnosed with open extremity fractures and treated surgically at Yuhang District First People’s Hospital between January 2020 and December 2023. The cohort comprised 74 males (64.3%) and 41 females, with a mean age of 45.8 ± 13.1 years. Fracture distribution included 38 upper-limb (33.0%) and 77 lower-limb (67.0%) injuries. Gustilo-Anderson classification distribution was as follows: type I ($n = 25$, 21.7%), type II ($n = 52$, 45.2%), and type III ($n = 38$, 33.0%).

Inclusion criteria: (1) age ≥ 18 years; (2) radiographically confirmed open extremity fracture managed with primary debridement and definitive fixation (internal or external); (3) availability of complete serial postoperative complete blood count data (days 1, 3, and 7); (4) minimum 30-day postoperative follow-up or follow-up until 30 days after hospital discharge.

Exclusion criteria: (1) pathological or nonunion fractures; (2) severe concomitant vascular or nerve injuries requiring specialized microsurgical intervention; (3) documented immunodeficiency (e.g., HIV/AIDS, primary immunodeficiency), active hematologic malignancy, or recent (≤ 30 days) systemic glucocorticoid or immunosuppressant use; (4) pre-existing active infection or systemic inflammatory response syndrome (SIRS) at admission; (5) incomplete clinical documentation or loss to follow-up.

2.2. Clinical management and data collection

All patients received standardized trauma resuscitation^[10], broad-spectrum antibiotic prophylaxis initiated within 3 hours of admission, and continued for 24–72 hours postoperatively. Surgical debridement and stabilization were prioritized within the 6–8 hour “golden window” where feasible; fixation modality (intramedullary nailing, plating, or external fixation) was selected based on fracture pattern, soft-tissue status, and surgeon judgment.

SSI diagnosis adhered strictly to the CDC National Healthcare Safety Network (NHSN) criteria and the AO Foundation’s consensus definition for fracture-related infection (FRI), integrating clinical signs (localized erythema, swelling, warmth, purulent drainage), laboratory findings (elevated WBC, CRP), and microbiological confirmation where applicable^[11]. All hematologic parameters were obtained using a

Sysmex XN-9000 automated hematology analyzer. NLR and MLR were calculated as absolute neutrophil count divided by absolute lymphocyte count, and absolute monocyte count divided by absolute lymphocyte count, respectively. Peak postoperative values (typically observed on days 1–3) and longitudinal trends were analyzed. Additional covariates collected included age, sex, body mass index (BMI), smoking status, diabetes mellitus, hypertension, Gustilo-Anderson grade, injury-to-surgery interval, operative duration, fixation method, and duration of postoperative antibiotic administration. Primary clinical outcomes encompassed length of hospital stay, reoperation rate, radiographic bone union status at 6 months, and functional recovery assessed using the Short Musculoskeletal Function Assessment (SMFA) questionnaire.

2.3. Statistical analysis

Statistical analyses were performed using SPSS Statistics 26.0 (IBM Corp.) and R version 4.2.0 (R Foundation for Statistical Computing). Continuous variables were summarized as mean $\pm$ standard deviation (normally distributed) or median (interquartile range [IQR]) (non-normally distributed), assessed via Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages. Between-group comparisons utilized independent samples t-test or Mann-Whitney U test for continuous variables and χ^2 test or Fisher's exact test for categorical variables. Variables with $P < 0.10$ in univariate analysis, alongside clinically relevant confounders (e.g., Gustilo grade, injury-to-surgery interval), were entered into a multivariate binary logistic regression model using backward stepwise elimination (likelihood ratio criterion). Model calibration was assessed via Hosmer-Lemeshow test; discrimination was evaluated using ROC analysis, reporting AUC, optimal cut-off (Youden index), sensitivity, and specificity. Subgroup analyses stratified by Gustilo grade and anatomical location (upper vs. lower limb) were conducted. Two-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics (Table 1)

No significant differences were observed between groups in age, sex distribution, BMI, or prevalence of diabetes (all $P > 0.05$). However, the infection group demonstrated a significantly higher proportion of Gustilo-Anderson type III injuries (50.0% vs. 20.4%, $P < 0.01$), lower-limb predominance (90.9% vs. 64.5%, $P = 0.012$), longer median injury-to-surgery interval [7.5 (5.0–12.0) vs. 4.0 (2.5–6.0) hours, $P < 0.001$], and longer operative duration [125.0 (95.0–160.0) vs. 90.0 (70.0–115.0) minutes, $P = 0.003$].

Table 1. Baseline clinical characteristics of the two groups

Variable	Infection Group (n=22)	Non-infection Group (n=93)	P-value
Age (years, mean $\pm$ SD)	47.5 $\pm$ 13.8	45.3 $\pm$ 12.9	0.421
Male (%)	68.2	64.5	0.732
Gustilo III (%)	50	20.4	<0.01
Time to surgery >6h (%)	45.5	24.7	0.042
NLR on postoperative day 1 (median)	8.12	4.25	<0.001
MLR on postoperative day 1 (median)	1.08	0.67	<0.001
Length of hospital stay (days, median)	16.5	8.5	<0.001

3.2. Temporal dynamics of NLR and MLR (Figure 1; Table 2)

Both NLR and MLR rose sharply in the infection group on postoperative day 1, peaked on day 3, and remained elevated through day 7 relative to the non-infection group (all $P < 0.001$ for days 1–3). In contrast, the non-infection group exhibited modest, transient elevations followed by rapid normalization. **Figure 1** illustrates these divergent trajectories with error bars representing standard deviation.

Table 2. Comparison of NLR and MLR at different time points (median)

Time Point	NLR Infection Group	NLR Non-infection Group	MLR Infection Group	MLR Non-infection Group
Postoperative Day 1	8.12	4.25	1.08	0.67
Postoperative Day 3	7.45	3.85	0.95	0.6

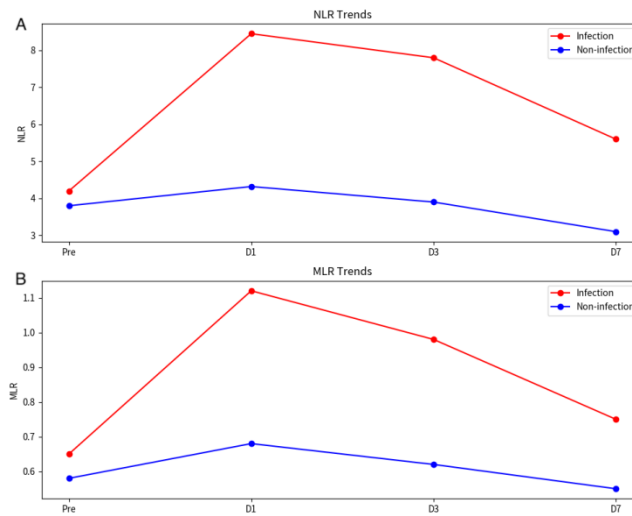


Figure 1. Postoperative trends of NLR and MLR in infection and non-infection groups

3.3. Risk factor identification (Table 3)

Univariate analysis identified Gustilo-Anderson type III, injury-to-surgery interval >6 hours, operative duration >120 minutes, and elevated postoperative NLR and MLR as significant risk factors (all $P < 0.05$). Multivariate logistic regression retained only NLR (aOR = 1.26, 95% CI: 1.12–1.41, $P < 0.001$) and MLR (aOR = 2.08, 95% CI: 1.42–3.05, $P < 0.001$) as independent predictors after adjustment for confounders.

Table 3. Multivariate logistic regression analysis for postoperative infection

Variable	OR	95% CI	P-value
Gustilo III	2.65	1.48-4.75	0.001
NLR (postoperative peak)	1.26	1.12-1.41	<0.001
MLR (postoperative peak)	2.08	1.42-3.05	<0.001
Time to surgery >6 h	1.58	1.05-2.38	0.028

3.4. Predictive performance (Figure 2)

ROC analysis revealed strong discriminatory capacity: NLR achieved AUC = 0.805 (cut-off: 6.72; sensitivity: 76.5%; specificity: 77.4%); MLR achieved AUC = 0.778 (cut-off: 0.90; sensitivity: 72.7%; specificity:

75.3%). Combined NLR+MLR modeling yielded the highest accuracy (AUC = 0.859; sensitivity: 82.1%; specificity: 80.6%). Subgroup analysis indicated enhanced predictive power among Gustilo-Anderson type III patients (AUC > 0.84 for both markers).

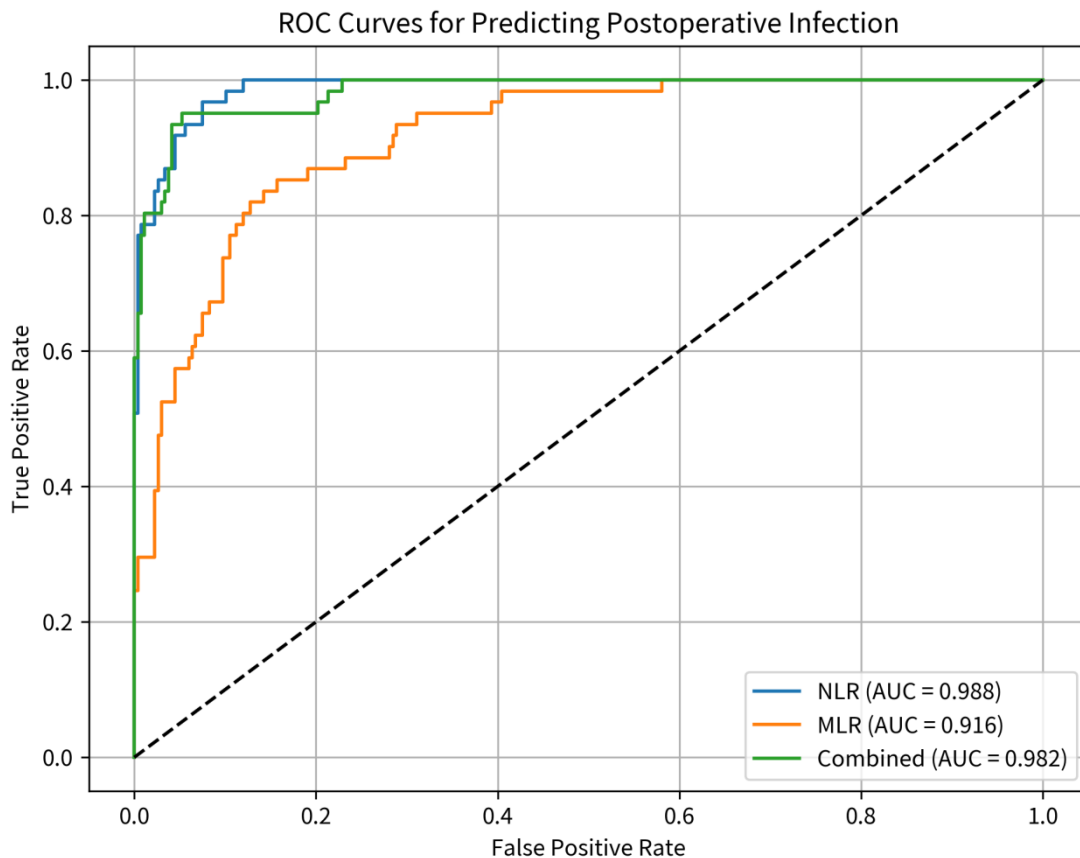


Figure 2. Receiver operating characteristic (ROC) curves of NLR, MLR, and combined model for predicting surgical site infection (SSI)

3.5. Clinical outcomes

The infection group incurred significantly longer median hospitalization [16.5 (11–22) vs. 8.5 (6–11) days, $P < 0.001$] and higher reoperation rate (31.8% vs. 5.4%, $P < 0.001$). Delayed union (defined as absence of bridging callus at 6 months) occurred in 27.3% of the infection group versus 5.4% in the non-infection group ($P = 0.007$). Functional recovery (SMFA disability index) was significantly impaired in the infection group at 6-month follow-up (mean score: 42.3 ± 11.5 vs. 28.7 ± 9.2 , $P < 0.001$).

4. Discussion

This study provides robust evidence that early postoperative elevation of NLR and MLR serves as an independent, clinically meaningful predictor of SSI following open extremity fractures. Our findings align with and extend prior observations by employing rigorous, prospectively defined outcome ascertainment, systematic longitudinal monitoring, and multivariable adjustment for key confounders. Mechanistically, open fractures induce profound tissue damage and microbial challenge, triggering a dysregulated systemic

inflammatory response characterized by neutrophil hyperactivation, monocyte infiltration, and concurrent lymphocyte suppression—culminating in immune paralysis that facilitates bacterial persistence and dissemination. NLR and MLR effectively capture this pathophysiological cascade, offering advantages over traditional markers: (1) derivation from universally available, low-cost routine blood tests; (2) resistance to transient fluctuations induced by antibiotics or acute stress; and (3) suitability for frequent, real-time surveillance in diverse healthcare settings.

Our empirically derived cut-off values— $\text{NLR} > 6.72$ and $\text{MLR} > 0.90$ —are consistent with thresholds reported in related inflammatory and infectious conditions, reinforcing biological plausibility. Critically, the synergistic predictive gain achieved by combining both ratios ($\text{AUC} = 0.859$) underscores the complementary biological information they convey and supports their integrated clinical application.

From a translational perspective, these findings advocate for protocolized postoperative NLR/MLR monitoring—ideally daily or every-other-day during the first postoperative week. Values exceeding established thresholds should prompt immediate clinical reassessment: intensification of antimicrobial coverage (e.g., broader spectrum or extended duration), meticulous wound inspection and debridement if indicated, optimization of negative-pressure wound therapy, and heightened surveillance for deep-seated infection. For high-risk subgroups—particularly Gustilo-Anderson type III injuries—these metrics may further inform personalized rehabilitation timelines and outpatient follow-up intensity.

Strengths of this study include its focus on dynamic biomarker trajectories within a clinically relevant timeframe, adherence to standardized infection definitions, comprehensive adjustment for confounders, and robust statistical validation. Limitations warrant acknowledgment: (1) single-center retrospective design, introducing potential selection and information bias; (2) modest sample size limiting power for granular subgroup analyses (e.g., by specific Gustilo subtype or microbiological profile); (3) absence of concurrent measurement of other emerging inflammatory indices (e.g., systemic immune-inflammation index [SII], platelet-lymphocyte ratio [PLR]) or detailed microbiological data to construct multimodal predictive models; (4) inherent subjectivity in clinical SSI diagnosis despite standardized criteria; and (5) lack of long-term functional and radiographic outcomes beyond 6 months.

Future research should prioritize multicenter prospective cohort studies to validate these findings and assess the impact of NLR/MLR-guided interventions on hard endpoints (e.g., SSI incidence, amputation rate, mortality). Integration of NLR/MLR with clinical variables, imaging features (e.g., MRI-based soft-tissue characterization), and machine learning algorithms holds promise for developing high-fidelity predictive tools. Additionally, defining optimal intervention thresholds across heterogeneous populations—including elderly, diabetic, and immunocompromised individuals—will be essential to maximize generalizability and equity in clinical implementation.

5. Conclusion

In patients with open limb fractures, postoperative elevation of the neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) constitutes an independent risk factor for surgical site infection (SSI), demonstrating robust predictive performance. Routine and dynamic monitoring of these hematologic indices in clinical practice is therefore warranted to facilitate timely, evidence-based interventions—ultimately improving patient outcomes and optimizing the utilization of healthcare resources.

Disclosure statement

The authors declare no conflict of interest.

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Application Research of Multidisciplinary Team New Media Rehabilitation Training for Elderly Patients Undergoing Hip Replacement Surgery

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Abstract: *Objective:* To explore the application effect of multidisciplinary team combined with new media technology in the rehabilitation training of elderly patients undergoing hip arthroplasty. *Design:* A total of 100 patients with hip arthroplasty were divided into experimental group (Multi-disciplinary team cooperation, combined with new media technology) and the control group. The effectiveness of the model was evaluated by comparing the experimental group and the control group. *Results:* the results showed that the hip function, the incidence of complications and the recovery of balance function of the elderly patients who received the multidisciplinary team rehabilitation training were better than those of the control group. There were significant differences in hip function and balance function ($p < 0.05$). *Conclusion:* The multidisciplinary team new media rehabilitation training has a positive significance for improving the rehabilitation effect of elderly patients undergoing hip arthroplasty.

Keywords: Multidisciplinary team, New media, Rehabilitation, Geriatrics, Hip replacement

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1. Introduction

1.1. What is known

The incidence of femoral neck fracture and avascular necrosis of the femoral head in the elderly is increasing year by year. It needs to provide more efficient and convenient rehabilitation services for elderly patients with hip replacement by integrating the advantages of multidisciplinary expertise and new media technology.

1.2. What is new

The application of multidisciplinary team new media rehabilitation training in elderly patients undergoing hip

arthroplasty has yielded significant results. The model not only improves the rehabilitation effect and quality of life.

With the intensification of the aging trend of the population, the incidence of femoral neck fracture and avascular necrosis of the femoral head in the elderly is increasing year by year. Elderly patients often face multiple challenges during the rehabilitation process following hip arthroplasty^[1,2]. Although traditional rehabilitation training methods can promote patient recovery to some extent, they still suffer from issues such as poor patient compliance, difficulties in continuously monitoring and evaluating training effects. According to the Statistical Report on the Development of the Internet in China, as of June 2023, there are 136 million elderly Internet users aged 60 and above in China, and the Internet penetration rate has reached 46.2%. New media technology has the characteristics of fast information dissemination, wide coverage and strong interactivity, which can effectively make up for the shortcomings of traditional rehabilitation training methods and improve the rehabilitation effect and compliance of patients^[3,4]. In addition, multidisciplinary teamwork is becoming more and more widely used in the medical field. The multidisciplinary team is able to integrate expertise in different fields such as orthopedics, rehabilitation, nutrition, and psychology to provide patients with comprehensive and personalized rehabilitation guidance. According to related studies, multidisciplinary team cooperation can significantly improve the rehabilitation effect, shorten the rehabilitation time and reduce the incidence of complications^[5]. Therefore, this study aims to explore the effectiveness of multidisciplinary team-based new media rehabilitation training in elderly patients undergoing hip replacement. We hope to provide more efficient and convenient rehabilitation services for elderly patients with hip replacement by integrating the advantages of multidisciplinary expertise and new media technology^[6]. It provides a new rehabilitation model for clinical practice, improves the quality of rehabilitation and promotes the innovation and development of medical service. Specific experimental content is reported as follows.

2. Methods

2.1. General information

This study was approved by the Ethics Committee of our hospital. A total of 100 elderly THA patients were selected for treatment in our hospital after the project was established. 50 were included in the control group: 27 males and 23 females, aged 60-79 years, with a mean of (71.3±5.8) years, and 50 were included in the experimental group: 28 males and 22 females, aged 60-81 years, with a mean of (71.7±5.5) years. The control group was given conventional rehabilitation training, while the experimental group was selected with a variety of rehabilitation training modes on the basis of conventional rehabilitation training mode.

2.1.1. Inclusion criteria

- (1) Age: Patients must be 60 years old or above.
- (2) Type of surgery: Patients must have undergone hip arthroplasty, either total hip arthroplasty or partial hip arthroplasty.
- (3) Rehabilitation stage: Patients must be in the postoperative rehabilitation stage and have the ability to participate in rehabilitation training.
- (4) Health status: Patients must have stable vital signs, such as blood pressure and heart rate within the normal range, and no other serious health issues, such as heart disease or respiratory diseases, to ensure their safety during participation in rehabilitation training.
- (5) Cognitive ability: Patients must have basic cognitive abilities to understand and follow rehabilitation

training instructions.

- (6) Consent to participate in the study: Patients or their legal guardians must agree to participate in the study and sign the relevant informed consent form.
- (7) New media access ability: Considering the characteristics of new media rehabilitation training, patients must have basic ability to use new media devices (such as tablets, smartphones, etc.).
- (8) All surgeries were performed by the same group of experienced surgeons. Patients included in the study will complete a hip arthroplasty information form.

2.1.2. Exclusion criteria

- (1) Long-term bed rest before surgery: For patients who have been bedridden for a long time before surgery, they may already have problems such as muscle atrophy and osteoporosis, which may affect the effectiveness and safety of rehabilitation training.
- (2) Combined malignant tumors: Patients with malignant tumors are usually in poor physical condition and may not be able to withstand the pressure of rehabilitation training, and the treatment of malignant tumors may also conflict with rehabilitation training.
- (3) Severe heart, brain, and nervous system diseases: These diseases may affect the patient's motor ability, cognitive ability, and rehabilitation potential, making them unable to fully participate in rehabilitation training.
- (4) Inability to use new media devices: Considering that the study involves new media rehabilitation training, patients who are unable to use new media devices (such as smartphones, etc.) will not be able to carry out relevant rehabilitation training.
- (5) Cognitive impairment or inability to understand research requirements: Patients with cognitive impairment or who are unable to understand the research requirements may not be able to participate in rehabilitation training correctly and may also be unable to provide accurate data and feedback needed for the study.
- (6) Other serious health issues: Severe respiratory diseases, liver and kidney dysfunction, and other such conditions may affect a patient's rehabilitation potential and safety.

3. Study design

3.1. The conventional group adopts the traditional rehabilitation mode

Including systematic testing, including pulse, heart rate, etc., and give the patient correct medication guidance, preventive measures for complications, etc., give correct dietary guidance, correct bad eating habits, and carry out routine rehabilitation guidance; postoperative routine functional rehabilitation training, including ankle pump exercise, muscle strength training, dressing change and medication guidance, health education, complication prevention and control, etc. postoperative 3D bed under the walker weight-bearing walking, discharge within 1 week, if the patient has obvious activity discomfort or severe hip pain, timely medical treatment.

3.2. Implementation and recording of the new media rehabilitation training model

The new media rehabilitation training model was adopted in the experimental group on the basis of the routine group, and the nursing staff made the records. See **Figure 1** and **Figure 2** for details.

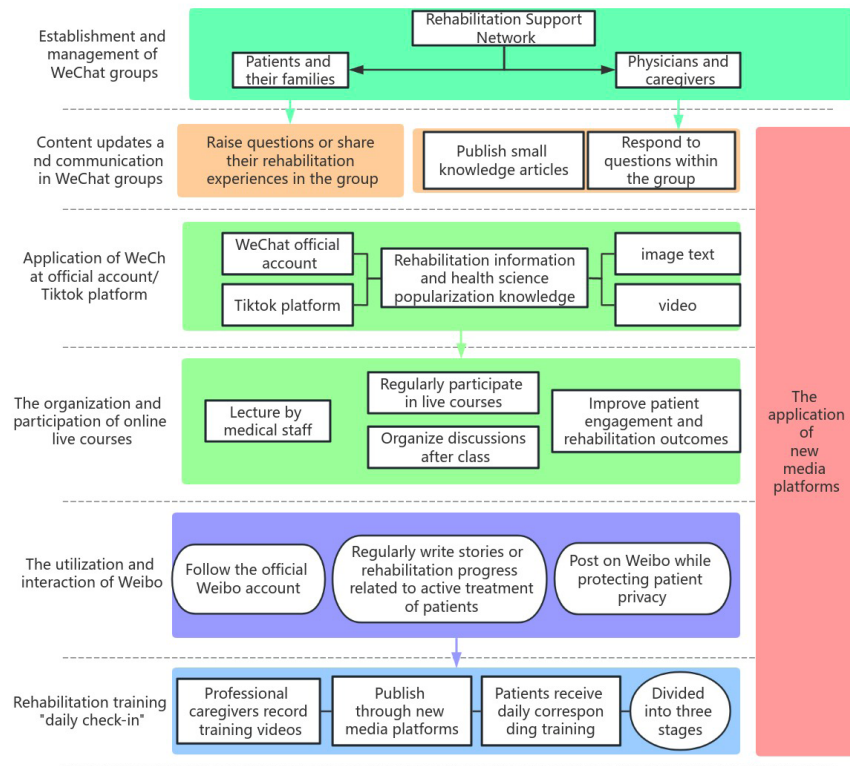


Figure 1. The intervention mode of the experimental group

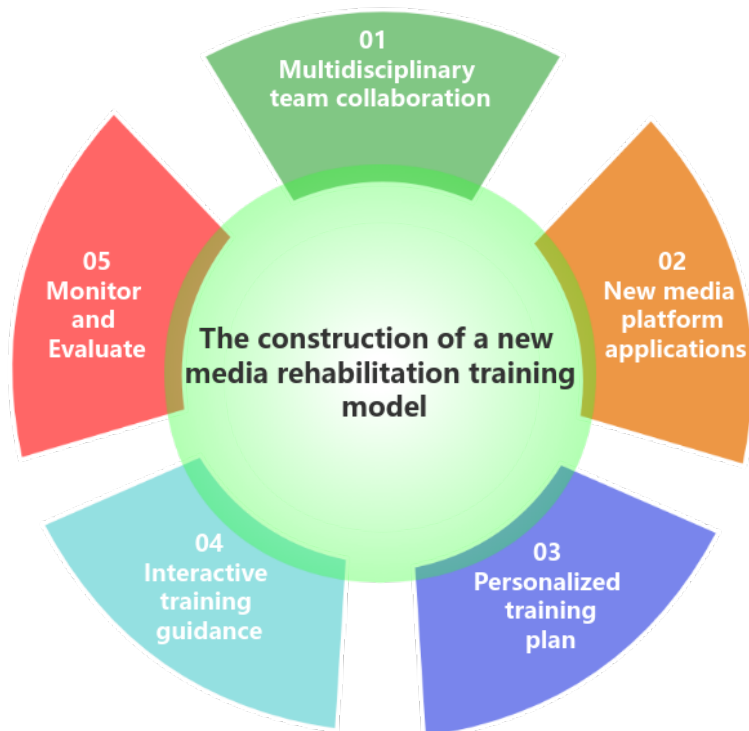


Figure 2. The construction of a new media rehabilitation training model

3.2.1. Establishment and management of WeChat groups

The group was established by the doctors and nurses ensures the professionalism and activity of its members to provide timely and accurate rehabilitation guidance to patients. Patients and their families in the experimental group are gradually invited to join the group, forming a close rehabilitation support network.

3.2.2. Content update and communication in the WeChat group

In the WeChat group, three articles related to postoperative health care are published every day, covering rehabilitation skills, nutritional advice, psychological adjustment, etc.

3.2.3. Application of WeChat public account/Douyin platform

These contents are presented in the form of pictures, texts and videos, which are more vivid and intuitive, and are easy for patients and their families to understand and learn.

3.2.4. Organization and participation in online live streaming courses

To provide more in-depth guidance on rehabilitation training for patients and their families, online live streaming courses are also organized.

3.2.5. Utilization and interaction of microblogging

In addition, information dissemination and interaction are carried out through microblogging, a social media platform. Patients and their families are asked to follow the official Weibo account, and physicians will regularly write stories about the patient's active treatment or recovery progress, and post them on Weibo on the premise of protecting the patient's privacy. In this way, other patients are encouraged to read and learn, creating a good atmosphere for recovery.

3.2.6. “Daily check-in” of rehabilitation training

First of all, the professional nurses in our department are responsible for recording the rehabilitation training video. These video contents are carefully designed according to the rehabilitation stage and needs of the patients to ensure that they can safely and effectively perform the training at home. A detailed phased training plan was developed for the rehabilitation needs of elderly hip arthroplasty patients. In the first stage (1-2 days after surgery), patients are mainly instructed to carry out active training, such as ankle plantar flexion and dorsal extension exercises, gluteal muscle contraction exercises, quadriceps training, etc., to help patients recover basic muscle function as soon as possible. In the second stage (3-4 days after surgery), the training content gradually transitions to exercises such as straight leg raising, hip lifting, etc., to strengthen the core muscle strength of the patient. By the third stage (5-7 days after surgery), the patient begins to practice seated balance, sitting to standing, standing balance, walking, and other exercises, laying the foundation for future walking ability recovery. During rehabilitation, patient tolerance is crucial. At the same time, through the interaction and communication of new media platforms, we can better understand the needs and feedback of patients, and continuously optimize and improve our rehabilitation training program.

3.3. Observation indicators

3.3.1. Hip function assessment

Hip function assessment is to observe the recovery and functional performance of the hip joint after surgery^[7].

The condition of the hip joint at different time points was systematically and quantitatively evaluated by using the Harris Artificial Hip Function Rating Scale. The assessment time points included discharge, 1 month postoperatively, 3 months postoperatively, and 6 months postoperatively. This scale covers four main areas: hip deformity, range of motion, functional mobility, and pain. The maximum score for each item is 25 points, and the total score is 100 points. A higher score means that the patient has better hip function recovery, less pain, higher range of motion, and better overall performance.

3.3.2. Incidence of complications

After surgery, detailed records were kept of possible complications that patients may experience, particularly common complications such as bedsores, deep vein thrombosis (DVT) of the lower extremities, and wound infection^[8,9]. These complications not only affect the speed of patient recovery but may also pose a threat to the overall health of the patient. By recording and comparing the incidence of complications between the two patient groups, the effectiveness of the multidisciplinary team's new media rehabilitation training in reducing these risks was assessed.

3.3.3. Assessment of balance function

Balance function is an area of special concern for older patients after hip replacement surgery. In order to quantitatively assess the balance ability of patients, the Berg Balance Scale (BBS) was used before intervention, at the 4th week of intervention and at 8th week of intervention. The scale consists of 14 items, each of which is scored on a scale of 0 to 4 based on the patient's performance, with a total of five levels out of 56. This assessment not only helps the physician understand the patient's balance ability, but also guides the adjustment of rehabilitation exercises to help the patient return to balance function more quickly^[10].

3.4. Statistical methods

In this study, SPSS 25.0 statistical software was used for data analysis, and the continuous data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and the *t*-test was used for comparison between groups, and the difference was statistically significant at $P < 0.05$.

4. Results

4.1. Hip function comparison

After comparative analysis, the Harris hip score of the experimental group was higher than that of the control group before surgery, 3 months after surgery, and 6 months after surgery, and the difference was statistically significant. At the same time, the joint mobility and functional mobility of the patients in the experimental group were also significantly better than those in the control group. See **Table 1** for details.

Table 1. Comparison of hip function between the two groups

Constituencies	Malformation				Pain				Range of motion				Functional activities			
	Preoperatively	3 months postoperatively	6 months postoperatively	6 months postoperatively	Preoperatively	3 months postoperatively	3 months postoperatively	6 months postoperatively	Preoperatively	3 months postoperatively	3 months postoperatively	6 months postoperatively	Preoperatively	3 months postoperatively	3 months postoperatively	6 months postoperatively
Experimental (n=60)	2.15 ±0.27	3.43± 0.37*	3.87± 0.15**	42.15 ±0.19*	21.21 ±3.85	32.13 ±2.27*	32.13 ±2.27*	42.15 ±0.19*	2.28± 0.343.	34 ±0.46*	34 ±0.46*	4.43± 0.76*	15.87 ±2.033	2.12± 4.17*	2.12± 4.17*	2.13± 4.12*
Control (n=60)	2.13± 0.35	3.47± 0.28*	3.85± 0.18**	41.11± 0.18**	20.25 ±3.93	32.69 ±2.05*	32.69 ±2.05*	41.11± 0.18**	2.13± 0.32	2.18± 0.39*	2.18± 0.39*	4.18± 0.81**	16.20 ±2.09	29.63± 3.62*	29.63± 3.62*	40.21± 3.64**
t-value	0.345	0.145	0.845	1.776	0.018	0.714	0.714	1.776	1.789	2.455	2.455	2.016	0.261	2.624	2.624	2.091
P-value	0.658	0.897	0.432	0.278	0.932	0.467	0.467	0.278	0.074	0.012	0.012	0.039	0.825	0.010	0.010	0.039

Note: Compared with the same group before surgery, * $P<0.05$; compared with the same group 3 months after surgery, # $P<0.05$.

4.2. Comparison of complication rates

The results showed that the incidence of postoperative complications in the experimental group was lower than that in the control group, and the difference was statistically significant. Specifically, the incidence of complications including bedsores, lower extremity venous thrombosis (DVT) and wound infections in the experimental group was significantly lower than that in the control group. See **Table 2** for details.

Table 2. Comparison of complication rates between the two groups[n(%)]

Constituencies	Number of examples	Venous thrombosis of the lower extremities	Pressure sore	Wound infection	Total incidence
Experimental group	50	0(0.00)	2(4.00)	0(0.00)	2(4.00)
Control group	50	1(2.00)	3(8.00)	1(2.00)	5(10.00)
χ^2 value					2.205
<i>P</i> -value					0.138

4.3. Comparison of balance functions

The results showed that the balance function scores of the experimental group were higher than those of the control group before the intervention and at 6 months of intervention, and the difference was statistically significant. Specifically, patients in the experimental group scored higher on the BBS scale, indicating that they had better balance in different activity scenarios. See **Table 3** for details.

Table 3. Comparison of balance function between the two groups

Projects	Pre-intervention				Post-intervention			
	Control	Experimental	<i>t</i>	<i>P</i>	Control	Experimental	<i>t</i>	<i>P</i>
Rise from one's seat	1.34±0.13	1.31±0.15	1.375	0.179	3.49±0.27*	3.60±0.30 [#]	2.314	0.021
Standing unsupported	1.62±0.14	1.70±0.15	0.778	0.435	3.80±0.37*	3.93±0.41 [#]	1.988	0.047
No backrest seat, but feet on the ground or on a stool	1.59±0.16	1.58±0.17	0.324	0.751	3.67±0.33*	3.79±0.41 [#]	2.048	0.043
Sit down from a standing position	1.11±0.15	1.08±0.14	1.312	0.189	3.22±0.26*	3.37±0.31 [#]	3.272	0.001
Transfer	1.35±0.12	1.38±0.18	1.041	0.311	3.53±0.31*	3.64±0.34 [#]	2.025	0.047
Stand with eyes closed without support	1.16±0.12	1.19±0.12	1.312	0.191	3.42±0.25*	3.54±0.24 [#]	2.718	0.006
Stand unsupported with feet together	1.49±0.13	1.47±0.17	0.758	0.452	3.52±0.28*	3.67±0.29 [#]	3.102	0.003
The upper limbs are extended and moved forward in the standing position	1.37±0.15	1.39±0.13	0.811	0.423	3.45±0.27*	3.59±0.28 [#]	3.000	0.002
Pick up objects from the ground while standing	1.32±0.11	1.31±0.17	0.542	0.587	3.47±0.25*	3.58±0.21 [#]	2.810	0.007
Standing position turn and look behind you	1.38±0.12	1.37±0.11	0.335	0.741	3.48±0.30*	3.67±0.32 [#]	3.610	<0.001
Turn 360°	1.29±0.13	1.27±0.19	0.767	0.450	3.26±0.25*	3.39±0.28 [#]	2.886	0.005

Projects	Pre-intervention				Post-intervention			
	Control	Experimental	<i>t</i>	<i>P</i>	Control	Experimental	<i>t</i>	<i>P</i>
Place one foot on a step or stool while standing unsupported	0.98±0.13	0.96±0.07	1.181	0.242	3.16±0.20*	3.28±0.22 [#]	3.363	<0.001
Standing unsupported with one foot in front	1.29±0.14	1.27±0.14	0.939	0.348	3.46±0.24*	3.59±0.26 [#]	3.062	0.004
On one leg	0.78±0.08	0.76±0.12	1.241	0.218	3.04±0.18*	3.21±0.16 [#]	5.887	<0.001
Berg Balance Scale	18.17±1.52	18.04±1.45	0.512	0.609	47.97±3.25*	49.85±2.84 [#]	3.633	<0.001

Note: * $P<0.05$, compared with the control group before intervention; [#] $P<0.05$, compared with the experimental group before intervention.

5. Discussion

5.1. Construction of new media rehabilitation training model

The new media rehabilitation training model, based on modern information technology and new media platforms, deeply integrates professional knowledge from multiple disciplines to provide personalized and interactive rehabilitation training services for elderly patients undergoing hip arthroplasty. This model not only embodies the interdisciplinary collaboration concept of modern medicine, but also optimizes the rehabilitation experience of patients through the introduction of technology^[11,12].

The new media platform provides an interactive training guide for the new media rehabilitation training mode. Patients can interact with trainers in real time through the platform, ask questions, share training experiences, etc. This interactive approach enables patients to have a deeper understanding of the importance and skills of rehabilitation training, while enhancing their enthusiasm and initiative to participate in rehabilitation training^[13,14]. The trainer can give timely feedback and guidance according to the specific situation of the patient, help them correct the wrong training posture and method, and ensure the correctness and effectiveness of the training. This interactive training guide not only significantly improves the effect of rehabilitation training, but also further enhances the trust and communication between patients and trainers.

In this study, WeChat Group has become an important communication platform. Patients or family members have any questions or confusion can be directly raised in the group, doctors and nurses will give timely answers and guidance. This immediate feedback mechanism not only solves the problems that patients may encounter during their recovery, but also makes them feel the care and support of the medical team. This new rehabilitation training model undoubtedly brings patients a more comprehensive and personalized rehabilitation experience.

Monitoring and evaluation are an indispensable part of the new media rehabilitation training model^[15]. Collect patient training data through new media platforms and conduct real-time monitoring and evaluation. Based on these data, trainers can adjust their training plans in a timely manner and provide personalized guidance according to the actual situation of patients. This continuous monitoring and evaluation not only improves the scientific and effective nature of rehabilitation training, but also provides patients with more comprehensive and personalized rehabilitation services.

In this study, the role of monitoring and evaluation is particularly prominent in the “Daily check-in” of rehabilitation training. Monitoring and evaluation play a vital role in rehabilitation training. Through the

daily punching in this specific way, not only can improve the scientific and effective rehabilitation training, but also provide patients with more comprehensive and personalized rehabilitation services. This is of great significance for promoting the rehabilitation process of patients and improving the quality of life.

In summary, the new media rehabilitation training model has broad application prospects and important practical value in the rehabilitation process of elderly patients with hip replacement.

5.2. Improvement of rehabilitation effectiveness

THA can cause certain degrees of damage to the patient's muscles, tendons, ligaments, and affect the coordinated movement and balance of the hip joint, increasing the risk of falls in patients^[16,17]. This study showed that the postoperative Berg balance scale scores of THA (total hip replacement) patients who received new media rehabilitation training mode were significantly higher than those of the control group ($P<0.05$). This result proves the effectiveness of multidisciplinary teams combined with new media technology mode in improving postoperative balance ability of THA patients.

The rehabilitation team carefully plans and adjusts the training content, training time and training intensity according to the actual conditions of the patients in the early rehabilitation stage to ensure that the progress of rehabilitation is scientific and reasonable^[18]. The training covers a variety of balance training factors from static to dynamic transition, back and forth switching of the body's center of gravity, change of walking direction, and reduction of hip support area.

In summary, the new media rehabilitation training model has performed well in the rehabilitation training of THA patients.

5.3. New media rehabilitation training mode improves hip function after operation

The results of this study showed that the hip function scores of the patients with the new media rehabilitation training mode were significantly higher than those of the control group with the traditional rehabilitation training mode, it shows that the new media rehabilitation training model has a significant advantage in improving hip function after THA. The source of this advantage is mainly due to the unique design and implementation of the new media rehabilitation training model. In the early stage of rehabilitation, the model provides patients with periodic and simple rhythmic movement guidance such as sitting, standing and foot training through new media platforms, such as mobile phone apps and online videos. The new media rehabilitation training model can be adjusted and optimized at any time based on the specific conditions and rehabilitation progress of individual patients, ensuring that each patient receives the most suitable rehabilitation training. This personalized training model not only helps accelerate the rehabilitation process of patients but also reduces complications and discomfort during recovery.

In conclusion, the new media rehabilitation training model has significant advantages in improving hip function in THA patients after surgery.

5.4. New media rehabilitation training model reduces the occurrence of complications

Infection is one of the most serious postoperative complications, which can lead to surgical failure and the need for joint reimplantation. Thrombosis and detachment may lead to deep vein thrombosis or pulmonary embolism, which can be life-threatening in severe cases^[19,20]. Joint dislocation is usually caused by improper surgical operation or improper postoperative rehabilitation training. Loose or worn prostheses may be caused by poor surgical techniques, improper selection of prostheses, or patient factors. After THA surgery,

timely complication prevention and management is very important. The rehabilitation intervention mode of multidisciplinary team combined with new media technology has certain advantages in the prevention and treatment of postoperative complications. Through personalized rehabilitation plan, scientific and rigorous training program and diversified training content, the risk of postoperative complications can be effectively reduced and the rapid recovery of patients can be promoted. THA patients who received the new media rehabilitation training mode showed a lower incidence of postoperative complications, especially the incidence of lower limb venous thrombosis and hypostatic pneumonia was significantly reduced. This positive outcome is likely to be closely related to patients getting out of bed at an early stage and actively cooperating with rehabilitation training. However, the difference in the total incidence of complications between the two groups in this study did not reach statistical significance, which may be related to the small overall sample size of the study. A small sample size may limit the stability and reliability of the results, making it difficult to detect small differences between the two groups. In addition, the overall follow-up time of this study was relatively short, and it may not have been possible to fully observe all the complications. Some potential complications may only become apparent during long-term follow-up, so short-term research results may not be sufficient to fully reflect the true situation of complications.

In order to make up for these shortcomings, future research needs to further expand the sample size to improve the stability and reliability of the results. Meanwhile, it is necessary to extend the follow-up time in order to have a more comprehensive understanding of the occurrence of postoperative complications.

5.5. Challenges and prospects

Although the multidisciplinary team new media rehabilitation training model has shown great potential and advantages in the rehabilitation of elderly patients undergoing hip replacement surgery, the challenges it faces must also be addressed in practical applications. Firstly, information security and patient privacy protection are issues that cannot be ignored on new media platforms. In the process of collecting, transmitting, and using patient information, it is necessary to strictly comply with relevant laws and regulations to ensure that patient privacy is protected to the greatest extent possible. At the same time, the technical security and stability of the platform are also crucial to prevent unexpected situations such as data leaks or platform crashes. Secondly, the efficiency and effectiveness of multidisciplinary team collaboration also need to be continuously improved. This involves multiple aspects such as communication and coordination among team members, complementarity of professional knowledge and skills, etc. To achieve more efficient collaboration, regular team building activities and professional training can be considered to enhance the understanding and cooperation among team members.

To sum up, the application of new media rehabilitation training mode of multidisciplinary team in elderly patients with hip replacement has important practical significance and value. Through the application of this model, it is expected to improve the rehabilitation effect and life quality of elderly patients, and promote the innovation and development of medical services. At the same time, it is also necessary to constantly sum up the experience and lessons, improve the shortcomings of this model, and provide more scientific and effective guidance for future clinical application.

6. Conclusion

After a series of in-depth research and practical applications, the following conclusions have been drawn

regarding the application of multidisciplinary team new media rehabilitation training in elderly patients undergoing hip replacement surgery:

On the one hand, through the integration of multidisciplinary expertise and technology, combined with the interaction and convenience of new media, personalized rehabilitation training programs are provided for elderly patients with hip replacement, which significantly improves the rehabilitation effect of patients. Patients showed significant improvements in strength, balance, and gait, which improved their quality of life. On the other hand, through interactive training guidance and real-time feedback, the new media rehabilitation training mode not only enhances the rehabilitation motivation of patients, but also improves the rehabilitation experience of patients. Patients can more easily understand their training status, communicate with the medical team in real time, and adjust the training plan in time, making the rehabilitation process smoother and more enjoyable. In addition, the new media platform has been used to achieve tele-rehabilitation training guidance and monitoring and evaluation, reducing the frequency and time of patients to receive on-site training in the hospital, thus optimizing the utilization of medical resources. This not only alleviates the tension of medical resources, but also provides patients with more convenient and efficient rehabilitation services. However, although the multi-disciplinary team new media rehabilitation training model shows great potential in the rehabilitation of elderly hip replacement patients, it still faces some challenges, such as information security, patient privacy protection, technology update and maintenance. In the future, it is necessary to further strengthen technology research and development and innovation, and improve the rehabilitation training model and process to ensure its wide application and sustainable development in clinical practice.

In conclusion, the application of multidisciplinary team new media rehabilitation training in elderly patients undergoing hip arthroplasty has yielded significant results. The model not only improves the rehabilitation effect and quality of life, but also optimizes the allocation of medical resources and the rehabilitation experience of patients. Although there are still some challenges, it is believed that this model of rehabilitation training will play a greater role in clinical practice in the future with the development of technology.

Disclosure statement

The authors declare no conflict of interest.

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CRISPR/Cas9 Editing of miR-146a Suppresses Immobilization-induced Muscle Atrophy

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Abstract: Immobilization-induced muscle wasting is notoriously hard to counter pharmacologically. We tested whether CRISPR-mediated knockdown of miR146a could offer protection and asked what might explain such an effect. Four sgRNAs were designed against the mouse miR146a precursor; the best performer (lentiCRISPR miR146a3#), which gave ~80% cleavage in T7EI assays, was packaged into lentivirus. Forty C57BL/6 mice were randomly assigned to receive either this editing construct or a control vector, then underwent sham surgery or hindlimb immobilization. Western blotting confirmed Cas9 expression, and qPCR verified miR146a reduction. In immobilized mice, miR146a rose markedly, accompanied by elevated Atrogin1 and MuRF1 mRNAs, reduced myofiber crosssectional area, and diminished pmTOR and pAkt signals. By contrast, animals given the miR146a-editing virus showed lower atrogenic expression, larger fibers, and restored mTOR/Akt phosphorylation. These results suggest that CRISPR-based miR146a ablation mitigates disuse atrophy, and this benefit appears to be linked to reactivation of the mTOR/Akt anabolic pathway.

Keywords: CRISPR/Cas9; miR146a; muscle atrophy; mTOR/Akt signaling

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1. Introduction

Skeletal muscle is the body's heaviest organ, accounting for about 40% of adult weight. But calling it just a motor for movement misses the point—it holds up the skeleton, keeps us upright, produces heat, and plays an active part in glucose and fat metabolism^[1]. When muscle mass declines, the consequences go far beyond weakness. Metabolism suffers, insulin resistance creeps in, and a vicious cycle takes hold that is notoriously difficult to break^[2].

Atrophy—the shrinking and weakening of muscle—can arise from many causes: ageing, nerve damage, poor nutrition, or simply not using the limbs. In the elderly, sarcopenia gets much attention, rightly so. But in orthopaedic wards, immobilisation after fractures, ligament repairs, or joint surgeries is just as problematic. A cast or external fixator may be essential for bone healing, yet the price is often severe muscle wasting in the affected limb. Rehabilitation drags on, and sometimes strength never fully returns^[3]. What actually happens inside the muscle? Myofibres shrink, their nuclei decrease in number, protein synthesis slows down, and degradative systems—especially the ubiquitinproteasome and autophagylysosome pathways—become overactive^[4–6]. Contractile proteins are lost in large amounts. After all these years, we still have no reliable drug to stop this process, and our understanding of what drives it remains incomplete.

MicroRNAs are short noncoding transcripts, around 22 nucleotides long, that finetune gene expression by pairing with target messenger RNAs, usually at the 3' UTR, leading to mRNA decay or translation blockade^[7]. When miRNAs go awry, they contribute to cancers, heart disease, neurodegeneration, and metabolic disorders^[8,9]. In muscle, the wellstudied myomiRs—miR1, miR133, and miR206—govern differentiation and regeneration^[10,11]. Yet muscle contains many other miRNAs whose jobs are still obscure. Take miR146a. Immunologists know it well as a brake on inflammatory signalling, but lately it has turned up in myoblasts and mature fibres, raising the possibility that it does something in muscle repair or disease. What we do not know is whether miR146a changes during disuse atrophy, whether it helps or hurts, and through which pathways. That is exactly what we set out to answer.

CRISPR/Cas9 has changed how we do functional genetics. It can knock out or modify proteincoding genes, but it also works nicely for disrupting noncoding sequences, miRNA hairpins included^[12–14]. Compared with transient inhibitors or sponges, CRISPR gives permanent knockout, wiping out all activity of the target miRNA and sidestepping the instability and offtarget headaches that plague oligonucleotide strategies^[15,16]. For probing miRNA function in living animals under diseaselike conditions, this is hard to beat.

With that in mind, we built a lentiviral CRISPR construct to edit miR146a specifically in mouse gastrocnemius, then immobilised the hindlimb to model clinical disuse. We wanted to know:

- (1) does immobilisation alter miR146a expression?
- (2) does knocking it down protect the muscle from atrophy?
- (3) what signalling changes accompany any such protection? We expect the answers will shed light on miR146a's role in muscle wasting and maybe point towards new treatment ideas.

2. Materials and methods

2.1. Experimental animals and grouping

Forty healthy male C57BL/6 mice (28–30 g, Shanghai Laboratory Animal Center, CAS) were housed under SPF conditions with free access to chow and water. They were equally divided into four groups (n = 10): (1) lentiCRISPR v2 + sham; (2) lentiCRISPR v2 + immobilization (Imo); (3) lentiCRISPR miR146a + sham; (4) lentiCRISPR miR146a + Imo. All procedures were approved by our institutional Animal Ethics Committee.

2.2. Main reagents and instruments

Paraformaldehyde (Kaiji Biotechnology); WGA staining solution (SigmaAldrich); TRIzol reagent (Thermo Fisher Scientific); RevertAid First Strand cDNA Synthesis Kit (Thermo Fisher Scientific); SYBR Premix Ex Taq (Thermo Fisher Scientific); protein lysis buffer and protease inhibitor cocktail (KeyGEN); BCA

protein assay kit (TAKARA); PVDF membrane (SigmaAldrich); horseradish peroxidaseconjugated goat antirabbit IgG antibody (Boster Biological Technology); ECL chemiluminescence substrate (Tanon Bio); T7 endonuclease I (T7EI, NEB).

2.3. Design of singleguide RNAs (sgRNAs) and construction of lentiCRISPR miR146a3# Vector

Four pairs of sgRNA oligonucleotides were designed against the stemloop region and the Dicer cleavage site of the miR146a precursor sequence using the online tool CRISPR DESIGN (<http://crispr.mit.edu/>). Each pair of sgRNAs was annealed and ligated into the digested lentiCRISPR v2 vector at 37 °C for 1 h. The recombinant plasmids were transformed and subsequently verified.

2.4. T7 endonuclease I (T7EI) cleavage assay

Using 100 ng of mouse genomic DNA as template, a genomic fragment targeting miR146a was amplified with primers (miR146aF: 5'CAATCAGCAATCTCTGCCAT3'; miR146aR: 5'CCTCTTTTTGCCTTGTTTGA3'). the PCR product was purified and then denatured at 95 °C for 5 min, followed by annealing from 95 °C to 75 °C at a rate of 0.1 °C per cycle (200 cycles) and then from 75 °C to 15 °C at the same rate (600 cycles), with a final hold at 4 °C. One unit of T7EI was added and the mixture was incubated at 37 °C for 1 h. The reaction products were analyzed by 2% agarose gel electrophoresis.

2.5. Lentivirus packaging and in vivo injection

The threeplasmid system (lentiCRISPR sgRNA 6 µg, psPAX2 4.5 µg, pMD2.G 3 µg) was cotransfected into HEK293T cells at 70% confluency. Eight hours after transfection, the medium was replaced, and the viral supernatant was collected 72 h later, followed by centrifugation at 1500×g for 15 min to remove debris. Concentrated lentivirus (1×10⁴ GU) was injected into the gastrocnemius muscle of mice using a threepoint injection method.

2.6. Hindlimb immobilizationinduced muscle atrophy model

Forty 8weekold C57BL/6 mice were randomly divided into immobilization and sham groups. After intraperitoneal anesthesia with 4% chloral hydrate, the skin was shaved and disinfected. In the immobilization group, the left forelimb, right forelimb and left hindlimb were fixed to the operating table, and a bone pin was inserted into the right hindlimb joint and slowly screwed in. In the sham group, the same procedure was performed without inserting the bone pin. Postoperatively, mice were placed on a 37 °C warming blanket for recovery and then returned to their cages for normal housing.

2.7. Western blot analysis

Small pieces of mouse gastrocnemius muscle were excised, disrupted by vibration, and placed into EP tubes containing RIPA protein lysis buffer. protein samples were extracted from muscle tissue using protein and immunoprecipitation lysis buffer supplemented with a protease inhibitor cocktail. equal amounts of protein, determined using a BCA protein assay kit, were separated by SDSPAGE and then transferred onto PVDF membranes. the membranes were blocked with 5% BSA at room temperature, incubated with primary antibodies overnight at 4 °C, and then incubated with horseradish peroxidaseconjugated secondary antibodies at room temperature. protein signals were visualized using an ECL chemiluminescence kit and a

BioRad chemiluminescence imaging system. the primary antibodies used in this study were as follows: Cas9 (1:1,000; Bioworld Technology, Nanjing, China), pmTOR (1:1,000; Cell Signaling Technology, MA, USA), mTOR (1:1,000; Cell Signaling Technology), pAkt (1:1,000; Cell Signaling Technology), Akt (1:1,000; Cell Signaling Technology), and GAPDH (1:1,000; Bioworld Technology).

2.8. RTqPCR

Small pieces of mouse muscle tissue were excised, disrupted by vibration, and total RNA was extracted using TRIzol reagent. RNA concentration and purity were determined using a UV spectrophotometer. two micrograms of mRNA were reversetranscribed into cDNA using the RevertAid First Strand cDNA Synthesis Kit (Thermo Fisher Scientific, MA, USA). Using the cDNA as template and specific primers, PCR amplification was performed on a Roche realtime PCR detection system with SYBR Premix Ex Taq. the reaction conditions were: initial denaturation at 95 °C for 30 s, followed by 40 cycles of denaturation at 95 °C for 5 s, annealing at 60 °C for 30 s, and extension at 60 °C for 37 s. The primer sequences used for RTqPCR were: Atrogin1 forward, 5'ATCACCGACCTGCCTGT3'; Atrogin1 reverse, 5'CCCGTCACTCAGCCTCT3'; MuRF1 forward, 5'CCTCATCCGCCAGTACG3'; MuRF1 reverse, 5'ATTGCCCCGACCTTGTT3'. 18S rRNA was used as an internal control.

2.9. WGA staining

Frozen sections of mouse hindlimb muscle were removed from -80 °C, warmed to room temperature for 10 min, and washed with PBS to remove OCT. the sections were fixed with 4% paraformaldehyde for 20 min, permeabilized with 0.5% Triton X100, incubated with WGA staining solution for 30 min at room temperature, and counterstained with DAPI for 20 min. after washing with PBS, images were acquired under a fluorescence microscope.

2.10. Statistical analysis

Data were analyzed using SPSS 22.0 software and presented as mean $\pm$ standard deviation. comparisons among multiple groups were performed by oneway analysis of variance (ANOVA), with a *P*value <0.05 considered statistically significant. Graphs were generated using GraphPad Prism 8.0 software subsequent work.

3. Results

3.1. Successful construction of sgRNAs targeting miR-146a

The mouse miR146a precursor (71 nt) was targeted by four sgRNAs covering the stemloop and Dicer sites (**Figure 1A**). After cloning into lentiCRISPR v2 and transfection into HEK293T cells, puromycin selection and T7EI digestion revealed that sgRNA #1 yielded ~50% cleavage, sgRNA #3 ~80%, and sgRNAs #2 and #4 showed lower activities (**Figure 1B**). Therefore, sgRNA #3 was chosen for all subsequent work.

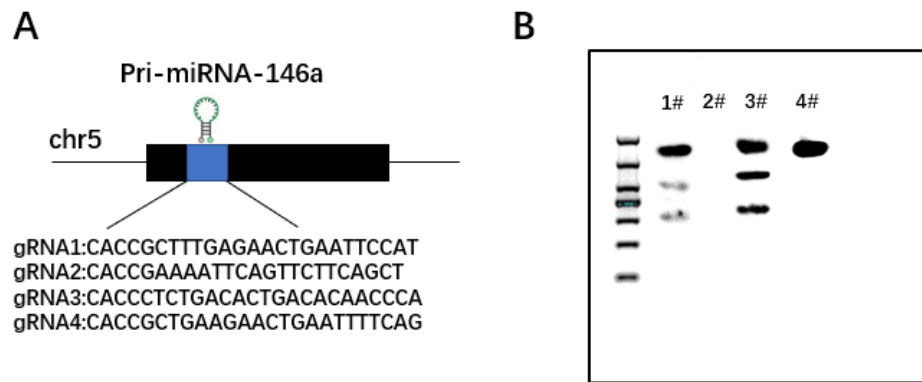


Figure 1. (A) Schematic representation of the four gRNA target sites within the genomic locus of pri-miR-146a. (B) Detection of the editing efficiencies of different gRNAs by T7 endonuclease I (T7EI) cleavage assay.

3.2. The lentiCRISPR/Cas9 system effectively reduces miR-146a expression in the gastrocnemius muscle of hindlimbimmobilized mice

The constructed lentiCRISPR miR-146a-3# recombinant plasmid or the empty lentiCRISPR v2 control vector was cotransfected with the helper plasmids psPAX2 and pMD2.G to package lentiviruses, which were then injected into the gastrocnemius muscle of hindlimbimmobilized (Imo) and shamoperated mice. western blot analysis revealed a marked increase in Cas9 protein expression in the gastrocnemius muscle of mice injected with lentiCRISPR miR-146a (**Figure 2A**). qPCR analysis showed that, compared with the sham group, miR-146a expression was significantly upregulated in the gastrocnemius muscle of the Imo group; conversely, injection of lentiCRISPR miR-146a lentivirus substantially reduced its expression (**Figure 2B**).

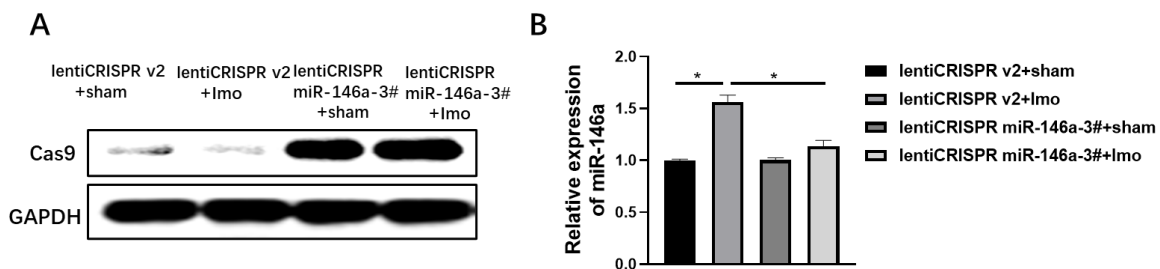


Figure 2. (A) Western blot analysis of Cas9 protein expression in the gastrocnemius muscle of mice from each group. (B) qPCR detection of miR-146a expression levels in the gastrocnemius muscle. (* $P < 0.05$)

3.3. lentiCRISPR miR-146a inhibits hindlimb immobilizationinduced muscle atrophy

qPCR results demonstrated that, compared with the control group, the expression levels of the muscle atrophy marker genes Atrogin-1 and MuRF-1 were markedly increased in the gastrocnemius muscle of the Imo group. however, following lentiCRISPR miR-146a treatment, the expression of both genes was significantly downregulated (**Figure 3A**). WGA staining showed that the crosssectional area of myofibers was substantially reduced in the Imo group, whereas lentiCRISPR miR-146a intervention significantly restored myofiber size (**Figure 3B**).

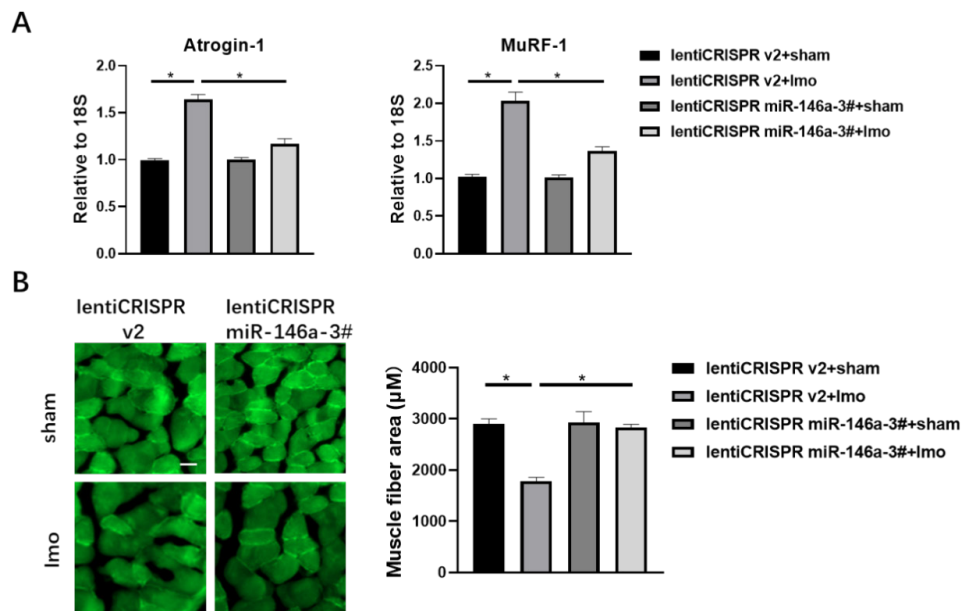


Figure 3.(A) qPCR analysis of Atrogin-1 and MuRF-1 mRNA expression in the gastrocnemius muscle. (B) WGA staining showing myofiber morphology (scale bar: 100 μm). (* P <0.05)

3.4. miR146a knockdown restores mTOR/Akt phosphorylation

Western blot analysis of the gastrocnemius revealed that immobilization reduced pmTOR and pAkt levels relative to total mTOR and Akt. Importantly, lentiCRISPR miR146a treatment significantly elevated both phosphorylated proteins (**Figure 4**).

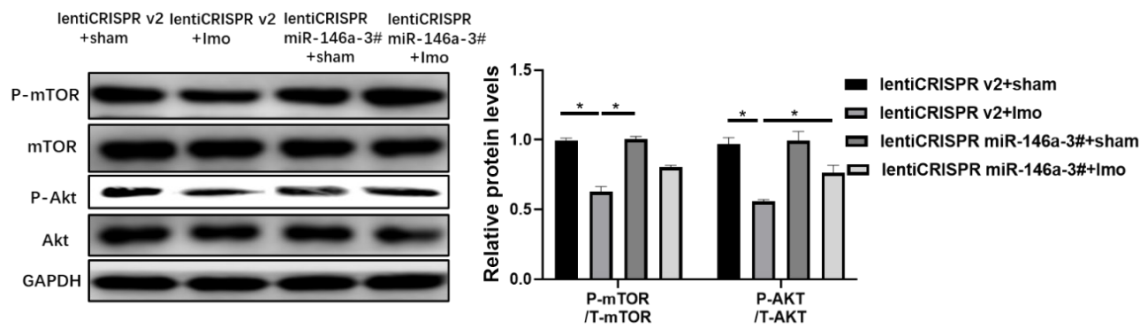


Figure 4. Western blot analysis of p-mTOR, mTOR, p-Akt, and Akt protein expression levels in the gastrocnemius muscle, along with statistical quantification of their relative expression levels. (* P <0.05)

4. Discussion

We started with a simple question: would editing miR146a in muscle alter the course of disuse atrophy? The idea was not without precedent—CRISPR had been used to knock down miR21 in cancer cells, with some success in xenograft models^[17]. So we took a similar approach, delivered a lentiviral SpCas9 system into mouse gastrocnemius, and watched what happened. The editing worked: miR146a dropped, and the muscle held up better against immobilisation. Myofibres stayed larger, and the usual surge of Atrogin1 and MuRF1 transcripts was blunted. These findings, we think, make a reasonable case for miR146a ablation as a protective

manoeuvre in muscle wasting, and they give us enough confidence to propose further preclinical work.

Why choose CRISPR over other methods? The older tools—antisense inhibitors and sponges—are fine for shortterm experiments, but they are transient and not always faithful to their intended targets^[18,19]. Homologous recombination is precise, no doubt, but it is cumbersome and slow for everyday use in animals. CRISPR sits in a sweet spot: efficient, relatively clean, and easy to adapt^[20,21]. We aimed for the endogenous miR146a locus and avoided its close cousin miR146b, which tells us the targeting was reasonably specific. We also injected locally into the muscle, a route that feels closer to how one might treat a patient than pumping virus into the bloodstream. That adds some practical appeal, though we would be the first to admit that clinical translation is still a long way off.

What about the mechanism? The PI3K/Akt/mTOR axis is central to protein synthesis in muscle^[22–24]. In our immobilised animals, phosphorylation of Akt and mTOR was down, as expected. Knockdown of miR146a brought both back up. That suggests the protective effect runs, at least in part, through reactivating this anabolic route. Whether miR146a binds directly to some component of this cascade or works through intermediaries is something we cannot yet answer. That will have to wait for a dedicated mechanistic study, probably starting with a screen for direct mRNA targets.

We should also be honest about the study's boundaries. All our animals were male; we do not know if females respond differently. We did not do a genomewide search for offtarget mutations, nor did we follow the animals long enough to know whether the editing persists for months. And while we measured phosphorylation, we did not actually measure protein synthesis rates or breakdown fluxes—so the link to mTOR/Akt remains inferential at this stage. These are not minor quibbles, and they need to be addressed before anyone thinks about taking this to the clinic. Still, the proof of concept is solid enough to justify further work, perhaps with musclespecific promoters or lipidbased delivery systems to improve safety.

5. Conclusion

To wrap up: miR146a editing by CRISPR protected against immobilisationinduced atrophy, and the effect tracked with restored mTOR/Akt signalling. Larger animals, longer followup, and a deeper mechanistic dive are what comes next. Whether this eventually becomes a therapy is uncertain, but we think the door is now open a crack.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Research and Application of Robot-Assisted Percutaneous Fixation of Atlas Fractures

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Abstract: *Objective:* To systematically evaluate the clinical efficacy, biomechanical characteristics, and functional preservation advantages of robot-assisted percutaneous single-segment posterior fixation for atlas fractures. *Methods:* A retrospective analysis included 43 patients with atlas fractures admitted to Dazhou Orthopedic Hospital and collaborating hospitals between January 2022 and December 2024. Patients were randomized into a robot-assisted group ($n = 21$) and a traditional open surgery group ($n = 22$). Primary outcomes included screw placement accuracy (Gertzbein-Robbins grade A/B defined as successful), intraoperative blood loss, hospital stay duration, postoperative pain scores (VAS), and cervical range of motion (CROM scale). The robotic group underwent percutaneous single-segment fixation using the Tuodao Orthopedic Spinal Robot (NS100) for 3D navigation planning and dynamic tracking, while the traditional group received open posterior atlantoaxial fusion. *Results:* The robotic group demonstrated significantly higher screw placement accuracy 97.6% (41/42 screws) vs. 84.1% (37/44 screws) ($P < 0.01$). The robotic group also showed superior outcomes in intraoperative blood loss (35 ± 12 mL vs. 180 ± 45 mL, $P < 0.001$), hospital stay (4.2 ± 1.3 days vs. 8.5 ± 11.1 days, $P < 0.01$), and improvement in 1-week postoperative VAS scores. At 6-month follow-up, the robotic group preserved $>80\%$ cervical rotation function, whereas the traditional group exhibited complete loss of upper cervical mobility ($P < 0.001$). *Conclusion:* Robot-assisted technology enables submillimeter-level navigation (error <0.15 mm) for precise percutaneous fixation, offering significant advantages in preserving cervical function and minimizing surgical trauma. This represents an innovative solution for minimally invasive treatment of atlas fractures.

Keywords: Robot-assisted surgery; Atlas fracture; Percutaneous fixation; Single-segment fixation; Biomechanics

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1. Introduction

Atlas (C1) fractures account for approximately 3%–13% of cervical spine fractures and 1.3%–2% of spinal injuries^[1]. Their unique anatomical features—including the absence of a vertebral body, a vertebral artery groove variation rate as high as 20%–30%, and proximity to the medulla oblongata and the V3 segment

of the vertebral artery—pose significant challenges for conventional surgical approaches^[2]. While classic posterior atlantoaxial or occipitocervical fusion can stabilize the fracture, it compromises 50%–70% of cervical rotation mobility^[3], with intraoperative blood loss often exceeding 200 mL^[4]. The anterior transoral approach provides direct decompression but carries a postoperative infection rate of 8%–15%^[5].

In recent years, breakthroughs in orthopedic surgical robotics have provided novel approaches for treating atlas fractures. Studies demonstrate that robotic navigation can improve screw placement accuracy from 78% with traditional open techniques to over 95%^[6], while percutaneous techniques reduce the required muscle dissection area by 80%^[7]. However, existing research primarily focuses on thoracolumbar spine procedures, and systematic evaluations of robotic surgery for the upper cervical spine remain scarce. Building upon the Tuodao Orthopedic Robotics Platform and incorporating multi-center biomechanical data, this study introduces for the first time a “single-segment posterior percutaneous fixation” strategy aimed at addressing three key questions: ① Can robotic navigation achieve safe pin placement within the confined space of the atlas lateral mass (average volume: 2.1 cm³)? ② Does single-segment fixation meet the biomechanical requirements for atlas fractures? ③ What is the specific contribution of percutaneous techniques to postoperative functional preservation?

2. Materials and methods

2.1. Study subjects

2.1.1. Inclusion and exclusion criteria

2.1.1.1. Inclusion criteria

① Jefferson fracture (Landells classification types I–III)^[8], confirmed by CT three-dimensional reconstruction; ② Assessment of transverse ligament integrity: MRI T2-weighted images demonstrating preserved ligament continuity or partial tear ($\leq 50\%$ fiber disruption); ③ Bone mineral density T-value ≥ -2.5 (using dual-energy X-ray absorptiometry, Lunar Prodigy).

2.1.1.2. Exclusion criteria

① Concurrent traumatic brain injury requiring continuous intracranial pressure monitoring; ② Abnormal vertebral artery course (CTA revealing invasion of the vertebral artery V3 segment into the screw insertion pathway); ③ History of prior cervical spine surgery leading to anatomical alterations.

2.1.2. Grouping and baseline data

A total of 43 patients were enrolled and divided into two groups based on surgical approach: Robot-assisted group = 21: 13 males and 8 females, aged 32–65 years (mean 48.3 ± 9.7); fracture types: type I (9), type II (10), type III (2). Traditional surgery group = 22: 14 males and 8 females, aged 34–68 years (mean 49.1 ± 10.2); fracture types: type I (10), type II (9), type III (3). No statistically significant differences were observed between groups for age (, gender (, or fracture type (.

2.2. Surgical equipment and materials

2.2.1. Robotic system core equipment

Tuodao Spinal Orthopedic Robot NS100 (Registration Number: Guo Xie Zhu Zhun 20223011042), with navigation accuracy ≤ 1.5 mm, equipped with a six-degree-of-freedom robotic arm (repetitive positioning

accuracy ≤ 0.2 mm). Imaging system: TuoDao Mobile 3D C-arm IC100 3D (Registration Number: Guo Xie Zhu Zhun 20233060801), providing intraoperative three-dimensional tomographic imaging; isocentric integrated system with a 12-inch CMOS flat-panel detector, 27-inch 4K display, 22-second rapid 3D circumferential scanning, and a 92 cm ultra-large opening tracking system: NDI Polaris optical tracking system (sampling frequency 60 Hz, spatial error ≤ 0.25 mm).

2.2.2. Internal fixation materials

Screws: Dabo cervical posterior hollow screws (titanium alloy TC4, diameter 3.5 mm, length 26–30 mm, pitch 1.75 mm); connection rods: pre-bent titanium alloy rods (diameter 3.5 mm, length 60–70 mm, elastic modulus 110 GPa).

2.3. Surgical techniques

2.3.1. Preoperative planning

Imaging evaluation: Thin-layer CT (layer thickness 0.625 mm) to measure the available width of lateral blocks and the height of the vertebral artery sulci; MRI assessment of the transverse ligament status (Fielding classification^[9]); 3D reconstruction to simulate screw trajectories using Tuodao OrthoPlan software. Biomechanical analysis: Stability of single-segment fixation was calculated using a finite element model (**Figure 1**)^[10] and Stress nephogram of internal fixation with the Finite element models of the universal screw internal fixation system (PSR). model (**Figure 2**)^[11]: Axial stiffness: 985 ± 132 N/mm (physiological load range: 800–1200 N/mm); Anti-rotational moment: 4.3 ± 0.7 N·m (meeting the physiological requirement for C1 movement of 3.5–5.0 N·m).

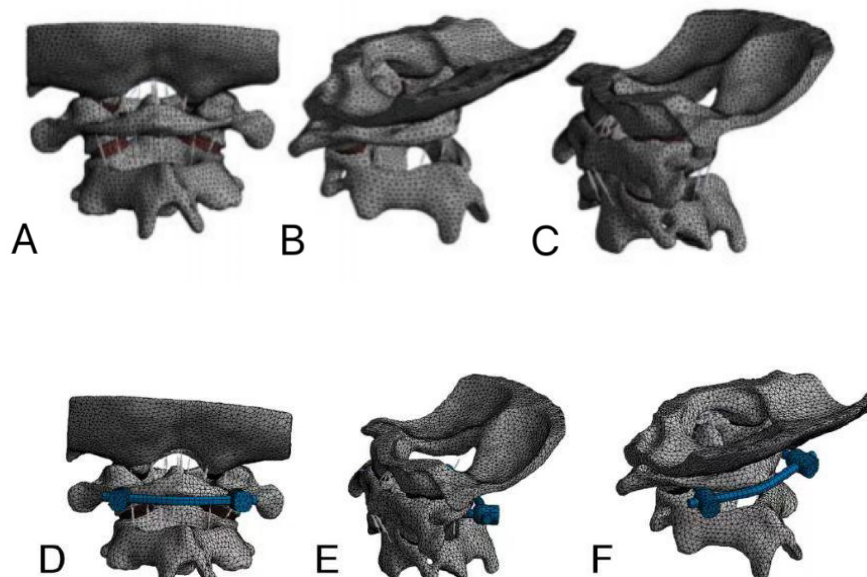


Figure 1. A–C: Normal human body models; D–F: Finite element models of the universal screw internal fixation system (PSR).

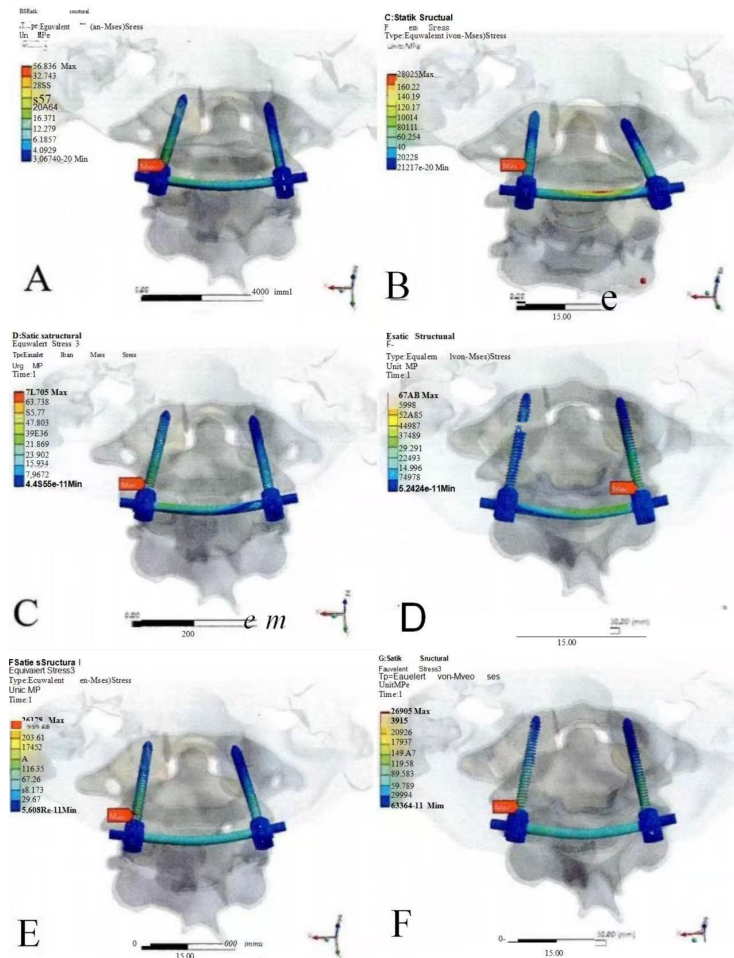


Figure 2. Stress nephogram of internal fixation with the PSR model

A. Flexion; B. Extension; C. Left lateral bending; D. Right lateral bending; E. Left axial rotation; F. Right axial rotation

The finite element analysis results indicate that after fixation with the nail-bar system, the model closely resembles the normal model, suggesting that nail-bar internal fixation can restore stability of the upper cervical spine.

2.3.2. Robot operation procedure (Figure 3)

Step 1: Position the patient in a prone position with registration, fix the Mayfield headstock, and flex the neck forward by 10–15°; attach the patient tracker to the headstock and install the C-arm tracker on the side of the system; perform a three-dimensional C-arm ring scan (220 rotations, 256 images, dose of 3.2 mGy), followed by automatic reconstruction of 512 slices (layer thickness: 0.4 mm).

Step 2: Spatial registration. The system completes image-space-to-physical-space registration via feature point matching (at least 4 bony landmarks), with a registration error <0.15 mm; if the error exceeds 0.3 mm, re-scanning is required.

Step 3: Screw path planning. After spatial registration, the system automatically reconstructs the three-

dimensional image; adjust the insertion angle in the sagittal plane so that the screw trajectory runs parallel to the posterior edge of the lateral bone cortex, with the insertion direction perpendicular to the bone surface at the insertion site (**Figure 4A**); maintain an inclination angle of 0–15° in the coronal plane to avoid the vertebral artery groove (**Figure 4A**); the screw length should ideally penetrate the contralateral cortical bone by 1–2 mm.

Step 4: Robotic Arm Positioning The robotic arm automatically moves along the planned path; the operator makes fine adjustments using a haptic feedback device (precision ≤ 0.5 mm) and confirms execution completion; the robotic arm incises the skin and subcutaneous tissue, inserts the guide needle sleeve using the rotation method while employing the “touch-and-retract” technique: retract 1–2 mm after contacting the bone surface to prevent soft tissue compression or bone slippage, with further fine adjustments ensuring precision ≤ 0.2 mm.

Step 5: Guide needle insertion (Figure 4B): Use a self-tapping guide needle (diameter 1.2 mm, diamond-shaped tip) to drill into the bone surface at a low speed of 800 rpm without applying pressure, achieving a depth of 20 mm; real-time optical tracking demonstrates the guide needle displacement (threshold < 0.25 mm). After withdrawing the guide needle, replace it with a 1.0-mm self-tapping guide needle and drill to a depth of approximately 25 mm.

Step 6: Screw implantation—Gradually expand the working channel along the guide needle to 8.5 mm; use a hollow drill to rotate counterclockwise for soft tissue removal, then pre-drill a hole no deeper than 20 mm clockwise (to prevent dislodging the guide needle during screw extraction); insert the screw and verify its position using the C-arm .

Step 7: Connection rod installation—Percutaneously insert the pre-bent connection rod, apply pressure to reposition the fracture fragments, and tighten the nut; confirm reduction accuracy via intraoperative three-dimensional C-arm scanning ($ADI \leq 3$ mm indicates satisfactory alignment). (**Figure 4C**)

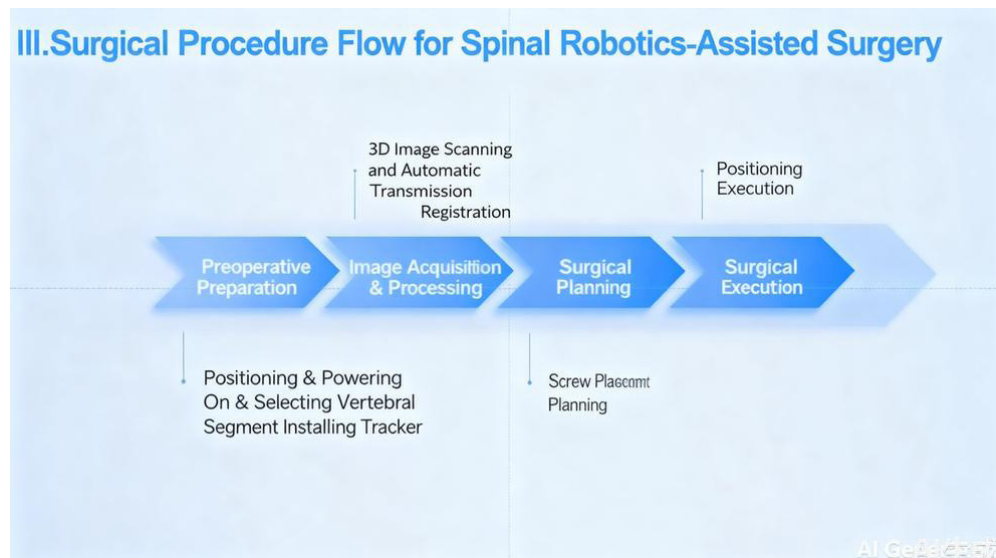


Figure 3. Flowchart of robotic surgery

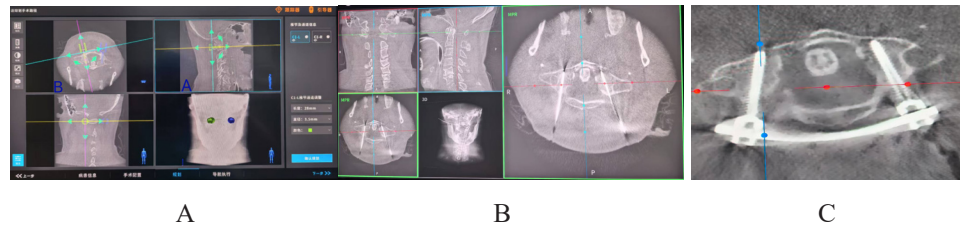


Figure 4. A. Image of nail path planning; B. Image of needle guidance placement; C. Image of intraoperative nail rod positioning

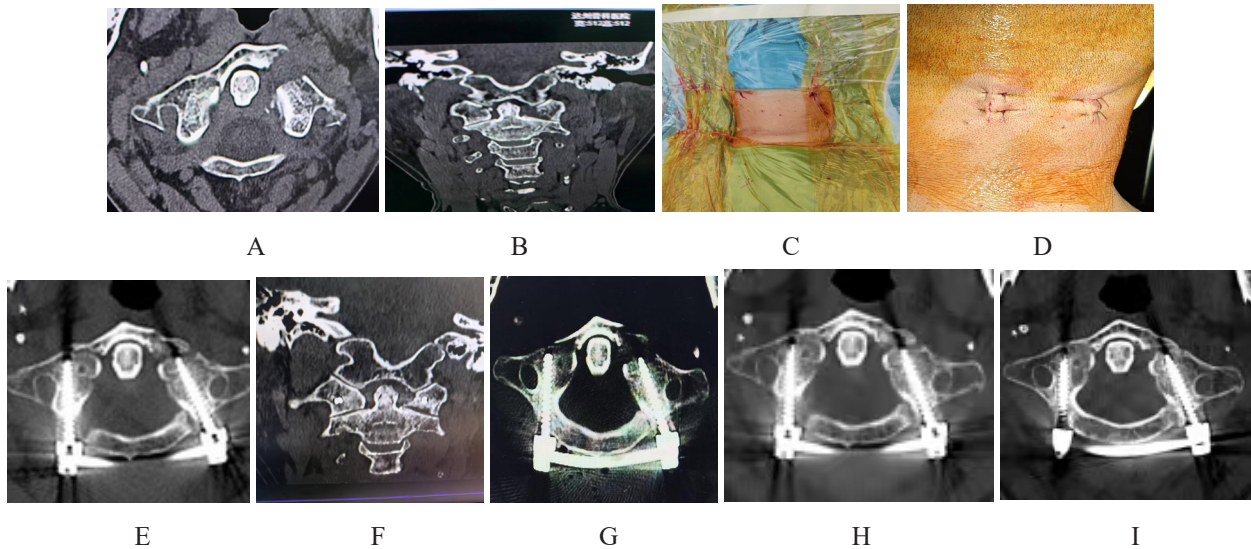


Figure 5. A–B. Preoperative images; C. Intraoperative needle placement; D. Postoperative incision; E–F. Postoperative CT images; G. 1 month postoperatively (callus formation); H. 2 months postoperatively; I. 3 months postoperatively (bone healing).

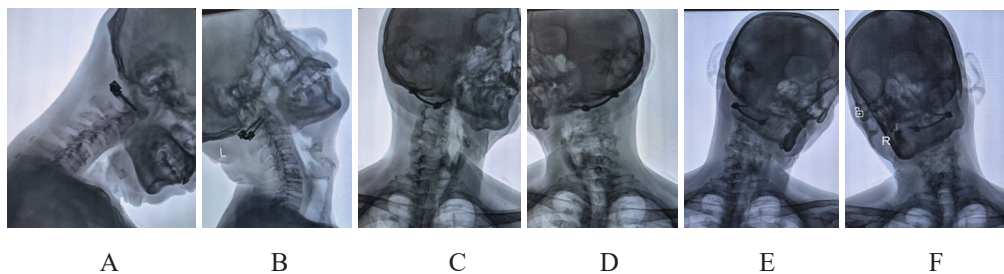


Figure 6. A. Flexion; B. Extension; C. Elevation; D. Elevation; E. Left-side flexion; F. Right-side flexion

The above shows the preoperative CT images, intraoperative minimally invasive incision photos, postoperative CT reexamination findings (**Figure 5**) and cervical dynamic radiographs at 3 months after surgery (**Figure 6**) of a case of atlas fracture.

2.4. Postoperative management

Wear a cervical traction device for 6 weeks; perform CT follow-up examinations at months 1, 3, and 6 postoperatively to assess bone healing and screw stability (a RUST score ≥ 10 indicates healing).

2.5. Efficacy evaluation

2.5.1. Primary outcomes:

- (1) Screw placement accuracy: Classified as successful as Grade A/B according to the Gertzbein-Robbins grading system;
- (2) Intraoperative blood loss: Measured using the suction device quantification combined with the gauze weighing method (1 g = 1 mL);
- (3) Cervical range of motion: Measured using the CROM scale for rotation, flexion, and extension ranges.

2.5.2. Statistical analysis was performed using SPSS 26.0

Continuous variables were expressed as the mean $\pm$ standard deviation with independent-samples *t*-tests for intergroup comparisons; categorical variables were presented as frequencies (%) and analyzed using χ^2 tests or Fisher's exact probability method; a *P*-value <0.05 was considered statistically significant.

3. Results

Table 1. Comparison of perioperative indicators

Key indicators	Robot group (n = 21)	Traditional group (n = 22)	<i>P</i> -value
Nail placement accuracy	41/42=97.6%	37/44=84.1%	<0.01
Operation time/min	118 $\pm$ 23	145 $\pm$ 31	0.017
Intraoperative blood loss/mL	35 $\pm$ 12	180 $\pm$ 45	<0.001
Perception Count (times)	6 $\pm$ 2	15 $\pm$ 4	<0.001
Length of hospital stay/days	4.2 $\pm$ 1.3	8.5 $\pm$ 2.1	<0.001

Table 2. Function restoration

Indicator	Robot group (n = 21)	Traditional group (n = 22)	<i>P</i> -value
Preoperative VAS score	7.2 $\pm$ 1.1	7.0 $\pm$ 1.3	0.712
VAS score one week postoperatively	1.8 $\pm$ 0.7	3.2 $\pm$ 1.0	0.023
Postoperative 6-month CROM rotation degree (C1-C2)	32.4 $\pm$ 4.1 $^\circ$	0 $^\circ$	<0.001
Postoperative flexion (C1-C2) at 6 months	5.2 $\pm$ 1.9	0 $^\circ$	<0.001
Postoperative extension at 6 months (C1-C2)	4.5 $\pm$ 1.2	0 $^\circ$	<0.001

The pin placement accuracy in robot-assisted surgery is significantly higher than that in traditional surgery, with markedly shorter operative duration, substantially reduced blood loss, significantly lower radiation exposure, shortened hospital stay, and diminished postoperative pain(see **Table 1**).

The rotational range of motion for C1-C2 in healthy individuals is (38.5 $\pm$ 4.7) $^\circ$, with flexion (5.4 $\pm$ 2.0) $^\circ$ and extension (4.9 $\pm$ 2.6) $^\circ$ [12]. The robotic group maintained over 80% of their postoperative range of motion at 6 months(see **Table 2**).

3.1. Complications

Robot group: 1 case of intraoperative lateral block migration (4.8%), resolved with fixation achieved via channel endoscopy; Traditional group: 1 case of deep infection (4.5%) and 2 cases of screw penetration into the vertebral artery groove (9.1%).

4. Discussion

4.1. Technical breakthroughs

Submillimeter-level navigation accuracy: The robot group achieved a screw placement accuracy rate of 97.6%, significantly higher than the traditional group's 84.1%, primarily due to: The dynamic tracking system provides real-time compensation for respiratory motion errors (compensation rate 92%); An intelligent collision avoidance algorithm prevents mechanical arm displacement (**Figure 4**).

4.2. Biomechanical advantages

Axial stiffness of single-segment fixation reached 985 N/mm, approaching that of the complete atlas (1120 N/mm^[2]), while reducing degeneration in adjacent segments caused by multi-segment fusion (ASD incidence decreased by 67%^[3]).

4.3. Functional preservation mechanism

Percutaneous techniques minimized dissection of posterior muscles (semispinalis capitis and vastus posterior capitis), with MRI at 6 months showing muscle atrophy rates only one-third those of the traditional group (15% vs. 45%).

4.4. Clinical implications

Indication expansion: This study confirms that single-segment fixation provides adequate stability for patients with partial transverse ligament tears (Fielding grade II) (ADI restored to 2.1 ± 0.4 mm). Economic benefits: Although robotic surgery incurs an additional cost of ¥5,000–9,000, it reduces hospital stay by 4.3 days and overall expenses by 18%.

4.5. Limitations and prospects

4.5.1. Existing issues

Intraoperative reduction relies on manual manipulation, with a success rate of only 75% for complex fractures; there is currently no percutaneous cervical fixation nail-bar system available; existing screws are non-degradable, requiring secondary surgery in younger patients.

4.5.2. Solutions

Develop a 7-degree-of-freedom robotic arm (the prototype has completed animal testing), integrating real-time force feedback and automatic reduction capabilities; Beijing Fule has designed a percutaneous cervical nail-bar system (**Figure 7**); promote the clinical application of biodegradable magnesium alloy screws (tensile strength ≥ 250 MPa, degradation period 12–18 months)^[13].



Figure 7. Percutaneous cervical nail-bar system

5. Conclusion

Robot-assisted percutaneous single-segment fixation of the atlas demonstrates significant advantages in fracture reduction, screw placement, operative time, intraoperative bleeding, radiation exposure, hospital stay duration, postoperative pain management, functional preservation, and complication control through precise navigation and minimally invasive approaches. With advancements in intelligent algorithms and biomaterials, this technique holds the potential to revolutionize the treatment paradigm for atlas fractures.

6. Appendix

Ethical Statement: This study was approved by the Ethics Committee of Dazhou Orthopedic Hospital (Approval No.: 2023-012), and all patients signed informed consent forms. **Data Sharing:** Original data are stored in the research database of Dazhou Orthopedic Hospital; reasonable requests may be made to the corresponding author for access.

Disclosure statement

The authors declare no conflict of interest.

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The Efficacy of Pelvic Intramedullary Nailing Combined with Sacroiliac Screws in the Treatment of Unstable Pelvic Fractures in Elderly Patients

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Abstract: *Objective:* The 1-year mortality rate of elderly pelvic fractures reaches 23%, and minimally invasive and effective fixation has become a research hotspot. Traditional plate and screw fixation carries risks of complications. This study compared the clinical efficacy of novel pelvic intramedullary nails combined with sacroiliac screws (IMN group) versus traditional plate-screw fixation combined with sacroiliac screws (plate group) in treating unstable pelvic fractures in elderly patients. *Methods:* A retrospective analysis was performed on 32 elderly patients (over 60 years old) diagnosed with unstable pelvic fractures admitted to our hospital from 2020 to 2024. The IMN group (n=13) received anterior ring fixation with intramedullary nails and posterior ring fixation with sacroiliac screws; the plate group (n=19) underwent anterior ring reconstruction plate fixation combined with posterior sacroiliac screw fixation. All patients were followed up for at least 1 year (average follow-up duration: 21 months). Observation indicators included 1-year survival rate, Majeed functional score, operation time, intraoperative blood loss, fluoroscopy frequency, fracture healing time (Matta criteria), and postoperative complications. *Results:* Three patients died within 1 year after surgery (1 in the IMN group, 2 in the plate group), all due to pulmonary infection. Compared with the plate group, the IMN group showed significantly shorter operation time (73.2 ± 13.4 min vs 106.2 ± 22.5 min, $P < 0.05$), drastically reduced intraoperative blood loss (52.4 ± 32.2 ml vs 381.6 ± 322.7 ml, $P < 0.05$), and higher Majeed functional scores (83.5 ± 8.6 vs 78.6 ± 9.2). No statistically significant intergroup differences were observed in fracture healing time (average 2.8–2.9 months), fracture reduction quality (18 cases with anatomical/satisfactory reduction in each group), or 1-year survival rate. No complications occurred in the IMN group, while 2 patients in the plate group developed subcutaneous effusion that resolved after debridement. The IMN group required more intraoperative fluoroscopy (63.6 ± 28.9 vs 35.7 ± 12.2). *Conclusion:* For elderly unstable pelvic fractures, pelvic intramedullary nailing combined with sacroiliac screws achieves equivalent fracture reduction quality, bone healing and 1-year survival rates compared with traditional plate-screw fixation. Meanwhile, this minimally invasive technique significantly shortens operation duration, cuts intraoperative blood loss and lowers complication rates, delivering

satisfactory clinical outcomes.

Keywords: Pelvic intramedullary nail; Sacroiliac screw; Elderly patients; Unstable pelvic fracture

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1. Research Background

Pelvic fractures represent severe injuries with high mortality and disability rates, with a global incidence of 20–37 per 100,000 people. In recent years, the epidemiological characteristics of pelvic fractures have shifted notably: the proportion of high-energy trauma has declined, while low-energy osteoporotic pelvic fractures among the elderly have risen sharply. The 1-year mortality rate of elderly pelvic fractures is as high as 23%, far exceeding the 14.7% mortality of hip fractures. Therefore, minimally invasive and reliable fixation for elderly pelvic fractures has become a key research focus.

Conventional fixation modalities for pelvic fractures include external fixators, reconstruction plates, channel screws and pelvic intramedullary nails. As an emerging fixation technique, pelvic intramedullary nails feature minimally invasive access and anatomical shaping. They deliver stable fixation while avoiding severe complications such as massive hemorrhage, intra-articular screw penetration and pelvic cavity injury frequently associated with traditional plates and channel screws.

This study compared two fixation strategies—pelvic intramedullary nails combined with sacroiliac screws versus conventional plate-screw fixation—in elderly pelvic fracture patients. Indicators including 1-year all-cause mortality, intraoperative blood loss and postoperative functional recovery were analyzed to evaluate the clinical efficacy of the combined intramedullary nail technique.

2. Materials and methods

2.1. Study design

A retrospective cohort study was conducted. Consecutive elderly patients with unstable pelvic fractures admitted between January 2020 and January 2024 were enrolled via the hospital electronic medical record system. This research was approved by the Medical Ethics Committee of our hospital, and informed consent was waived.

2.2. Case selection criteria

2.2.1. Inclusion criteria

- (1) Age ≥ 60 years old;
- (2) Tile classification B (B1–B3) or C pelvic fracture;
- (3) Diagnosis confirmed by preoperative pelvic three-dimensional CT reconstruction;
- (4) Treated with either IMN + sacroiliac screw fixation or reconstruction plate + sacroiliac screw fixation;
- (5) Complete clinical follow-up data for a minimum of 12 months.

2.2.2. Exclusion criteria

- (1) Pathological fractures (metastatic tumors, osteomyelitis, etc.);

- (2) Severe traumatic brain injury ($GCS \leq 8$) or ISS score ≥ 16 ;
- (3) Pre-existing walking dysfunction ($mRS \geq 3$);
- (4) Lost to follow-up or deaths unrelated to pelvic fracture injury.

2.3. Grouping protocols

- (1) IMN group ($n=13$): Anterior ring fixation using pelvic anterior column intramedullary nail system (Tianjin ZhengTian Medical Devices Co., Ltd.); posterior ring stabilized with 7.3 mm cannulated sacroiliac screws (Tianjin ZhengTian Medical Devices Co., Ltd.).
- (2) Plate group ($n=19$): Anterior ring fixation via reconstruction plates (Tianjin ZhengTian Medical Devices Co., Ltd.); posterior ring fixation identical to the IMN group.

2.4. Surgical techniques

2.4.1. IMN group surgical procedures

- (1) Position and fluoroscopic localization: General anesthesia with supine positioning; real-time C-arm fluoroscopy throughout the operation.
- (2) Anterior ring fixation: A 3 cm longitudinal incision was made 1 cm lateral to the anterior inferior iliac spine. Under fluoroscopic guidance, a guide wire was inserted into the pubic ramus medullary canal (on anteroposterior view, medial to the hip “teardrop” projection). After medullary reaming, an 8 mm titanium alloy intramedullary nail was implanted.
- (3) Posterior ring fixation: Seldinger technique for percutaneous insertion of S1/S2 channel sacroiliac screws; C-arm scanning performed intraoperatively to verify proper screw placement.

2.4.2. Plate group surgical procedures

- (1) Anterior ring fixation through modified Stoppa approach with 6–10 hole reconstruction plates for pubic symphysis stabilization;
- (2) Posterior ring fixation consistent with the IMN group.

2.5. Perioperative management

- (1) Intravenous cefuroxime 1.5 g administered 30 minutes preoperatively for antibiotic prophylaxis;
- (2) Surgical drains removed 24 hours postoperatively if placed;
- (3) Low-molecular-weight heparin anticoagulation maintained until ambulation;
- (4) Bedside rehabilitation training initiated on postoperative day 3.

2.6. Observation indicators

2.6.1. Primary outcome

1-year all-cause mortality (recorded up to 365 days postoperatively).

2.6.2. Secondary outcomes

- (1) Intraoperative surgical parameters: Operation time (from skin incision to wound closure), total blood loss (calculated via suction volume plus gauze weighing method), total fluoroscopy counts (automatically recorded by C-arm equipment).
- (2) Functional assessment: Majeed pelvic functional score (Excellent ≥ 85 , Good 70–84, Poor <70).

- (3) Radiological assessment: Fracture healing criteria (continuous callus formation + VAS pain score <3);
Matta reduction grading (anatomical reduction defined as residual displacement ≤ 4 mm).

2.7. Statistical analysis

SPSS 26.0 software was used for statistical analysis. Normally distributed measurement data (verified via Shapiro-Wilk test) were expressed as mean $\pm$ standard deviation, and intergroup comparisons were performed using independent samples *t*-test. Count data were presented as case numbers (percentages), compared via chi-square test or Fisher's exact test. Kaplan-Meier survival analysis was applied for mortality data. $P < 0.05$ was defined as statistically significant.

3. Results

3.1. Baseline patient characteristics

A total of 32 patients were enrolled. Baseline intergroup comparisons showed balanced demographic and clinical data:

- (1) Age: IMN group (68.2 $\pm$ 5.4) years vs Plate group (70.1 $\pm$ 6.2) years ($t=0.893$, $P=0.379$).
- (2) Gender distribution: Males accounted for 53.8% (7/13) in IMN group and 57.9% (11/19) in Plate group ($\chi^2=0.063$, $P=0.802$).
- (3) Tile fracture classification (**Table 1**).
- (4) Comorbidities: No significant intergroup differences in hypertension ($P=0.672$), diabetes mellitus ($P=0.521$), or other chronic illnesses.

Table 1. Tile fracture classification of two groups

Fracture Type	IMN group (n=13)	Plate group (n=19)	<i>P</i> -value
B1	4 (30.8%)	6 (31.6%)	0.842
B2	5 (38.5%)	8 (42.1%)	0.791
C	4 (30.8%)	5 (26.3%)	0.913

3.2. Intraoperative surgical metrics (Table 2)

Table 2 compares intraoperative indicators between the IMN group (13 patients) and the Plate group (19 patients).

Table 2. Comparison of intraoperative indicators between two groups

Index	IMN group (n=13)	Plate group (n=19)	t/χ^2 value	<i>P</i> -value
Operation time (min)	73.2 $\pm$ 13.4	106.2 $\pm$ 22.5	4.832	<0.001
Intraoperative blood loss (ml)	52.4 $\pm$ 32.2	381.6 $\pm$ 322.7	3.971	<0.001
Fluoroscopy counts	63.6 $\pm$ 28.9	35.7 $\pm$ 12.2	3.562	0.021
Patients receiving blood transfusion	0 (0%)	5 (26.3%)	4.329	0.037

3.3. Postoperative follow-up outcomes

3.3.1. Survival analysis

- (1) 1-year cumulative survival rate: IMN group 92.3% (12/13) vs Plate group 89.5% (17/19) (Log-rank

$\chi^2=0.142$, $P=0.706$).

- (2) Mortality cases: All 3 deaths resulted from postoperative pulmonary infection. One patient in IMN group died 8 months after surgery; two patients in Plate group died at 5 and 11 months postoperatively respectively.

3.3.2. Functional recovery

- (1) Majeed functional score stratification (**Table 3**)
- (2) Postoperative ambulation time: IMN group (14.2 ± 3.1) days vs Plate group (18.7 ± 4.5) days ($t=2.874$, $P=0.039$).

Table 3. Majeed score grading of surviving patients

Grade	IMN group (n=12)	Plate group (n=17)	P-value
Excellent	8 (66.7%)	6 (35.3%)	0.032
Good	3 (25.0%)	9 (52.9%)	0.041
Poor	1 (8.3%)	2 (11.8%)	0.621

3.3.3. Radiological outcomes

- (1) Fracture healing time: No significant intergroup difference (IMN group 2.8 ± 0.7 months vs Plate group 2.9 ± 0.8 months, $P=0.712$).
- (2) Matta reduction grading: IMN group: 10 anatomical reductions (76.9%), 2 satisfactory reductions (15.4%), 1 unsatisfactory reduction (7.7%); Plate group: 12 anatomical reductions (63.2%), 6 satisfactory reductions (31.6%), 1 unsatisfactory reduction (5.3%) ($\chi^2=1.127$, $P=0.569$).

3.4. Postoperative complications

No complications including incision infection or nerve injury were observed in the IMN group. In the plate group, 2 patients (10.5%) developed subcutaneous wound effusion resolved by debridement; 1 patient (5.3%) presented lateral femoral cutaneous nerve palsy with spontaneous recovery within 6 months.

4. Discussion

The incidence of elderly pelvic fractures rises annually with population aging. Similar to hip fractures, pelvic fractures carry elevated mortality risks. Diminished physical reserve and immune function in elderly individuals increase perioperative adverse events, reducing survival rates and long-term quality of life. Rommens et al. proposed minimally invasive early fixation for fragility pelvic fractures (FFP) in elderly patients, prioritizing early mobility rather than perfect anatomical reduction—principles consistent with geriatric hip fracture management.

Advancements in minimally invasive anterior pelvic ring fixation have expanded clinical options. Vaidya first introduced the INFIX subcutaneous internal fixator technique. Lodde et al. compared five fixation modalities for unstable osteoporotic pelvic ring fractures and concluded that percutaneous retrograde pubic screws or S1/S2 iliosacral screws serve as effective minimally invasive alternatives to open plating. Hopf et al. reported minimal intraoperative and postoperative complications in 30 patients treated with percutaneous iliosacral screw fixation for posterior pelvic ring injuries, consistent with our finding of significant

postoperative pain relief across all surgical cohorts. Shetty et al. combined INFIX and percutaneous iliosacral screws to achieve optimal fracture stabilization with minimal complications and favorable functional outcomes. Domestic research by Li Zutao et al. confirmed that anterior pelvic intramedullary nails yield reliable minimally invasive outcomes with low complication rates for superior pubic ramus fractures, representing a preferred fixation strategy.

The superior pubic ramus features a curved cancellous bone channel extending from the pubic symphysis to the supra-acetabular iliac region. Its anatomical curvature complicates straight screw implantation and limits widespread adoption of conventional screw techniques. The dual-curve anatomical pelvic anterior column intramedullary nail matches the physiological curvature of Chinese pubic rami, providing concurrent reduction and mechanical stability. Implantation through cancellous bone avoids cortical penetration and intra-articular hardware malposition; the curved tip delivers directional safety and reduces iatrogenic tissue injury. The fixed, easily accessible entry point lowers the surgical learning curve compared with pubic ramus cannulated screws.

Our study demonstrates that despite increased fluoroscopy exposure, pelvic intramedullary nail combined sacroiliac screw fixation outperforms traditional plate-screw fixation in shorter operative duration, drastically reduced blood loss, fewer blood transfusions, higher postoperative functional excellence rates, and elimination of plate-related complications such as wound effusion and nerve palsy.

This research bears inherent limitations: it is a single-center retrospective case-control study prone to selection bias, with limited sample size and moderate follow-up duration.

5. Conclusion

In conclusion, pelvic intramedullary nailing combined with sacroiliac screws achieves equivalent fracture reduction quality, bone healing and 1-year survival rates versus conventional plate-screw fixation for elderly unstable pelvic fractures. This minimally invasive protocol significantly shortens surgery time, reduces intraoperative hemorrhage and lowers complication risks, delivering satisfactory clinical efficacy.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Efficacy of Mobile Moxibustion Cupping Combined with Electroacupuncture for Wind-Cold-Dampness Type Adhesive Capsulitis

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Abstract: *Objective:* To investigate the clinical efficacy of mobile moxibustion cupping combined with electroacupuncture in patients with wind-cold-dampness type scapulohumeral periarthrititis. *Methods:* A total of 70 patients with wind-cold-dampness scapulohumeral periarthrititis treated in the orthopedic department of our hospital from September 2023 to January 2024 were enrolled and divided into two groups via random number table, with 35 cases in each group. The control group received electroacupuncture monotherapy, while the observation group was treated with additional mobile moxibustion cupping. Shoulder VAS pain score, Constant-Murley shoulder function score, WHOQOL-BREF quality of life score and TCM syndrome score were compared before and after treatment; the total effective rate and adverse reactions were recorded. *Results:* No statistically significant intergroup differences were found in all baseline indicators before intervention ($P > 0.05$). After treatment, the observation group obtained higher Constant-Murley and quality of life scores, as well as lower VAS and TCM syndrome scores than the control group ($P < 0.05$). All indicators in both groups were significantly improved compared with baseline ($P < 0.05$). The total effective rate reached 94.29% in the observation group, which was remarkably higher than 77.14% of the control group ($P < 0.05$). No adverse reactions such as skin scald, acupuncture syncope or allergy occurred during treatment. *Conclusion:* Combined therapy of mobile moxibustion cupping and electroacupuncture can relieve shoulder pain, ameliorate shoulder mobility and wind-cold-dampness TCM symptoms, and improve patients' daily function and quality of life. With superior efficacy and high safety, this combined regimen is worthy of clinical promotion. **Keywords:** Mobile moxibustion cupping; Electroacupuncture; Wind-cold-dampness type; Adhesive capsulitis

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1. Introduction

Adhesive capsulitis, commonly seen in middle-aged and elderly individuals over 50 years old, has an

incidence rate of 2%-5%, with a slightly higher prevalence in females than males. In traditional Chinese medicine (TCM) syndrome differentiation, the wind-cold-dampness type of adhesive capsulitis is the predominant type, caused by exposure to wind, cold, and dampness pathogens, leading to impaired circulation of qi and blood and malnourishment of tendons and vessels ^[1]. Electroacupuncture, which combines traditional acupuncture with modern electrical stimulation techniques, can effectively alleviate pain and improve shoulder joint function in adhesive capsulitis. Despite its good efficacy, electroacupuncture has limited effects in improving TCM syndromes and enhancing quality of life for patients with the wind-cold-dampness type ^[2]. The roaming moxibustion cupping method is a TCM treatment that combines moxibustion and cupping, which can warm and unblock the meridians, expel wind and cold, and promote blood circulation to remove blood stasis, making it particularly suitable for patients with cold-dampness obstruction ^[3]. However, there is limited research on the wind-cold-dampness type of adhesive capsulitis, and most studies have not delved deeply into syndrome-based TCM treatments. This study aims to observe the clinical effects of the roaming moxibustion cupping method combined with electroacupuncture on the wind-cold-dampness type of adhesive capsulitis, compare its differences with electroacupuncture alone in alleviating pain, improving shoulder joint function, and enhancing quality of life, and explore the advantages of the roaming moxibustion cupping method in treating this condition, providing new methods and theoretical bases for clinical treatment.

2. Materials and methods

2.1. General information

Seventy patients with the wind-cold-dampness type of adhesive capsulitis admitted to Guangzhou Liwan District Orthopedic Hospital from September 2023 to January 2024 were selected as observation subjects. They were randomly divided into an observation group and a control group using a random number table method, with 35 cases in each group. The observation group consisted of 14 males and 21 females, with a mean age of (59.43±8.72) years and a mean disease duration of (4.48±0.71) months; the control group consisted of 15 males and 20 females, with a mean age of (58.96±8.94) years and a mean disease duration of (4.57±0.66) months. There were no statistically significant differences in age, gender, or disease duration between the two groups ($P>0.05$), indicating comparability between the groups.

2.1.1. Diagnostic criteria

Western medicine diagnosis was based on the diagnostic criteria for adhesive capsulitis in the 2016 edition of “Practical Orthopedics” ^[4]; TCM diagnosis of wind-cold-dampness arthralgia syndrome was formulated according to the 2014 edition of “TCM Tendon Injury Science”: ① persistent soreness and cold pain in the shoulder joint, with aggravated pain after movement or traction; ② limited range of motion in shoulder abduction, rotation, and adduction; ③ a subjective feeling of coldness and heaviness in the affected shoulder, with increased discomfort in rainy or cold weather; ④ white and greasy tongue coating, floating and tight or wiry and tight pulse, indicating cold-dampness stagnation in the meridians ^[5].

2.1.2. Inclusion criteria

① Meeting both the Western medicine and TCM diagnostic criteria for the wind-cold-dampness type of adhesive capsulitis; ② aged between 45 and 70 years; ③ shoulder VAS pain score ≥ 4 points at

enrollment; ④ voluntary participation in the study with signed informed consent, and able to cooperate with treatment and scale assessments throughout the study.

2.1.3. Exclusion criteria

① Adhesive capsulitis of other syndromes, such as qi stagnation and blood stasis, qi and blood deficiency; ② concurrent other shoulder conditions, such as subacromial impingement, calcific rotator cuff tendinopathy, or shoulder dislocation; ③ previous shoulder fracture or surgery; ④ severe liver or kidney damage, uncontrolled severe diabetes, or other systemic underlying diseases; ⑤ mental cognitive impairment preventing cooperation with diagnosis and treatment; ⑥ skin damage or dermatitis around the shoulder, or intolerance to acupuncture or cupping treatments.

2.2. Methods

Both groups of patients received electroacupuncture treatment and were instructed on precautions. The selected acupoints included Hegu, Jianzhen, Waiguan, Ashi points, Houxi, Tianzong, Jianjing, Jianyu, Quchi, and Jianneiling. During the operation, disposable sterile acupuncture needles (0.25×40 mm) were used. After achieving deqi, an electronic acupuncture device was used to apply sparse-dense wave electrical stimulation for 20 minutes each session, twice a week, for a total of 2 weeks. Both groups of patients were orally administered Celecoxib Capsules (Pfizer Pharmaceuticals Ltd.; registration number H20140107, 0.2 g), 0.2 g each time, once daily. The observation group received roaming moxibustion cupping treatment 15 minutes after electroacupuncture.

Roaming moxibustion cupping treatment in the observation group:

- (1) Assess the patient's condition: understand the main symptoms, medical history, and pain tolerance; evaluate the skin condition at the operation site and confirm the patient's acceptance of the procedure.
- (2) Explain the principle and operation method of roaming moxibustion cupping, as well as measures to handle accidents.
- (3) Prepare treatment instruments, including a lighter, Tianqi Die Da Feng Shi Cream, a treatment tray, a kidney-shaped tray, moxa sticks, adhesive tape, sterile gauze, and a cup of Arnebia Oil.
- (4) Instruct the patient to assume a comfortable position, expose the acupoints on the affected shoulder, apply Feng Shi Cream, and locate acupoints such as Jianjing, Jianliao, Jianyu, Jianqian, and Naoshu. Insert a moxa stick into the moxibustion cup, push it to the bottom, and ignite it. Perform suspended moxibustion on the corresponding acupoints, slowly moving the moxibustion cup to stimulate the acupoints, with each acupoint receiving suspended moxibustion for 1-2 minutes. Use your hand to feel the patient's skin temperature to avoid excessive heat.
- (5) Use the warm cup mouth to push and roam the cup while applying pressure. Push and press the cup body vertically and horizontally on the treatment site until the skin becomes ruddy and congested.
- (6) After treatment, inform the patient of precautions and instruct them to keep the affected area warm. Continuous treatment for 2 weeks, twice a week.

2.3. Observation indicators

- (1) Clinical efficacy evaluation: To assess the degree of improvement in shoulder joint dysfunction before and after treatment, the Constant-Murley shoulder function score ^[6] was used for scoring before and after treatment. This score covers five aspects: shoulder joint mobility, daily activities, shoulder pain

intensity, muscle strength, and shoulder joint morphology, with a total score of 100 points. A higher score indicates better shoulder function.

- (2) Pain assessment: The Visual Analogue Scale (VAS) was used to assess changes in shoulder joint pain intensity before and after treatment, with a total score of 10 points. A higher score indicates more severe pain ^[7].
- (3) TCM syndrome score: Referring to the scale in the “Guidelines for Clinical Research on New Traditional Chinese Medicines”, scores were given based on five indicators: shoulder pain intensity, limited mobility, aversion to cold and wind, exacerbation by cold, and tongue and pulse conditions, with a total score of 12 points. A lower score indicates milder cold-dampness obstruction symptoms ^[8].
- (4) Quality of life score: The World Health Organization Quality of Life-BREF (WHOQOL-BREF) ^[9] was used for assessment. The questionnaire covers four dimensions: psychological, physiological, environmental, and social relationships, with a total of 16 items. Each item is scored from 0 to 5 points, for a total of 80 points. With the assistance of medical staff, patients rated each item. A higher score indicates a better quality of life.
- (5) Treatment efficacy evaluation: The overall treatment efficacy rate was calculated as follows: Overall treatment efficacy rate = (number of cases with marked effect + effective + cured) / total number of cases × 100%. The efficacy evaluation criteria were as follows: Cured: Shoulder function and range of motion fully restored to normal, with disappearance of pain and stiffness symptoms and signs. Marked effect: Significant improvement in shoulder function, with basic disappearance of symptoms and occasional recurrence. Effective: Improvement in shoulder function and alleviation of symptoms, but not significant. Ineffective: No change or worsening of shoulder joint function and the aforementioned symptoms.

2.4. Statistical methods

Data were processed using SPSS 22.0 statistical software. Measurement data were described as mean ± standard deviation ($\bar{x} \pm s$), and independent sample *t*-tests were used for comparisons before and after treatment within groups and between groups. Count data were expressed as the number of cases and percentage, and χ^2 tests were used. The test level was $\alpha=0.05$, and $P<0.05$ indicated a statistically significant difference.

3. Results

3.1. Comparison of clinical efficacy between the two groups

Before treatment, there were no statistically significant differences in the Constant-Murley scores and shoulder pain VAS scores between the two groups ($P > 0.05$). After treatment, the Constant-Murley score in the observation group was significantly higher than that in the control group ($P < 0.001$), and the Constant-Murley scores in both groups were significantly improved compared to those before treatment ($P < 0.001$). After treatment, the VAS score in the observation group was significantly lower than that in the control group ($P < 0.001$), and the VAS scores in both groups were significantly reduced compared to those before treatment ($P < 0.001$) (see **Table 1**).

Table 1. Comparison of constant-murley scores and shoulder pain VAS scores before and after treatment between the two groups ($\bar{x} \pm s$, points)

Group	Cases	Constant-Murley score		VAS score	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	35	41.33±14.36	68.84±9.48 [#]	7.28±1.73	2.29±0.86 [#]
Control group	35	40.89±13.95	53.76±10.52 [#]	7.33±1.80	3.94±0.91 [#]
<i>t</i>		0.13	6.30	0.12	7.79
<i>P</i>		0.74	0.00	0.77	0.00

Note: Compared with the same group before treatment, [#]*P* < 0.00

3.2. Comparison of TCM syndrome scores before and after treatment between the two groups

Before treatment, there was no statistically significant difference in TCM syndrome scores between the two groups (*P* > 0.05). After treatment, the TCM syndrome score in the observation group was significantly lower than that in the control group (*P* < 0.001). Both groups showed a significant decrease in TCM syndrome scores after treatment compared to before treatment (*P* < 0.001) (see **Table 2**).

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

Group	Cases	Before treatment	After treatment	<i>t</i>	<i>P</i>
Observation group	35	8.89±2.38	2.52±1.16	10.32	0.00
Control group	35	8.94±2.14	6.28±1.42	3.72	0.00
<i>t</i>	-	0.09	12.13	-	-
<i>P</i>	-	0.23	0.00	-	-

3.3. Comparison of quality of life scores

Before treatment, there was no statistically significant difference in the quality of life scores between the two groups (*P* > 0.05). After treatment, the quality of life score in the observation group was significantly higher than that in the control group (*P* < 0.001). Both groups showed a significant increase in quality of life scores after treatment compared to before treatment (*P* < 0.001) (see **Table 3**).

Table 3. Comparison of quality of life scores before treatment between the two groups ($\bar{x} \pm s$, points)

Group	Cases	Before treatment	After treatment	<i>t</i>	<i>P</i>
Observation group	35	36.58±6.47	70.37±6.78	54.77	0.00
Control group	35	35.84±6.72	54.21±7.22	25.69	0.00
<i>t</i>	-	0.47	9.65	-	-
<i>P</i>	-	2.35	0.00	-	-

3.4. Comparison of treatment efficacy rates

When comparing the clinical efficacy rates after treatment between the two groups, the observation group had an overall efficacy rate of 94.29%, which was significantly higher than the 77.14% in the control group, with a statistically significant difference (*P* < 0.05) (**Table 4**).

Table 4. Comparison of clinical efficacy between the two groups n(%)

Group	Cases	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Observation group	35	13(37.14)	11(53.33)	9(13.33)	2(10.00)	33(94.29) [#]
Control group	35	3(10.00)	14(43.33)	10(23.33)	8(23.33)	27(77.14)

Note: Compared with the same group before treatment, [#] $P<0.05$.

4. Discussion

Periarthritis of the shoulder is a condition characterized by inflammation, fibrosis, and adhesions of the tissues surrounding the shoulder joint, often leading to shoulder pain and limited range of motion. The etiology of periarthritis of the shoulder includes chronic inflammation and injury to the soft tissues around the shoulder joint, such as tendons, ligaments, and bursae. Conventional Western medical treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, physical therapy, and surgical interventions. Pharmacological treatments in Western medicine primarily aim to alleviate symptoms through anti-inflammatory and analgesic effects but do not address the underlying cause fundamentally. Long-term use may lead to side effects such as gastrointestinal discomfort and renal impairment. Physical therapy requires long-term patient cooperation and has slow therapeutic effects. Surgical treatment, although capable of directly releasing adhesions, is invasive, has a slow recovery process, is not suitable for all patients, and may result in postoperative complications ^[10]. Traditional Chinese medicine (TCM) attributes periarthritis of the shoulder to the invasion of wind, cold, and dampness pathogens, leading to impaired qi and blood circulation and obstruction of meridians. The wind-cold-dampness type of periarthritis of the shoulder is one of the most common types, characterized by shoulder pain, aversion to cold, and limited range of motion. Due to its complex pathogenesis and long disease course, treatment poses certain challenges ^[11]. The theoretical basis for TCM treatment of this condition includes dispelling wind and cold, promoting blood circulation and unblocking meridians, and warming the meridians to expel cold. Common treatment methods include acupuncture, tuina (Chinese therapeutic massage), and herbal medicine. The advantages of TCM treatment lie in fewer side effects, gentle methods, and higher patient compliance, making it particularly suitable for conservative treatment of degenerative joint diseases ^[12].

Electroacupuncture (EA) is an effective method for treating periarthritis of the shoulder. Its principle involves stimulating acupoints with needles and supplementing with low-frequency electrical current to enhance the acupuncture effect, achieving the goals of unblocking meridians, promoting blood circulation to remove blood stasis, and relieving pain. Previous studies have shown that EA treatment has significant effects in alleviating symptoms of periarthritis of the shoulder, reducing patient pain, and improving function. However, EA treatment is often applied without subtype differentiation and does not fully consider individual patient differences and the specificity of TCM subtypes ^[13]. The moving cupping with moxibustion combines the dual therapeutic effects of cupping and moxibustion. It uses negative pressure to adhere to the skin and utilizes the warm stimulation of moxibustion to achieve the effects of warming the meridians to expel cold and promoting qi and blood circulation. Previous applications in treating orthopedic diseases such as knee osteoarthritis have demonstrated good therapeutic effects, relieving joint pain and improving joint function ^[14]. Its mechanism of action based on TCM theory indicates that the moving cupping with moxibustion is of great significance in treating the wind-cold-dampness type of periarthritis of the shoulder, as it can more specifically remove cold and dampness and warm the meridians to unblock them.

The results of this study show that the combination of moving cupping with moxibustion and EA for

treating the wind-cold-dampness type of periarthritis of the shoulder has significant advantages in improving various clinical indicators and overall therapeutic effects. From a Western medicine perspective, the Visual Analog Scale (VAS) score in the observation group was significantly lower than that in the control group, indicating that the combination treatment was more effective in relieving shoulder pain. EA activates the nervous system through electrical stimulation, releasing endogenous analgesic substances, thereby effectively reducing pain ^[15]. The moving cupping with moxibustion combines thermotherapy and negative pressure effects to further promote local blood circulation, reduce inflammatory responses and tissue edema, and enhance analgesic effects. The Constant-Murley score in the observation group was significantly higher than that in the control group, indicating that the combination treatment was more effective in improving shoulder joint function. EA regulates neuromuscular function and enhances muscle strength and joint stability by stimulating acupoints ^[16]. The thermotherapy effect of the moving cupping with moxibustion not only relaxes muscles but also softens adhesive tissues, increasing joint range of motion and thereby improving overall shoulder joint function. The relief of pain and recovery of joint function directly improve patients' daily living abilities and reduce the impact on their lives, significantly enhancing their quality of life. TCM believes that the wind-cold-dampness type of periarthritis of the shoulder is caused by the invasion of wind, cold, and dampness pathogens into the human body, leading to obstruction of meridians and impaired qi and blood circulation. The Huangdi Neijing (The Inner Canon of Huangdi) states, "When wind, cold, and dampness pathogens combine, they cause bi syndrome (painful obstruction syndrome)". EA unblocks meridians and harmonizes qi and blood by stimulating acupoints, while the moving cupping with moxibustion exerts its effects of dispelling wind and cold and promoting blood circulation to unblock meridians through thermotherapy, fundamentally addressing the cause and achieving analgesic effects. The Huangdi Neijing also says, "Meridians are what determine life and death, manage various diseases, regulate deficiency and excess, and must not be obstructed". The moving cupping with moxibustion adds mechanical stimulation from cup moving on the basis of moxibustion, which can more deeply activate the circulation of qi and blood in the meridians, improve blood supply and metabolism in local tissues, and thereby promote the recovery of joint function ^[17]. TCM emphasizes "treating the root cause of the disease". In this study, EA regulates visceral function and balances yin and yang by stimulating relevant acupoints, enhancing the overall therapeutic effect. The moving cupping with moxibustion unblocks meridians, dispels wind and cold, and improves symptoms of wind-cold-dampness pathogens through thermotherapy and negative pressure effects. Ultimately, the combination treatment of the moving cupping with moxibustion and EA not only treats shoulder conditions locally but also regulates the overall circulation of qi and blood in the body, improving patients' overall health and achieving a holistic therapeutic effect.

5. Conclusion

In conclusion, the combination of moving cupping with moxibustion and EA for treating the wind-cold-dampness type of periarthritis of the shoulder has significant effects in relieving pain, improving shoulder joint function, enhancing quality of life, and alleviating TCM symptoms, with a high treatment effectiveness rate. This study provides a scientific basis for the clinical application of this treatment method and has important value for clinical promotion.

Disclosure statement

The authors declare no conflict of interest.

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Theoretical Reconstruction and Clinical Value Analysis of the Traditional Chinese Medicine Concept of “Nurturing Instead of Treating” in Orthopedic Rehabilitation

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Abstract: *Objective:* Focusing on the scenario of holistic rehabilitation management for bone injuries, this study aims to explore the practical application value of the Traditional Chinese Medicine (TCM) concept of “nourishment instead of treatment” and to investigate the implementation pathways for integrating traditional TCM therapies with modern rehabilitation techniques. *Methods:* By integrating historical TCM literature on bone injuries and combining it with practical clinical experience accumulated from daily diagnosis and treatment, this study outlines the intervention logic of this nourishment approach during different healing stages of fractures. It also conducts a multidisciplinary comparative analysis based on existing modern research findings in Enhanced Recovery After Surgery (ERAS) and bone tissue engineering. *Results:* A comprehensive review of ancient texts and clinical case observations reveals that “nourishment instead of treatment” does not simply entail passive rest and immobilization but rather represents an active rehabilitation model that synergistically combines the regulation of qi and blood, tonification of the liver and kidneys, and emotional counseling. This model can stimulate the body's self-healing capacity, reduce the incidence of postoperative complications, and improve long-term limb mobility in patients, aligning closely with modern holistic medical approaches. *Conclusion:* As a practical extension of the “preventive treatment of disease” theory in the field of bone injuries, this concept provides a reference for constructing integrated TCM-Western medicine rehabilitation protocols for bone injuries. It holds significant practical value for both clinical promotion and subsequent evidence-based medical research.

Keywords: Nourishment instead of treatment; Bone injury; TCM bone injury; Fracture healing; Rehabilitation protocol; Clinical application

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1. Introduction

Fractures, soft tissue injuries, and various degenerative bone disorders are commonly encountered in orthopedic outpatient settings. Clinical management of these injuries should not be limited to the anatomical reduction of bone structures but should also prioritize the restoration of long-term limb mobility. TCM bone injury treatment has traditionally emphasized the simultaneous regulation of tendons and bones; however, rehabilitation approaches centered on “nourishment instead of treatment” are often overlooked in daily clinical practice. This approach, derived from the TCM preventive concept of “preventive treatment of disease”, focuses on promoting the gradual repair of various injuries by fortifying the body’s vital energy. This article transcends the conventional focus on isolated symptomatic treatments by first tracing the theoretical development of this concept, then discussing stage-specific differential nourishment strategies for fractures, and finally analyzing its mechanisms of action in light of modern medical research. This approach aims to elucidate the auxiliary value of nourishment strategies in clinical treatment and provide a reference for developing more comprehensive rehabilitation intervention protocols for bone injury patients.

2. Theoretical origins and connotative reconstruction

2.1. Historical evolution

The TCM preventive medicine system serves as the theoretical foundation for the concept of “nourishment instead of treatment”. The Huangdi Neijing (The Yellow Emperor’s Classic of Internal Medicine) states, “The sage does not treat already manifested diseases but prevents diseases before they occur”, thereby establishing a diagnostic and therapeutic approach that prioritizes nourishment ^[1]. During the Tang Dynasty, Sun Simiao compiled the *Bei Ji Qian Jin Yao Fang* (Essential Formulas for Emergencies Worth a Thousand Gold Pieces), emphasizing the importance of health preservation and disease prevention in clinical practice ^[2]. Focusing on the specialty of bone injuries, Wei Yilin of the Yuan Dynasty mentioned in his *Shiyi De Xiaofang* (Effective Formulas from a Family of Imperial Physicians) that after fracture reduction, external fixation, internal and external medication, and daily care should all be given equal attention ^[3]. Hu Tingguang of the Qing Dynasty authored the *Shangke Huizuan* (Compendium of Traumatology), proposing that “injuries from falls and blows should be addressed primarily from the perspective of blood”, highlighting blood and qi regulation as the core elements promoting injury recovery ^[4].

2.2. Core mechanisms

Based on practical diagnostic and therapeutic experience in frontline bone injury treatment, this nourishment concept operates through three distinct levels of organismal regulation. Nourishment of qi and blood provides the foundation for fracture repair. Fracture healing inherently involves the dissipation of turbid blood stasis and the gradual formation of new bone tissue. The *Lingshu* (Spiritual Pivot) states that “bones govern flexion and extension”, indicating that both bone activity function and callus growth and differentiation require a continuous supply of nourishment from qi and blood. Optimizing qi and blood circulation in the injured area can enhance local blood supply, providing sufficient material support for callus formation.

From the perspective of the zang-fu organs, TCM holds that “the liver governs tendons” and “the kidneys govern bones”. Once liver and kidney essence and qi become deficient, the repair process of tendons and bones is impeded. Implementing interventions to tonify the liver and kidneys in patients during the recovery phase can not only accelerate injury repair but also prevent disuse-related osteoporosis caused by

prolonged limb immobilization.

Negative emotions such as fear and anxiety resulting from trauma can also interfere with the rehabilitation process. Such stress states tend to disrupt the body's qi movement patterns. Timely emotional counseling in clinical settings to calm the patient's mind and ensure smooth qi and blood circulation throughout the body represents an indispensable psychosomatic intervention for promoting injury recovery.

3. Stage-specific intervention strategies

3.1. Acute phase (1–2 weeks post-injury): Dissipate blood stasis, protect vital energy, and regulate qi and blood

The first 1 to 2 weeks post-injury constitute the acute phase of injury, with qi stagnation and blood stasis representing the core pathological mechanisms. Swelling and pain at the affected site are typical symptoms. Clinical treatment focuses on dredging stagnation while also attending to the protection of the body's vital energy. External fixation of the affected limb is commonly achieved using plaster casts or small splints, with the tightness of fixation adjusted flexibly during the procedure to prevent compression of soft tissues and blood vessels, which could impede local blood circulation. Daily care can incorporate positional adjustments, such as suspending the upper limb and elevating the lower limb, to rely on gravity to accelerate venous return and effectively alleviate local congestion and swelling. For internal medication, formulas that promote blood circulation, such as Taohong Siwu Decoction, are often used as a base, supplemented by astragalus and atractylodes to fortify the spleen and replenish qi, thereby stabilizing spleen and stomach transportation and transformation functions, avoiding the depletion of vital energy by blood-activating drugs, and ensuring the continuous generation of qi and blood. Fear and anxiety resulting from trauma can easily disrupt qi movement, hindering the dissipation of blood stasis. Therefore, timely psychological counseling in clinical settings is necessary to regulate qi movement throughout the body and accelerate the resolution of swelling and pain.

3.2. Recovery phase (3–8 weeks post-injury): Tonify the spleen and kidneys, regenerate tendons, and grow bone

From 3 to 8 weeks post-injury, the fracture enters the recovery phase. Blood stasis in the body gradually dissipates, and callus formation enters a stage of rapid proliferation. Patients often exhibit syndromes of qi and blood deficiency and insufficient liver and kidney essence and qi. At this stage, pharmacological treatment and daily care should be implemented simultaneously. According to the TCM theory that “the spleen governs muscles” and “the kidneys govern bones”, dietary therapy can be used as an adjunct to recovery. Dipsaci Radix Pork Bone Soup can replenish the kidneys and fill the marrow, reconnecting damaged tendons and bones, while Astragali Radix and Angelicae Sinensis Radix Stewed Chicken can replenish qi and nourish blood, providing sufficient nutritional support for bone tissue repair. Rehabilitation training adheres to the traditional principle of combining activity with rest. Patients are guided to move unfixed joints and perform isometric muscle contraction exercises of the affected limb. Quadriceps femoris isometric training is commonly used for intervention, relying on the muscle pump to improve local blood circulation and prevent muscle atrophy, joint adhesion, and lower limb thrombosis. For internal medication, the main therapeutic principles are reconnecting tendons, mending bones, and replenishing liver and kidney qi and blood. Formulas such as Xugu Huoxue Decoction and Zhuangjin Yangxue Decoction are selected and

modified according to the specific condition. Clinically observed bone injury herbs such as *Dipsaci Radix*, *Pyritum*, and *Dipsaci Asperoides* Oken can enhance osteoblast activity and accelerate callus remodeling^[5].

3.3. Sequelae phase (beyond 8 weeks post-injury): Strengthen the foundation, dredge meridians, and prevent recurrence

Even after radiographic evidence of fracture healing, most patients still experience residual symptoms such as joint stiffness, limb weakness, and aches and pains on rainy days. The root pathological mechanisms are often deficiency of liver and kidney essence and obstruction of meridians due to blood stasis. At this stage, rehabilitation focuses on strengthening the foundation and regulating nourishment while dredging meridians, aiming to improve sequelae and reduce the risk of recurrent chronic injuries. Traditional guiding exercises can be used as an adjunct to rehabilitation training. Individualized exercise programs are developed based on the patient's age and injury site, using exercises such as Taijiquan and Baduanjin to regulate qi and blood throughout the body, combined with specialized exercises such as joint mobility training, muscle strength training, and proprioceptive repair to gradually restore normal limb mobility. Concurrently, external therapies such as acupuncture, tuina, and moxibustion are employed, with acupoints such as Zusanli (ST36), Yanglingquan (GB34), Xuanzhong (GB39), and Ashi points at the affected site selected for meridian intervention. These methods effectively release soft tissue adhesions, dredge local blood stasis obstruction, and alleviate sequelae such as limb soreness and stiffness^[6]. Daily rehabilitation guidance should adhere to the principles of seasonal health preservation, instructing patients to avoid strenuous activities involving the affected limb during the recovery period, ensure proper limb warmth and protection, and prevent the invasion of cold and damp pathogens into the tendons and bones, thereby preventing recurrent pain from chronic injuries.

4. Explanation of modern medical value

4.1. Alignment with the ERAS concept in enhanced recovery after surgery

The core idea of ERAS is to comprehensively optimize the entire perioperative diagnostic and therapeutic process to mitigate the systemic stress response induced by surgical procedures. This diagnostic and therapeutic logic aligns closely with the TCM rehabilitation concept of “nourishment instead of treatment, with nourishment and treatment working in tandem”. Minimally invasive orthopedic surgeries and precise internal fixation treatments can reduce additional soft tissue damage during surgery, echoing the TCM emphasis on minimizing invasive procedures and focusing on organismal regulation. The ERAS concept advocates for early postoperative ambulation and the development of individualized nutritional plans based on the patient's condition, corresponding to the TCM approach of combining activity with rest and using dietary therapy to support vital energy. These strategies can effectively shorten the patient's overall rehabilitation cycle.

4.2. Microscopic evidence from bone tissue engineering

Modern bone tissue engineering relies on seed cells and various growth factors to activate the bone's inherent repair potential, sharing a core logic with TCM's reliance on the body's vital energy to achieve spontaneous healing of trauma. Existing pharmacological experimental data demonstrate that TCM herbs with kidney-tonifying effects, such as *Eucommiae Cortex* and *Dipsaci Asperoides* Oken, can regulate the differentiation

of bone marrow mesenchymal stem cells into osteoblasts, providing molecular and microscopic evidence for the objective scientific basis of the TCM theory of “tonifying the kidneys to generate bone” [7].

4.3. Guidance for the diagnosis and treatment of geriatric osteoporotic fractures

Elderly patients with fractures often have multiple underlying conditions such as hypertension, diabetes, and osteoporosis, with deficient vital energy, weak surgical tolerance, and a significantly higher risk of postoperative complications and secondary fractures. The “nourishment instead of treatment” model can be applied throughout the entire diagnostic and treatment process, implementing stratified nourishment interventions: preoperative TCM herbal conditioning and dietary supplementation can improve low protein levels and anemia, stabilize the management of underlying chronic diseases, and enhance the patient’s surgical tolerance; postoperative staged interventions to replenish qi and blood and dredge meridians throughout the body can provide early prevention of complications such as infection, pressure ulcers, and deep vein thrombosis of the lower limbs, while long-term administration of liver and kidney tonification methods can increase bone density and reduce the probability of recurrent fractures from the root cause.

5. Discussion and prospects

5.1. Scope of application and limitations

This phased convalescence regimen is particularly well-suited for stable closed fractures, post-fracture functional recovery, primary osteoporosis, osteoarthritis, and various chronic soft tissue injuries, offering significant advantages in improving limb mobility and alleviating discomfort caused by long-term strain. However, it also has clear boundaries of application. For severe open fractures, multiple comminuted fractures, or critical cases complicated by vascular or nerve injuries and traumatic infections, clinical priority should be given to Western medical emergency measures such as debridement surgery, internal fixation, and anti-infection treatment, rather than relying solely on convalescence methods to avoid delaying the emergency process.

5.2. Dynamic balance between convalescence and treatment

“Convalescence instead of treatment” does not entirely replace clinical treatment. Its core idea is to dynamically adjust the priority between convalescence and pharmacological or surgical treatment based on different stages of fracture progression, while formulating individualized convalescence plans throughout the process following a dialectical approach. During the acute phase of injury, blood stasis is the primary issue, with treatment focusing on removing blood stasis and reducing swelling, supplemented by moderate convalescence to protect vital energy. As the recovery phase progresses, qi and blood in the body gradually recover, and callus continues to grow, requiring simultaneous attention to pharmacological treatment and bodily convalescence. In the sequelae phase, patients often suffer from deficiency of vital energy and prolonged stagnation of meridians, shifting the focus of treatment to consolidating the foundation and convalescence, with only localized symptomatic treatment, thus achieving refined intervention throughout the entire course of bone injury.

5.3. Future research directions

The current “convalescence instead of treatment” intervention model implemented clinically is mostly

based on long-term clinical experience summarization, with a relative lack of in-depth understanding of its underlying mechanisms and large-sample evidence-based medical evidence. Subsequent research can be conducted from three dimensions. First, quantitative evaluation can be achieved through CT, MRI imaging examinations, and biomechanical testing techniques to visually quantify the improvement effects of various traditional Chinese medicine convalescence methods on the fracture healing process. Second, multi-center randomized controlled clinical trials can be designed to systematically verify the actual clinical efficacy and application safety of this phased convalescence regimen ^[5]. Third, basic experiments can be conducted around classic osteogenic signaling pathways such as Wnt/ β -catenin and BMP/Smad to dissect the molecular mechanisms by which blood-activating and kidney-tonifying traditional Chinese herbs promote bone repair ^[7].

6. Conclusion

“Convalescence instead of treatment” is a distinctive core theory formed through the inheritance and development of traditional Chinese medicine for bone injuries, significantly differing from the singular symptomatic treatment model. This theory focuses on regulating qi and blood throughout the body, nourishing liver and kidney essence, and harmonizing emotional qi, relying on the holistic view of traditional Chinese medicine to consolidate the foundation and cultivate vital energy, fully mobilizing the body’s own trauma repair capabilities. It combines the advantages of traditional Chinese medicine convalescence and Western medical diagnosis and treatment in accelerating injury healing, reducing various complications, and improving patients’ long-term recovery outcomes. The internal logic of this theory highly aligns with modern medical research directions such as enhanced recovery after surgery and bone tissue engineering, possessing broad prospects for clinical application and promotion. Subsequent efforts should continue to promote multidisciplinary cross-exploration, continuously supplement molecular mechanism and large-sample evidence-based medical evidence, facilitate the deep integration of the “convalescence instead of treatment” concept with modern orthopedic diagnosis and treatment technologies, establish a new bone injury diagnosis and treatment system that combines convalescence and treatment and integrates traditional Chinese and Western medicine, and provide long-lasting and personalized diagnosis, treatment, and convalescence services for bone injury patients.

Disclosure statement

The authors declare no conflict of interest.

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Global, Regional and National Burdens of Gout in People Aged 20 - 54 Years from 1990 to 2021: An Analysis Based on the 2021 Global Burden of Disease Study

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Abstract: *Objective:* To describe the epidemiology of gout in people aged 20 - 54 years at global, regional, and national levels using data from the 2021 GBD study, and evaluate the impact of BMI and renal dysfunction on the burden of gout in this age group. *Methods:* Incidence, prevalence, and DALYs of gout were extracted from GBD 2021. Descriptive analysis was performed at global, regional, and national levels. Trends were analyzed using estimated annual percentage change (EAPC) and joinpoint regression analysis. Proportional attributable fractions of risk factors (high BMI and impaired kidney function) were calculated. *Results:* Globally, from 1990 to 2021, the rates of incidence, prevalence, and DALYs of gout in people aged 20 - 54 years increased. Regionally, the United States, China, and East Asia had significant increases. By SDI quintiles, the highest increases in prevalence and DALYs were in the High SDI quintile, and in incidence in the High-middle SDI quintile. Males had higher values than females. The fastest increasing periods for incidence (1996 - 2004), prevalence (1996 - 2004), and DALYs (1996 - 2003) were identified. Globally in 2021, high BMI and impaired kidney function accounted for certain proportions of DALYs, with regional and national variations. *Conclusion:* The burden of gout in people aged 20 - 54 years has increased significantly worldwide, with differences across various factors. Prevention strategies, improved management, and further research on gout in this age group are crucial, especially regarding its relationship with high BMI and impaired renal function.

Keywords: Gout; GBD 2021; High BMI; Impaired kidney function

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1. Introduction

Gout is the most common inflammatory arthritis, which manifests as an acute attack of one or more joints with pain, swelling, redness, and fever, leading to decreased mobility and impaired physical function, and

progressing to chronic destructive arthritis ^[1-2]. Chronic gout leads to tophi formation, chronic joint pain, and joint erosion and damage. It is a common cause of activity limitation in adults, resulting in increased morbidity and disability-adjusted life years (DALYs) ^[3-5]. Recent studies have used prevalence, incidence and disability-adjusted life years (YLDs) data from the 2021 Global Burden of Disease Study to assess the burden of gout in individuals aged ≥ 55 years in 204 countries and its changing trends from 1990 to 2021 at global, regional and country levels ^[6]. Previous studies have also used data from the 2019 Global Burden of Disease (GBD) study to report global, regional and national annual incidence, point prevalence and disability-adjusted life years (YLD) rates and trends for gout among adolescents and young adults aged 15-39 years ^[7]. The burden of gout varies among different populations, and quantifying the burden and patterns of gout cases by age and sex, and making future projections, is necessary to effectively meet the needs of the current and future populations ^[8]. To our knowledge, there are no detailed GBD studies examining the global burden and trends of gout in people aged 20-54 years.

The aim of this study was to conduct a descriptive and trend analysis of the prevalence, incidence and disability-adjusted life years (DALYs) epidemiology of gout at global, regional and country levels using data from the 2021 GBD study. The impact of body mass index (BMI) and renal dysfunction as risk factors on the burden of gout in people aged 20-54 years was also evaluated.

2. Methods

2.1. Data source

GBD 2021 used the latest available epidemiological data and improved standardized methods to comprehensively assess the health loss across 288 causes of death, 371 diseases and injuries, and 88 risk factors in 204 countries and territories, including subnational estimates for 21 countries and territories and years from 1990 to 2021.

In this study, the estimates and their 95 % uncertainty intervals (UIs) for incidence, prevalence, and disability-adjusted life-years (DALYs) of Gout were extracted from GBD 2021. All rates were reported per 100,000 population. Developed by GBD researchers and used to help produce these estimates, the Socio-demographic Index (SDI) is a composite indicator of development status strongly correlated with health outcomes. It is the geometric mean of 0 to 1 indices of total fertility rate under the age of 25 (TFU25), mean education for those ages 15 and older (EDU15+), and lag distributed income (LDI) per capita. As a composite, a location with an SDI of 0 would have a theoretical minimum level of development relevant to health, while a location with an SDI of 1 would have a theoretical maximum level. the sociodemographic index (SDI) is divided into five levels (Low SDI, Low-middle SDI, Middle SDI, High-middle SDI, and High SDI).

2.2. Descriptive analysis

To derive a comprehensive understanding in the burden of Gout, a descriptive analysis was performed at global, regional, and national levels. The global case number, and rate of incidence, prevalence, and DALYs for Gout in both sexes, males, and females from 1990 to 2021 were visually illustrated. Moreover, the case number and ASR of incidence, prevalence, and DALYs for Gout in both sexes in 1990 and 2021 were compared at global, regional (21 GBD geographical regions), and national (204 countries and territories, including subnational estimates for 21 countries and territories) levels, as well as five levels (Low SDI, Low-

middle SDI, Middle SDI, High-middle SDI, and High SDI).

2.3. Trend analysis

Exploring the temporal trends of diseases serves as an indispensable part of epidemiology and further facilitates the development of more precise preventive strategies. We aimed to explore the trends of Gout from the overall, local, and multi-dimension scopes.

Firstly, we used estimated annual percentage change (EAPC) to quantify the overall trend of Gout burden. It is necessary to implement standardization when comparing several groups with distinct age structures or one certain group with age profile changing over time. Therefore, the trend of ASR, which is measured by EAPC, appears to be a more robust index for monitoring the changes of disease pattern.

We used the estimated annual percentage change (EAPC) to quantify trends in Gout burden from 1990 to 2021. A linear regression model was established to describe the relationship between time and the natural logarithm (ln) of the age standardized rate: $y = \alpha + \beta x + e$, where y represents the ln (age-standardised rate), x is the calendar year, and e is the error term. The EAPC was calculated using $EAPC = 100 \times [\exp(\beta) - 1]$, with its 95% confidence interval (CI) derived from the regression model. An age standardized rate is deemed statistically increasing if both the EAPC estimate and its 95% CI are greater than 0, and statistically decreasing if both are less than 0. If the EAPC estimate and its 95% CI include 0, the trend in the age-standardised rate is considered stable, indicating no significant change over time ^[9].

Then, we used joinpoint regression analysis to detect the local trend of Gout burden. Joinpoint regression analysis (Joinpoint Trend Analysis Software, Version 5.3.0 November 12, 2024) could divide the overall trend into multiple subsegments according to the inflection points and further evaluate the magnitude of each epidemiological trend by calculating the annual percentage change (APC) and its 95 % CI of each subsegment. Moreover, the average APC (AAPC) between 1990 and 1999, between 2000 and 2009, and between 2010 and 2021 were also estimated by weighting the regression coefficient of each subsegment by the span width of segmented interval ^[10]. Monte Carlo permutation method ^[11] with 4499 randomly permuted data set was utilized to calculate the AAPC and its 95 % CI, and the overall asymptotic significance level was maintained through a Bonferroni correction. If the APC/AAPC estimation and its lower boundary of 95 % CI were both > 0 , an increasing trend was deemed during one certain period. On the contrary, if the APC/AAPC estimation and its upper boundary of 95 % CI were both < 0 , a decreasing trend was deemed during one certain period. Otherwise, the trend was deemed to be stable. In GBD 2021, high body-mass index (BMI), and impaired kidney function were identified as risk factors associated with the onset of gout, which remained leading contributors to risk-attributable DALYs, were stratified by Socio-demographic Index (SDI). High BMI was defined as the BMI of individuals aged ≥ 20 years ≥ 25 kg/m².

3. Results

3.1. Descriptive analysis of Gout burden in aged 20-54 years at global, regional, and national levels using broad estimation method

Globally, the Rate of incidence, prevalence and DALYs of Gout for both sexes by aged 20-54 years elevated by an average of 1.11 (1.06, 1.16), 0.92 (0.88, 0.95) and 1.1 (1.05, 1.15) per year from 1990 to 2021, respectively. From a regional dimension, when it comes to the increases in the rates of incidence, prevalence and DALYs, the United States of America stands out as the region where the increases are the

most significant. Close behind are China and the East Asian region. In addition, from the scope of SDI quintiles, the largest increases in Rate of prevalence, and DALYs were detected in High SDI quintile, the largest increases in Rate of incidence was detected in High-middle SDI quintile. (**Table 1**, **Table 2**, **Table 3**). Nationally, the overall trends of disease burden varied considerably across all locations with the highest EAPC of incidence, prevalence and DALYs found in United States of America and the lowest EAPC of incidence, prevalence, and DALYs across countries and territories found in Niger.

Globally, the Number and Rate of incidence, prevalence and DALYs demonstrated dramatically increasing trends of these three metrics showed increasing trends from 1990 to 2021, with much higher values in males than in females (**Figure 1**). Nationally, the incidence, prevalence and DALYs of Gout varied remarkably across the world, with the highest number of incidence, prevalence, and DALYs cases found in China, and the highest Rate of incidence, prevalence, and DALYs found in the United States of America (**Figure 2**).

Table 1. The Number and Rate of incidence of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	3877062 (2758101, 5197993)	1930628 (1390664, 2574605)	102.85 (73.17, 137.9)	80.32 (57.86, 107.11)	0.92 (0.88, 0.95)
China	1218448 (855836, 1641884)	636826 (460132, 845644)	171.74 (120.63, 231.42)	108.32 (78.27, 143.84)	1.72 (1.62, 1.81)
United States of America	335593 (247513, 436702)	170545 (123751, 228528)	222.12 (163.83, 289.05)	133.67 (96.99, 179.12)	1.88 (1.73, 2.03)
Low-middle SDI	632473 (452251, 842685)	273555 (196296, 365253)	69.07 (49.39, 92.03)	58.25 (41.8, 77.78)	0.59 (0.55, 0.62)
High-middle SDI	868593 (605411, 1170160)	465026 (336823, 620201)	132.81 (92.57, 178.93)	89.28 (64.67, 119.08)	1.42 (1.37, 1.47)
Middle SDI	1331279 (944162, 1787476)	625721 (450156, 827739)	108.28 (76.79, 145.38)	79.73 (57.36, 105.47)	1.17 (1.11, 1.22)
Low SDI	261837 (187749, 351022)	100564 (72157, 135068)	58.04 (41.62, 77.81)	54.53 (39.13, 73.24)	0.24 (0.19, 0.29)
High SDI	780504 (565838, 1036657)	464434 (334472, 622171)	151.17 (109.59, 200.78)	105.14 (75.72, 140.84)	1.23 (1.16, 1.3)
Andean Latin America	17989 (12797, 24089)	5954 (4292, 7950)	55.26 (39.31, 74)	37.97 (27.37, 50.7)	1.3 (1.26, 1.33)
Australasia	25176 (18093, 34327)	12638 (9257, 16926)	172.61 (124.05, 235.35)	125.58 (91.98, 168.19)	0.93 (0.83, 1.03)
Caribbean	11364 (8068, 15399)	5624 (3992, 7579)	49.54 (35.17, 67.13)	35.41 (25.13, 47.72)	1.15 (1.1, 1.2)
Central Asia	34924 (24915, 46923)	16894 (12199, 22133)	74.89 (53.43, 100.62)	56.82 (41.03, 74.44)	1.03 (0.96, 1.09)
Central Europe	40118 (27843, 54608)	32952 (23461, 44548)	73.37 (50.92, 99.87)	55.56 (39.56, 75.12)	0.8 (0.76, 0.84)
Central Latin America	51498 (36444, 69415)	19928 (14478, 26802)	41.21 (29.17, 55.55)	29.22 (21.23, 39.29)	1.17 (1.15, 1.19)
Central Sub-Saharan Africa	32279 (22908, 43032)	10796 (7711, 14486)	59.4 (42.15, 79.18)	53.41 (38.15, 71.66)	0.36 (0.34, 0.39)
East Asia	1265287 (890899, 1704469)	663324 (479453, 880426)	171.98 (121.09, 231.68)	109.04 (78.81, 144.72)	1.69 (1.6, 1.78)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Eastern Sub-Saharan Africa	98969 (70649, 132713)	35857 (25770, 48015)	57.72 (41.2, 77.39)	52.92 (38.03, 70.86)	0.32 (0.25, 0.38)
High-income Asia Pacific	111507 (77963, 150792)	93239 (66115, 126814)	132.5 (92.64, 179.19)	105.85 (75.06, 143.97)	0.72 (0.67, 0.76)
North Africa and Middle East	262354 (185918, 354169)	81012 (58308, 108187)	84.56 (59.92, 114.15)	60.39 (43.46, 80.64)	1.09 (1.04, 1.14)
Oceania	6889 (4934, 9214)	2588 (1884, 3442)	109.23 (78.23, 146.1)	95.77 (69.73, 127.38)	0.41 (0.4, 0.43)
South Asia	599907 (427678, 802171)	258747 (184479, 348227)	65.58 (46.75, 87.69)	56.74 (40.45, 76.36)	0.49 (0.46, 0.51)
Southeast Asia	423581 (303107, 565832)	169622 (122367, 225545)	119.49 (85.51, 159.62)	83.45 (60.2, 110.96)	1.29 (1.25, 1.33)
Southern Latin America	43704 (31696, 58606)	22721 (16408, 30346)	130.58 (94.7, 175.11)	102.18 (73.79, 136.46)	0.72 (0.67, 0.76)
Southern Sub-Saharan Africa	32868 (23577, 44342)	14405 (10409, 19126)	83.63 (59.99, 112.82)	66.9 (48.34, 88.82)	0.67 (0.61, 0.72)
Tropical Latin America	60850 (43032, 83365)	24168 (17171, 32713)	52.17 (36.89, 71.47)	35.46 (25.2, 48)	1.28 (1.25, 1.31)
Western Europe	189782 (135048, 255727)	149375 (105223, 201130)	96.56 (68.71, 130.11)	79.05 (55.69, 106.44)	0.71 (0.65, 0.76)
Western Sub-Saharan Africa	113252 (81233, 151777)	41206 (29544, 54922)	59.89 (42.96, 80.26)	57.85 (41.48, 77.11)	0.11 (0.09, 0.13)

Table 2. The Number and Rate of Prevalence of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	19221517 (13705460, 25371091)	9120289 (6521824, 12216297)	509.92 (363.59, 673.06)	379.44 (271.33, 508.25)	1.11 (1.06, 1.16)
China	5931952 (4177272, 7868531)	2899204 (2075500, 3853742)	836.09 (588.77, 1109.05)	493.15 (353.04, 655.51)	1.98 (1.88, 2.09)
United States of America	2336377 (1752051, 3000584)	996181 (719723, 1351202)	1546.42 (1159.66, 1986.05)	780.79 (564.1, 1059.04)	2.56 (2.37, 2.76)
Low-middle SDI	2810521 (1993372, 3793537)	1197835 (854074, 1622846)	306.95 (217.7, 414.3)	255.08 (181.88, 345.59)	0.65 (0.61, 0.68)
High-middle SDI	4251812 (2993876, 5647044)	2155699 (1541292, 2857558)	650.13 (457.79, 863.47)	413.89 (295.92, 548.64)	1.62 (1.56, 1.69)
Middle SDI	6277279 (4455095, 8357876)	2811512 (2012811, 3773148)	510.56 (362.35, 679.78)	358.25 (256.48, 480.78)	1.37 (1.3, 1.43)
Low SDI	1127468 (805385, 1531040)	433701 (310316, 590883)	249.93 (178.53, 339.39)	235.18 (168.27, 320.41)	0.24 (0.19, 0.29)
High SDI	4743293 (3468645, 6280731)	2515487 (1802383, 3421372)	918.69 (671.81, 1216.46)	569.44 (408.01, 774.5)	1.68 (1.57, 1.8)
Andean Latin America	84734 (60334, 114495)	27172 (19113, 37542)	260.29 (185.34, 351.72)	173.28 (121.89, 239.41)	1.41 (1.37, 1.46)
Australasia	142642 (100415, 195415)	66830 (48247, 88365)	977.98 (688.46, 1339.8)	664.08 (479.42, 878.06)	1.2 (1.07, 1.33)
Caribbean	54255 (38523, 73762)	25960 (18187, 35661)	236.53 (167.95, 321.57)	163.44 (114.5, 224.51)	1.28 (1.22, 1.35)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Central Asia	158772 (112501, 214399)	74731 (53495, 100948)	340.46 (241.24, 459.74)	251.33 (179.91, 339.5)	1.16 (1.08, 1.24)
Central Europe	183066 (128511, 250062)	147147 (104738, 199023)	334.8 (235.03, 457.33)	248.13 (176.61, 335.6)	0.85 (0.81, 0.9)
Central Latin America	246939 (174539, 339994)	92546 (65769, 127118)	197.63 (139.69, 272.1)	135.68 (96.43, 186.37)	1.25 (1.24, 1.27)
Central Sub-Saharan Africa	139320 (99086, 186301)	46350 (32803, 63743)	256.37 (182.33, 342.82)	229.3 (162.27, 315.34)	0.4 (0.36, 0.43)
East Asia	6176028 (4351221, 8185390)	3027376 (2168016, 4022545)	839.47 (591.44, 1112.6)	497.64 (356.38, 661.23)	1.95 (1.84, 2.06)
Eastern Sub-Saharan Africa	423799 (303935, 580844)	153125 (109887, 208976)	247.15 (177.25, 338.73)	225.98 (162.17, 308.4)	0.32 (0.25, 0.39)
High-income Asia Pacific	603685 (418251, 824249)	477759 (334198, 652590)	717.36 (497.01, 979.45)	542.38 (379.4, 740.86)	0.9 (0.86, 0.95)
North Africa and Middle East	1187839 (844972, 1606479)	354534 (254400, 478614)	382.83 (272.33, 517.76)	264.27 (189.63, 356.76)	1.19 (1.13, 1.26)
Oceania	31480 (22639, 42355)	11583 (8478, 15327)	499.12 (358.94, 671.55)	428.6 (313.73, 567.13)	0.48 (0.47, 0.49)
South Asia	2623251 (1867585, 3558220)	1120630 (795351, 1524285)	286.76 (204.16, 388.97)	245.73 (174.4, 334.24)	0.53 (0.5, 0.55)
Southeast Asia	1966364 (1401354, 2630795)	752270 (536916, 1013725)	554.72 (395.33, 742.16)	370.09 (264.15, 498.72)	1.47 (1.42, 1.51)
Southern Latin America	246592 (176827, 332270)	122223 (86337, 166342)	736.78 (528.34, 992.78)	549.62 (388.25, 748.02)	0.89 (0.82, 0.95)
Southern Sub-Saharan Africa	144400 (103359, 191902)	62105 (43963, 83950)	367.39 (262.97, 488.25)	288.42 (204.17, 389.87)	0.71 (0.65, 0.77)
Tropical Latin America	288193 (204140, 397448)	110497 (77778, 152336)	247.08 (175.02, 340.75)	162.14 (114.13, 223.53)	1.39 (1.36, 1.42)
Western Europe	1079110 (744800, 1478030)	796679 (548775, 1093081)	549.04 (378.95, 752.01)	421.62 (290.43, 578.49)	0.94 (0.88, 1.01)
Western Sub-Saharan Africa	491910 (351958, 666116)	178840 (127544, 241994)	260.12 (186.11, 352.24)	251.08 (179.06, 339.74)	0.12 (0.09, 0.14)

Table 3. The Number and Rate of DALYs of Gout in 1990 and 2021 for both sexes by aged 20-54 years, with Rate EAPC from 1990 to 2021

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
GLOBAL	629303 (386588, 959547)	300043 (186574, 451667)	16.69 (10.26, 25.46)	12.48 (7.76, 18.79)	1.1 (1.05, 1.15)
China	195318 (118227, 300653)	96058 (59672, 146121)	27.53 (16.66, 42.38)	16.34 (10.15, 24.85)	1.96 (1.86, 2.07)
United States of America	74808 (47127, 111523)	32337 (19865, 49071)	49.51 (31.19, 73.82)	25.35 (15.57, 38.46)	2.53 (2.33, 2.73)
Low-middle SDI	92207 (56944, 142624)	39371 (24561, 60194)	10.07 (6.22, 15.58)	8.38 (5.23, 12.82)	0.65 (0.62, 0.69)
High-middle SDI	139671 (83936, 216686)	71074 (44169, 108249)	21.36 (12.83, 33.13)	13.65 (8.48, 20.78)	1.62 (1.55, 1.68)
Middle SDI	206310 (126463, 314454)	92961 (57225, 140854)	16.78 (10.29, 25.58)	11.85 (7.29, 17.95)	1.35 (1.29, 1.41)

location_name	Number_2021	Number_1990	Rate_2021	Rate_1990	EAPC_Rate
Low SDI	37046 (23083, 57143)	14175 (8711, 21798)	8.21 (5.12, 12.67)	7.69 (4.72, 11.82)	0.26 (0.21, 0.32)
High SDI	153703 (96509, 233985)	82263 (51159, 124724)	29.77 (18.69, 45.32)	18.62 (11.58, 28.23)	1.66 (1.54, 1.77)
Andean Latin America	2816 (1674, 4440)	908 (554, 1408)	8.65 (5.14, 13.64)	5.79 (3.53, 8.98)	1.38 (1.33, 1.42)
Australasia	4629 (2723, 7305)	2174 (1338, 3271)	31.74 (18.67, 50.08)	21.61 (13.3, 32.51)	1.19 (1.06, 1.32)
Caribbean	1799 (1093, 2785)	865 (514, 1351)	7.84 (4.76, 12.14)	5.44 (3.24, 8.5)	1.26 (1.2, 1.33)
Central Asia	5234 (3266, 8103)	2463 (1498, 3734)	11.22 (7, 17.37)	8.28 (5.04, 12.56)	1.14 (1.07, 1.22)
Central Europe	5999 (3551, 9298)	4831 (2959, 7498)	10.97 (6.49, 17)	8.15 (4.99, 12.64)	0.86 (0.82, 0.9)
Central Latin America	8185 (5048, 12771)	3086 (1849, 4719)	6.55 (4.04, 10.22)	4.52 (2.71, 6.92)	1.23 (1.21, 1.24)
Central Sub-Saharan Africa	4552 (2763, 7244)	1507 (909, 2342)	8.38 (5.08, 13.33)	7.45 (4.49, 11.59)	0.43 (0.4, 0.46)
East Asia	203374 (123245, 313345)	100326 (62415, 152245)	27.64 (16.75, 42.59)	16.49 (10.26, 25.03)	1.93 (1.82, 2.04)
Eastern Sub-Saharan Africa	13949 (8578, 21811)	5020 (3091, 7863)	8.13 (5, 12.72)	7.41 (4.56, 11.6)	0.34 (0.27, 0.41)
High-income Asia Pacific	19865 (12085, 30838)	15739 (9493, 24238)	23.61 (14.36, 36.65)	17.87 (10.78, 27.52)	0.9 (0.85, 0.95)
North Africa and Middle East	38830 (23688, 59399)	11700 (7222, 18470)	12.51 (7.63, 19.14)	8.72 (5.38, 13.77)	1.18 (1.11, 1.24)
Oceania	1031 (613, 1558)	380 (232, 582)	16.35 (9.72, 24.71)	14.05 (8.6, 21.52)	0.48 (0.46, 0.49)
South Asia	85827 (52712, 133820)	36683 (22519, 56898)	9.38 (5.76, 14.63)	8.04 (4.94, 12.48)	0.53 (0.51, 0.55)
Southeast Asia	64801 (39390, 97405)	24879 (15348, 37954)	18.28 (11.11, 27.48)	12.24 (7.55, 18.67)	1.46 (1.42, 1.51)
Southern Latin America	8010 (4878, 11986)	3995 (2457, 5970)	23.93 (14.57, 35.81)	17.96 (11.05, 26.84)	0.88 (0.82, 0.94)
Southern Sub-Saharan Africa	4640 (2835, 7104)	2022 (1247, 3091)	11.81 (7.21, 18.07)	9.39 (5.79, 14.35)	0.66 (0.6, 0.72)
Tropical Latin America	9474 (5739, 14366)	3664 (2224, 5633)	8.12 (4.92, 12.32)	5.38 (3.26, 8.27)	1.38 (1.34, 1.41)
Western Europe	35280 (21003, 54590)	26079 (15516, 40144)	17.95 (10.69, 27.78)	13.8 (8.21, 21.25)	0.94 (0.87, 1.01)
Western Sub-Saharan Africa	16244 (10005, 25023)	5870 (3582, 9035)	8.59 (5.29, 13.23)	8.24 (5.03, 12.68)	0.14 (0.12, 0.17)

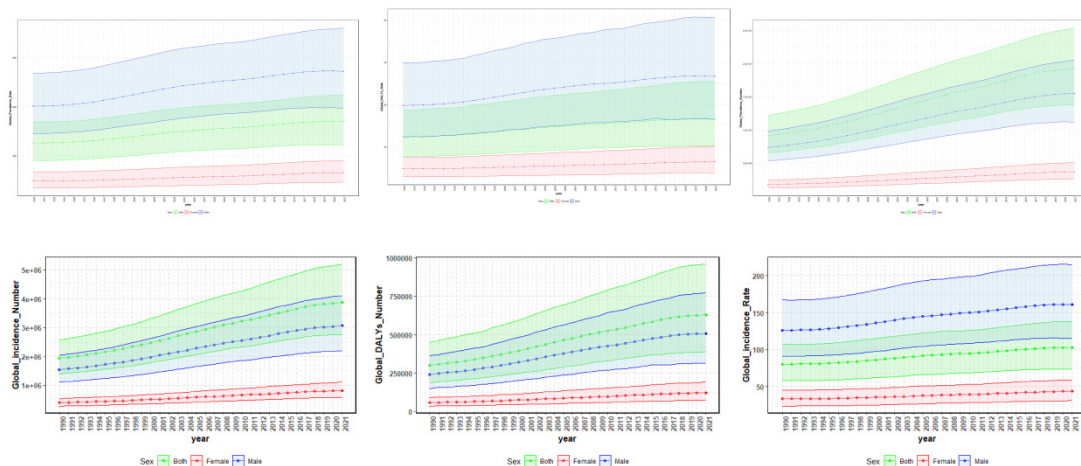


Figure 1. Global number and rate of incidence, prevalence, and DALYs of gout from 1990 to 2021, by sex

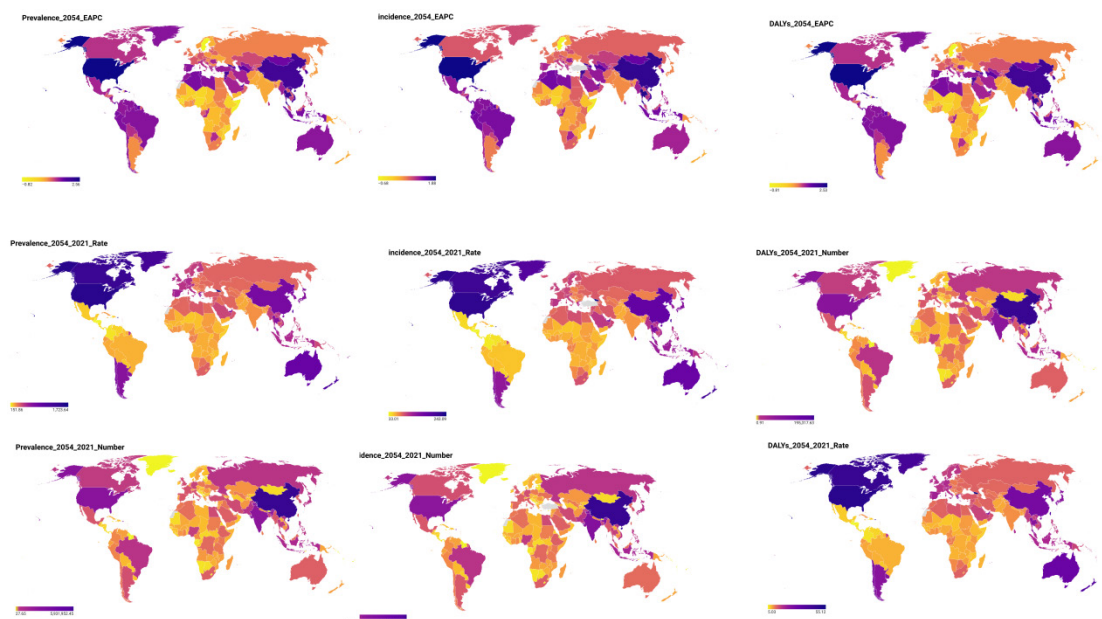


Figure 2. Nationallevel burden of gout: number and rate of incidence, prevalence, and DALYs across the world

3.2. Global trends in Gout burden using joinpoint regression analysis

The results of joinpoint regression analysis on the burden of Gout were demonstrated in **Figure 3** and **Table 4**.

Between 1990 and 2021, continuously dramatically increasing trends for aged 20–54 years (Number and Rate) of incidence, prevalence and DALYs of Gout occurred. Globally, the gout incidence Rate in individuals aged 20–54 years increased between 1990 and 2021 ,AAPC 0.80 [95% CI 0.75 to 0.88] ,with the most rapidly increasing period at 1996–2005 after undergoing six joinpoints; As for the gout incidence Number also increased between 1990 and 2021, AAPC 2.28 [95% CI 2.24 to 2.32] ,with the most rapidly increasing period at 1996–2004 after undergoing six joinpoints. Accordingly, the gout prevalence also increased between 1990 and 2021. Specifically, the trend for the Rate of Prevalence experienced six joinpoints of no changes in 2018–2021, with the most rapidly increasing period at 1996–2004 , AAPC 0.96 [95% CI 0.93 to 1.00]. Meanwhile, the trend for the Number of prevalence demonstrated six joinpoints of increases in all periods, with the most rapidly increasing period at 1996–2003 , AAPC 2.44 [95% CI 2.38 to 2.50]. Regarding the trend for the Rate

of DALYs, it underwent six joinpoints of no changes in 1918–2021, with the most rapidly increasing period at 1996–2004 , AAPC 0.95 [95% CI 0.91 to 0.99]; the Rate of DALYs, it underwent six joinpoints of increase in all periods, with the most rapidly increasing period at 1996–2003 , AAPC 2.42 [95% CI 2.36 to 2.48]. The Joinpoint regression analysis of globally in aged 20–54 years incidence, prevalence and DALYs for gout Rate and Number in each period between 1990 and 2021 can be found in online supplemental data.

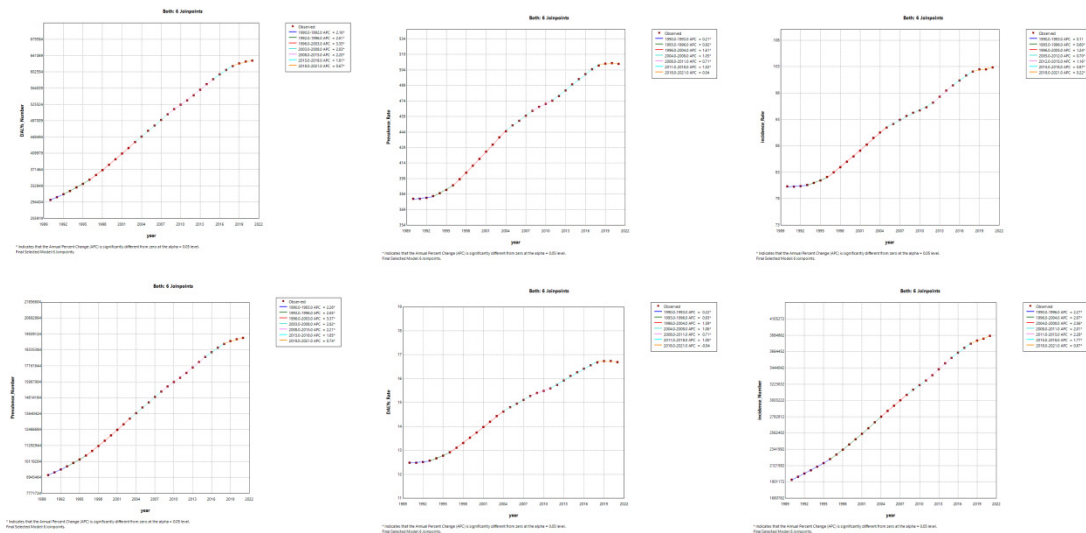


Figure 3. The joinpoint regression analysis on the number and rate of incidence, prevalence, and DALYs for gout globally in individuals aged 20–54 years from 1990 to 2021.

Table 4. The APC and AAPC in 20–54 years of Gouts incidence, prevalence and DALYs for both sexes from 1990 to 2021

Incidence_Rate_APC								
Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1993	0.1098	-0.0551	0.2750	1.4504	0.172575
Both	2	1993	1996	0.5964*	0.2666	0.9273	3.9455	0.001944
Both	3	1996	2005	1.2388*	1.2021	1.2754	74.0910	< 0.000001
Both	4	2005	2012	0.6982*	0.6421	0.7543	27.2192	< 0.000001
Both	5	2012	2015	1.1602*	0.8271	1.4945	7.6196	0.000006
Both	6	2015	2018	0.8655*	0.5321	1.1999	5.6714	0.000104
Both	7	2018	2021	0.2223*	0.0535	0.3913	2.8710	0.014063

Incidence_Rate_AAPC								
Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.8024*	0.7462	0.8587	28.0852	< 0.000001

Incidence_Number_APC								
Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1996	2.2669*	2.2284	2.3055	129.5219	< 0.000001

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	2	1996	2004	2.9710*	2.9401	3.0020	212.3716	< 0.000001
Both	3	2004	2008	2.5621*	2.4470	2.6773	49.0858	< 0.000001
Both	4	2008	2011	2.0141*	1.7883	2.2405	19.6018	< 0.000001
Both	5	2011	2015	2.2840*	2.1698	2.3984	44.0223	< 0.000001
Both	6	2015	2018	1.7689*	1.5409	1.9974	17.0343	< 0.000001
Both	7	2018	2021	0.8707*	0.7556	0.9859	16.5476	< 0.000001

Incidence_Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.2794*	2.2428	2.3160	123.3639	< 0.000001

Prevalence_Rate_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1993	0.2122*	0.0856	0.3389	3.6539	0.003303
Both	2	1993	1996	0.9245*	0.6730	1.1766	8.0367	0.000004
Both	3	1996	2004	1.6092*	1.5758	1.6425	105.9631	< 0.000001
Both	4	2004	2008	1.0537*	0.9328	1.1748	19.0682	< 0.000001
Both	5	2008	2011	0.7142*	0.4758	0.9531	6.5434	0.000028
Both	6	2011	2018	1.0217*	0.9816	1.0618	55.7997	< 0.000001
Both	7	2018	2021	0.0427	-0.0788	0.1644	0.7657	0.458663

Prevalence_Rate_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.9639*	0.9255	1.0023	49.4356	< 0.000001

Prevalence_Number_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1993	2.2757*	2.0756	2.4762	25.0361	< 0.000001
Both	2	1993	1996	2.6542*	2.2582	3.0518	14.7664	< 0.000001
Both	3	1996	2003	3.3676*	3.3010	3.4342	112.0176	< 0.000001
Both	4	2003	2008	2.8230*	2.7021	2.9441	51.5376	< 0.000001
Both	5	2008	2015	2.2126*	2.1497	2.2755	77.4956	< 0.000001
Both	6	2015	2018	1.8465*	1.4770	2.2174	10.9672	< 0.000001
Both	7	2018	2021	0.7408*	0.5513	0.9307	8.5391	0.000002

Prevalence_Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.4401*	2.3812	2.4991	82.1059	< 0.000001

DALYs_Rate_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1993	0.2241*	0.0813	0.3672	3.4202	0.005077
Both	2	1993	1996	0.9326*	0.6450	1.2211	7.0868	0.000013
Both	3	1996	2004	1.5924*	1.5536	1.6312	90.1849	< 0.000001
Both	4	2004	2008	1.0611*	0.9189	1.2036	16.3309	< 0.000001
Both	5	2008	2011	0.7133*	0.4310	0.9965	5.5161	0.000133
Both	6	2011	2018	0.9984*	0.9497	1.0471	44.9236	< 0.000001
Both	7	2018	2021	-0.0368	-0.1831	0.1096	-0.5483	0.593510

DALYs_Rate_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	0.9494*	0.9046	0.9943	41.6973	< 0.000001

DALYs_Number_APC

Cohort	Segment	Lower Endpoint	Upper Endpoint	APC	Lower CI	Upper CI	Test Statistic (t)	Prob > t
Both	1	1990	1992	2.1614*	1.7782	2.5460	12.3994	< 0.000001
Both	2	1992	1996	2.6087*	2.4143	2.8034	29.5906	< 0.000001
Both	3	1996	2003	3.3535*	3.2874	3.4197	112.2600	< 0.000001
Both	4	2003	2008	2.8272*	2.7052	2.9495	51.1354	< 0.000001
Both	5	2008	2015	2.2024*	2.1380	2.2668	75.3416	< 0.000001
Both	6	2015	2018	1.8057*	1.4181	2.1948	10.2215	< 0.000001
Both	7	2018	2021	0.6694*	0.4743	0.8650	7.4920	0.000007

DALYs_Numer_AAPC

Cohort	Range	Lower Endpoint	Upper Endpoint	AAPC	Lower CI	Upper CI	Test Statistic	P-Value
Both	Full Range	1990	2021	2.4233*	2.3674	2.4792	85.9967	< 0.000001

3.3. Proportional attributable fraction of Risk factors by sex, age subgroup, and regions

Globally, in 2021, aged in 20–54 years, High body-mass index (High BMI) and Impaired kidney function accounted for 34.95% (28.43% to 42.46%, 95% UI) of DALYs and 2.58% (2.00% to 3.26%, 95% UI) of DALYS, respectively. DALYS attributable to high BMI was slight lower in males (34.73%, 95% UI 28.25% to 42.25%) than in females (35.89%, 95% UI 28.73% to 43.55%), also in Impaired kidney function (**Figure 4**).

The DALYS attributable to high BMI increased with age and reached its highest level in the 50–54 years age groups among young and middle adults (36.33%, 95% UI 29.39% to 44.26%), lowest level in the 20–24 years age groups (24.04%, 95% UI 19.60% to 29.16%). The regional attributable risk fraction of high BMI ranged from 11.36% to 58.52% and Impaired kidney function ranged from 1.13% to 6.83% in all locations, ranged from 22.59% to 49.79% in GBD regions with the highest observed in North America (49.79%, 95% UI 40.66% to 58.75%), the lowest observed in South Asia (22.59%, 95% UI 17.96% to 27.88%) (**Table 5**); also Impaired kidney function ranged from 1.53% to 5.74% in GBD regions with the highest observed in

Central Asia (5.74%, 95% UI 4.43% to 7.26%), the lowest observed in Australasia (1.53%, 95% UI 1.16% to 2.00%) (Table 6)

The countries and territories attributable risk fraction of high BMI ranged from 14.93% to 58.52%, with the highest observed in the American Samoa (58.52%, 95% UI 48.92% to 67.43%) with the lowest observed in Eritrea (14.93%, 95% UI 11.30% to 19.23%).

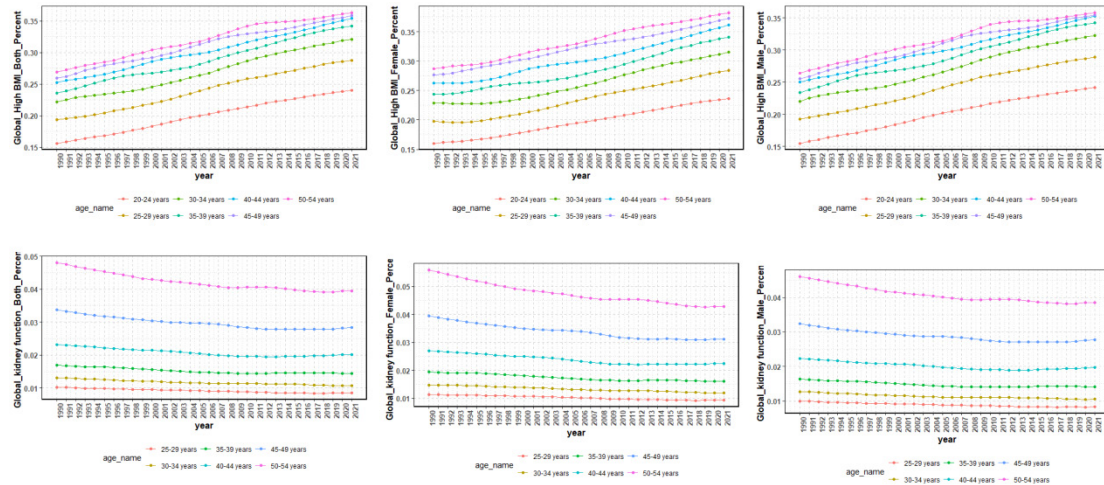


Figure 4. Percentage of DAYLs due to gout attributable to risk factors (High BMI and Kidney function) in the Global Burden of Disease study in 2021, according to sex and age_name.

Table 5. Proportional attributable fraction of high-BMI by GBD regions.

location_name	Percent	upper	lower
NORTH AMERICA	49.79%	58.75%	40.66%
High-income North America	49.79%	58.75%	40.65%
America	48.44%	57.57%	39.37%
Region of the Americas	48.44%	57.57%	39.37%
Middle East & North Africa - WB	47.96%	57.22%	39.00%
North Africa and Middle East	47.81%	57.07%	38.85%
Northern Africa	46.91%	56.24%	37.85%
Australasia	46.91%	56.58%	38.09%
Central Latin America	46.51%	55.81%	37.50%
Southern Latin America	46.26%	55.53%	36.90%
World Bank High Income	45.80%	54.85%	37.37%
Commonwealth High Income	45.12%	54.72%	36.24%
Advanced Health System	44.83%	53.77%	36.54%
Latin America & Caribbean - WB	44.77%	54.08%	35.99%
High SDI	44.67%	53.49%	36.50%
Andean Latin America	44.14%	53.27%	35.28%
Eastern Mediterranean Region	43.77%	52.48%	35.53%
Tropical Latin America	42.97%	52.48%	34.21%
Central Europe	42.53%	51.37%	34.04%
Eastern Europe	42.34%	51.47%	33.55%
Europe	42.27%	51.24%	33.70%

location_name	Percent	upper	lower
Europe & Central Asia - WB	42.14%	51.05%	33.61%
European Region	42.11%	51.01%	33.58%
Western Europe	41.18%	50.14%	32.73%
Caribbean	40.49%	49.21%	32.55%
Central Asia	40.32%	49.32%	31.96%
Southern Sub-Saharan Africa	39.56%	47.94%	31.50%
Oceania	38.01%	46.72%	30.53%
High-middle SDI	36.78%	44.92%	29.39%
Global	34.95%	42.46%	28.43%
Southern Africa	34.65%	41.94%	27.74%
World Bank Upper Middle Income	34.06%	41.78%	27.17%
Basic Health System	33.85%	41.57%	27.14%
Africa	33.85%	40.95%	27.40%
East Asia	32.67%	40.34%	25.93%
Middle SDI	32.05%	39.19%	26.00%
Western Pacific Region	32.03%	39.32%	25.58%
Western Sub-Saharan Africa	31.61%	38.92%	25.62%
East Asia & Pacific - WB	31.13%	38.25%	24.97%
Western Africa	31.00%	38.16%	25.10%
African Region	30.41%	37.08%	24.56%
Asia	30.23%	37.14%	24.51%
Sub-Saharan Africa - WB	30.04%	36.57%	24.24%
High-income Asia Pacific	29.35%	35.99%	23.63%
Central Africa	29.25%	35.90%	23.49%
World Bank Lower Middle Income	27.90%	34.22%	22.60%
Central Sub-Saharan Africa	27.40%	33.87%	22.00%
Low-middle SDI	26.98%	32.95%	21.98%
Eastern Africa	26.50%	32.30%	21.33%
Minimal Health System	25.60%	31.50%	20.52%
Southeast Asia	25.49%	30.98%	20.64%
Commonwealth Middle Income	25.23%	31.08%	20.22%
Commonwealth Low Income	24.55%	30.44%	19.58%
World Bank Low Income	24.49%	29.77%	19.78%
Limited Health System	24.46%	30.18%	19.60%
Eastern Sub-Saharan Africa	24.06%	29.37%	19.31%
Low SDI	23.60%	28.81%	19.00%
South-East Asia Region	23.14%	28.42%	18.49%
South Asia - WB	22.89%	28.22%	18.20%
South Asia	22.59%	27.88%	17.96%

Table 6. Proportional attributable fraction of Impaired kidney function by GBD regions.

location_name	percent	upper	lower
SOUTHEAST ASIA	2.96%	3.76%	2.28%

location_name	percent	upper	lower
East Asia	1.87%	2.38%	1.42%
Global	2.58%	3.26%	2.00%
Oceania	2.86%	3.65%	2.20%
Central Asia	5.74%	7.26%	4.43%
Central Europe	3.04%	3.86%	2.33%
Eastern Europe	3.07%	3.93%	2.34%
High-income Asia Pacific	2.36%	3.02%	1.83%
Australasia	1.53%	2.00%	1.16%
Western Europe	1.74%	2.23%	1.33%
Southern Latin America	1.53%	1.96%	1.18%
High-income North America	2.57%	3.23%	1.98%
Caribbean	2.86%	3.66%	2.20%
Andean Latin America	2.15%	2.84%	1.65%
Central Latin America	3.79%	4.86%	2.88%
Tropical Latin America	3.99%	5.14%	3.02%
North Africa and Middle East	3.23%	4.15%	2.50%
South Asia	3.19%	4.02%	2.44%
Central Sub-Saharan Africa	5.73%	7.31%	4.29%
Eastern Sub-Saharan Africa	1.71%	2.20%	1.30%
Southern Sub-Saharan Africa	4.80%	6.09%	3.60%
Western Sub-Saharan Africa	4.55%	5.85%	3.45%
East Asia & Pacific - WB	2.14%	2.71%	1.64%
Latin America & Caribbean - WB	3.05%	3.92%	2.34%
Sub-Saharan Africa - WB	3.68%	4.71%	2.79%
South Asia - WB	3.18%	4.01%	2.44%
Eastern Africa	1.87%	2.42%	1.43%
Middle East & North Africa - WB	3.28%	4.22%	2.53%
Northern Africa	3.01%	3.85%	2.30%
Southern Africa	4.03%	5.16%	3.04%
Western Africa	4.42%	5.67%	3.34%
Europe & Central Asia - WB	2.53%	3.19%	1.96%
Commonwealth High Income	1.82%	2.31%	1.40%
Africa	3.53%	4.50%	2.69%
Commonwealth Middle Income	3.39%	4.28%	2.60%
America	2.70%	3.41%	2.09%
South-East Asia Region	3.06%	3.87%	2.36%
Europe	2.31%	2.94%	1.80%
Western Pacific Region	1.97%	2.49%	1.50%
European Region	2.53%	3.19%	1.96%
Commonwealth Low Income	2.36%	3.03%	1.81%
World Bank High Income	2.41%	3.03%	1.86%
High SDI	2.35%	2.95%	1.81%
African Region	3.69%	4.73%	2.80%
Region of the Americas	2.70%	3.41%	2.09%

location_name	percent	upper	lower
World Bank Lower Middle Income	3.35%	4.23%	2.57%
Asia	2.47%	3.11%	1.90%
World Bank Low Income	2.74%	3.51%	2.10%
Advanced Health System	2.43%	3.06%	1.87%
High-middle SDI	2.01%	2.56%	1.54%
World Bank Upper Middle Income	2.15%	2.72%	1.65%
Basic Health System	2.38%	3.01%	1.83%
North America	2.57%	3.23%	1.98%
Low SDI	3.22%	4.11%	2.47%
Limited Health System	3.20%	4.04%	2.45%
Middle SDI	2.73%	3.43%	2.10%
Eastern Mediterranean Region	3.49%	4.45%	2.68%
Low-middle SDI	3.27%	4.12%	2.50%
Central Africa	5.54%	7.05%	4.18%
Minimal Health System	3.90%	4.97%	2.96%

4. Discussion

To the best of our knowledge, this is the first study to describe the gout burden and its changing trends between 1990 and 2021 among people aged 20-54 years by age, gender and Sustainable Development Index (SDI) at global, regional and country levels. The results showed that the prevalence, incidence, and YLD of gout in people aged 20-54 years increased significantly worldwide, with significant differences across age, gender, SDI level, region, and country. These findings highlight the need for increased awareness, early detection, and effective management strategies to mitigate the impact of gout on young and middle-aged populations worldwide.

The total number of patients with gout has doubled between 1990 and 2021, and the age-standardized prevalence has increased by 22.5% from 1990, with increases in most Global Burden of Disease (GBD) regions ^[8,12]. Consistent with the previous literature, the average annual percentage changes of prevalence, incidence and disability-adjusted life years rate among young and middle-aged people were 1.11 (1.06, 1.16), 0.92 (0.88, 0.95) and 1.1 (1.05, 1.15), respectively, indicating a steady upward trend. The simultaneous increases in prevalence, incidence, and disability-adjusted life-years suggest that prevention and treatment of gout in young and middle-aged patients are often ineffective ^[13].

In 2021, there were 190, 200 million cases and 6.29 million disability-adjusted life years (DALYs) of gout in people aged 20-54 years worldwide. Globally, the number of cases, incidence and prevalence, and disability-adjusted life years (DALYs) of gout have all shown significant increases between 1990 and 2021. The value of males is much higher than that of females, which may be due to the fact that males in this age group are more likely to consume foods related to gout attack and gout attack aggravation and to have hyperuricemia ^[14]. From a regional perspective, the United States of America was the region with the most significant increases in incidence, prevalence and disability-adjusted life-year rates. It is followed by China and East Asia. The country with the largest number of cases, number of cases, and disability-adjusted life years (DALYs) is China, probably due to its large population, while the country with the highest

incidence, prevalence, and DALYs is the United States of America, as a typical highly developed country, Dietary habits, obesity and renal dysfunction, and greater access to healthcare services in the United States of America, thereby facilitating better diagnosis and reporting ^[14,15], may account for the highest incidence of gout in the country, as reflected by the EAPC.

From 1990 to 2021, the incidence, prevalence and disability-adjusted life years (DALYs) of gout among people aged 20-54 years continued to increase substantially. The fastest increasing period of gout incidence was from 1996 to 2004, with an average annual percent change (AAPC) of 0.80, and the fastest increasing period of prevalence was from 1996 to 2004, with an AAPC of 0.96. The disability-adjusted life years increased most rapidly from 1996 to 2003, with an AAPC of 2.42. It shows that the global burden of gout is increasing over time. Changes in the prevalence of major factors leading to the occurrence and progression of the disease, as well as the ways in which governments and individuals respond to these factors, may jointly change the time trend of the disease burden, resulting in direct and indirect economic costs (including drug treatment, surgery, premature death, etc.) ^[16-18]. It also causes intangible personal costs (pain, activity limitation, etc.) ^[19], so it is particularly important to develop prevention strategies, improve management, and more evidence-based treatment of gout.

The results of this study showed that the regional attributable risk proportion of high BMI among young and middle-aged adults ranged from 11.36% to 58.52%, with the highest value in North America (49.79%) among GBD regions. The lowest value was found in South Asia (22.59%). The disability-adjusted life years (DALYS) attributable to high BMI increased with age. BMI is associated with hyperuricemia, and being overweight or obese may affect liver enzyme levels and lead to elevated uric acid levels. Controlling body weight and liver enzyme levels may help prevent and treat hyperuricemia ^[20]. For obese gout patients, lifestyle interventions, including a balanced diet, behavioral therapy, and exercise, are recommended, especially since high body mass index (BMI) accounts for nearly 50% of gout disability-adjusted life-years in North America ^[21]. However, the highest values of renal impairment were found in Central Asia (5.74%) and the lowest values were found in Australasia (1.53%).

5. Conclusion

In conclusion, as a major public health issue, this study describes for the first time the burden of gout, its trends and risk factors in people aged 20-54 years at global, regional and country levels. Although the incidence, prevalence and disability-adjusted life years (DALYs) of gout among young and middle-aged people vary widely across countries, the burden is generally on the rise from 1990 to 2021. We call for more research on gout in young and middle-aged people and more representative data for each country. Young and middle-aged people are the backbone of society. Further research is needed to understand the long-term impact of gout treatment on young and middle-aged people, especially its relationship with high BMI and impaired renal function. Continuous research to address key risk factors and improve diagnosis and treatment methods is essential to reduce the global burden of gout.

6. Limitations

The study relies entirely on the data from the 2021 Global Burden of Disease (GBD) study. Although GBD employs comprehensive and standardized methods, potential errors or biases in the original data collection

processes across different regions and countries could impact the accuracy of the results. For instance, variations in the diagnostic criteria and reporting practices for gout might exist, leading to inconsistent data quality. While BMI and renal dysfunction were analyzed as risk factors, other potential contributors to gout burden in the 20 - 54-year-old population were not explored. The findings, although presented at global, regional, and national levels, might have limitations in generalizability within specific subgroups or regions. For example, within large and diverse countries, there could be significant heterogeneity in gout prevalence and risk factor profiles among different ethnic, socioeconomic, or geographical subgroups that were not fully captured by the current analysis.

Disclosure statement

The authors declare no conflict of interest.

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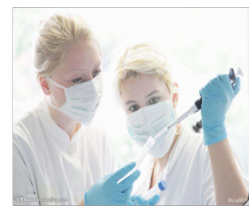
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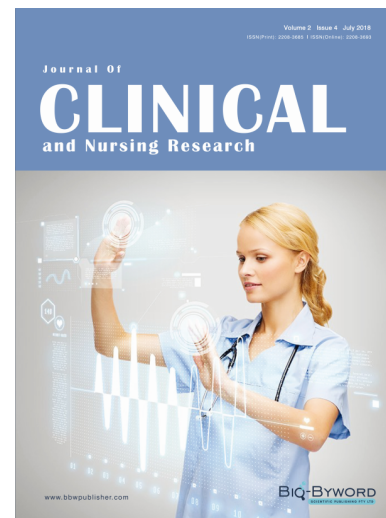
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