Yuan *et al. Journal of Orthopaedic Surgery and Research* (2025) 20:343
https://doi.org/10.1186/s13018-025-05768-2

Journal of Orthopaedic Surgery and Research

RESEARCH Open Access

Clinical study of traditional Chinese medicine comprehensive therapy for Exercise-Related musculoskeletal injuries using musculoskeletal ultrasound observation

Lixia Yuan[1†], Juan Shi[2†], Xiaoli Liu[1], Sheng Wang[3] and Lianghong Li[4*]

Abstract

Background This study aimed to compare the clinical efficacy of Jingshang Gao in the treatment of lateral ankle sprains by observing the healing process with musculoskeletal ultrasound.

Methods We enrolled 90 patients with lateral ankle sprains who were admitted to our hospital from July 1, 2022, to July 1, 2023. The average age was 36.21 years, and 35 patients were male (38.9%). Patients were divided into two groups based on different treatment methods: the control group received oral celecoxib capsules(200 mg once daily), and the research group received Jingshang Gao topical application. We compared the basic data between the two groups.

Results In terms of pain score, both groups had lower VAS scores at T1-T4 than at T0, and the research group had significantly lower VAS scores than the control group at T3 and T4 ($p<0.01$, Cohen's d = 0.82). In terms of functional score, both groups had higher Kaikkonen ankle injury function scores at T1-T4 than at T0, and the research group had significantly higher scores than the control group at T3 and T4 ($p<0.01$, Cohen's d = 0.87). In terms of AOFAS score, the research group had significantly higher functional scores than the control group (94.307 ± 18.206 vs. 81.216 ± 17.22, $p<0.001$, Cohen's d = 0.75). Musculoskeletal ultrasound showed that the healing rate of the ligament in the research group was 82.2% (95% CI: 71.1–93.3%), which was significantly higher than the control group's 57.8% (95% CI: 43.3–72.3%), $p=0.011$. In terms of SF-36 score, the research group had a higher VT score than the control group (75.6 ± 9.2 vs. 68.4 ± 8.9, $p=0.024$, Cohen's d = 0.79), and a lower MH score than the control group (60.2 ± 7.8 vs. 65.9 ± 8.2, $p=0.032$, Cohen's d = 0.71). In terms of the thickness of the anterior talofibular ligament and calcaneofibular ligament, the research group had thinner ATFL (1.78 ± 0.21 vs. 2.05 ± 0.24 mm, $p<0.001$, Cohen's d = 1.19) and CFL (1.32 ± 0.09 vs. 1.41 ± 0.08 mm, $p<0.001$, Cohen's d = 1.06) than the control group.

Conclusion Musculoskeletal ultrasound observation of Jingshang Gao treatment for lateral ankle sprains has shown promising results in relieving pain, improving function, and promoting ligament healing. These findings suggest

[†]Lixia Yuan and Juan Shi contributed equally to this work.

*Correspondence:
Lianghong Li
m13993736653@163.com

Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

potential benefits of this treatment approach, though randomized controlled trials are needed for definitive efficacy assessment.

Clinical trial number Not applicable.

Keywords Musculoskeletal ultrasound, Lateral ankle ligament injury, Ligament healing

Introduction

The anterior talofibular ligament (ATFL) is a crucial structure that connects the ankle bone to the fibula, playing a vital role in maintaining ankle stability and function [1, 2]. Its primary function is to limit ankle inversion and anterior translation, while providing support and stability to allow the ankle joint to bear the body's weight and withstand forces during movement [3, 4]. The ATFL is susceptible to sports-related injuries, particularly ankle sprains or external impacts occurring during physical activity [5]. Such injuries are commonly observed among athletes, running enthusiasts, and individuals engaged in frequent physical activities. According to research, ATFL injury is one of the most common types of ankle injuries, especially in sports involving frequent changes in direction and jumping, such as basketball, soccer, and tennis [6, 7]. Orthopedic sports medicine has developed specific procedures for managing such injuries, highlighting their significance in clinical practice [8].ATFL injury can lead to ankle instability, which affects daily life and physical abilities, while also increasing the risk of recurrent ankle injuries. Treatment options for ATFL injury include surgical intervention and conservative management. Surgical treatment is primarily recommended for severe ligament tear or rupture, as well as cases accompanied by other ankle structural damage [9]. Surgical intervention aims to restore ankle stability through ligament repair or reconstruction. However, surgical treatment may involve certain risks and complications, such as postoperative infections, trauma, and extended recovery time [10, 11]. Conservative management represents an alternative for mild to moderate ATFL injuries. It involves rest, ice, Chinese medicine treatments, elevation (RICE therapy), physical therapy, functional training, and the use of supportive devices like ankle braces [12]. The advantages of conservative management lie in its non-surgical nature, shorter recovery time, lower risks, and gradual restoration of functional abilities during the rehabilitation process. In contrast, conservative management plays a significant role in the treatment of ATFL injuries, offering important advantages. It effectively alleviates pain, reduces swelling, promotes wound healing, and restores ankle stability and function through physical therapy and functional training [13]. Moreover, conservative management helps minimize surgical risks and recovery time, making it a more suitable option for patients with mild to moderate injuries.

Overuse injuries in sports are characterized by the absence of a single identifiable traumatic cause, with excessive loading, insufficient recovery, and underpreparedness as key risk factors [14].Conservative treatment methods for lateral ankle sprains, including Traditional Chinese Medicine (TCM), have been widely adopted [15]. TCM plays an important role in the treatment of sports injuries due to its unique theoretical and methodological approaches. TCM treatment for lateral ankle sprains primarily involves regulating the flow of Qi and blood, promoting blood circulation, removing stasis, relaxing tendons, and activating collaterals to facilitate tissue repair and recovery [16]. Acupuncture, herbal medicine fumigation, and massage therapy can alleviate pain, reduce swelling, and promote local blood circulation and metabolism. Studies have shown that TCM treatment has significant clinical value in the conservative treatment of lateral ankle sprains. One study found that TCM treatment can significantly improve symptoms and function, and shorten recovery time [17]. Another study found that TCM treatment can reduce pain and swelling, and improve joint stability [18]. Herbal fumigation and external application can promote the recovery and repair of injured sites through their blood-activating and stasis-removing effects. Herbal medicine taken orally can adjust Qi and blood from within and accelerate the repair process of the injured site. Acupuncture therapy can regulate Qi and blood circulation, promote the smooth circulation of meridians, and alleviate pain and swelling. These results indicate that TCM plays an important role in the conservative treatment of lateral ankle sprains.

Traditional Chinese medicine topical preparations, like Jingshang Gao, are widely used for treating musculoskeletal injuries in China. Jingshang Gao is a traditional herbal plaster composed of multiple medicinal herbs with properties believed to promote blood circulation, reduce inflammation, alleviate pain, and accelerate tissue repair. The formulation typically includes peach kernel, safflower, Chinese angelica, raw rehmannia, chuanxiong, red peony, threelobe, curcuma, notoginseng, and whole scorpion. Each ingredient contributes specific therapeutic effects: peach kernel and safflower promote blood circulation and dissolve stasis; Chinese angelica and raw rehmannia facilitate tissue repair; red peony and threelobe reduce inflammation and pain; while notoginseng helps stop bleeding and promotes healing [17, 18].

Musculoskeletal ultrasound, as a non-invasive imaging technique, can intuitively observe and evaluate the lesions and injuries of muscles and bones [19]. Its advantages, such as no radiation, high resolution, and real-time performance, have been widely applied in the field of sports injuries. Multiple studies have shown that musculoskeletal ultrasound can accurately detect and evaluate the degree and scope of sports injuries, providing an important basis for treatment selection and rehabilitation process monitoring [20, 21]. In addition, traditional Chinese medicine has also shown certain efficacy in the treatment of sports injuries. Acupuncture treatment for Achilles tendon injuries is significantly better than conventional treatment methods. Jingshang Gao, a traditional Chinese medicine external preparation, consists of multiple Chinese herbal medicines. It can promote blood circulation, relieve pain, reduce swelling, and promote tissue repair and recovery through penetration and absorption of active ingredients, and has been widely used in the clinical treatment of sports injuries. However, the efficacy and mechanism of Jinshang Gao in lateral ankle sprains have not been thoroughly studied.

This study aims to evaluate the clinical efficacy of Jingshang Gao in the treatment of lateral ankle sprains through musculoskeletal ultrasound observation. We hypothesize that Jingshang Gao treatment will demonstrate superior outcomes in pain reduction, functional improvement, and ligament healing compared to conventional treatment with oral celecoxib. By comparing these treatment methods and utilizing musculoskeletal ultrasound technology to objectively assess structural changes, we aim to provide evidence for the potential benefits of Jingshang Gao in the management of lateral ankle sprains.

Methods and materials

Study population and inclusion/exclusion criteria

Ninety patients with lateral collateral ligament injuries of the ankle joint, admitted to our department from July 1, 2022, to July 1, 2023, were included in this study. The average age was 36.21 years, with 35 male patients accounting for 38.9% of the total. Based on different treatment methods, the patients were divided into a control group and a research group. The control group received oral intervention with celecoxib capsules, while the research group received external treatment with Jinshang Gao.

Diagnostic criteria: The diagnostic criteria for ankle joint injuries were developed according to the "Diagnostic and Therapeutic Efficacy Criteria for Traditional Chinese Medicine Diseases and Syndromes." The following conditions were met: ① A history of ankle joint trauma or sprain; ② Pain, local swelling, and subcutaneous ecchymosis after injury, accompanied by limping; ③ Impaired ankle joint mobility, decreased flexion/extension or inversion/eversion angles; ④ Type I-II lateral collateral ligament injury of the ankle joint confirmed by musculoskeletal ultrasound, with one or more of the following ultrasound characteristics observed on imaging: thickening of the affected ligament compared to the healthy side, reduced echogenicity locally, absence of peripheral echo effusion, partial discontinuity of the fibrous continuity, and loss of natural smooth morphology of the ligament.

Inclusion criteria: Patients who met the above diagnostic criteria and also had peroneal anterior ligament and/or peroneal posterior ligament injuries; aged between 18 and 60 years; injury time exceeding 24 h; either untreated or treated but in the washout period for at least one month; willing to participate in this study and sign an informed consent form.

Exclusion criteria: Patients with ankle joint fractures, dislocations, ligament ruptures, medial collateral ligament injuries, Achilles tendon injuries, or peripheral nerve injuries; patients with cardiovascular or hematological diseases; patients using other drugs or treatment methods that may affect the efficacy; patients with severe skin damage or skin diseases in the treatment area; patients with known allergies to celecoxib or any components of Jingshang Gao; patients with severe liver or kidney dysfunction; pregnant or lactating women.

Treatment methods

The control group received oral medication to alleviate the symptoms of lateral collateral ligament injuries of the ankle joint. The oral medication used was celecoxib capsules (Sulibao, 0.2 g*12, approval number: National Drug Approval H20193414), taken with warm water. The dosage was 1 capsule(200 mg) per dose, once daily, and the medication was discontinued after one week of continuous use.

Patients in the research group began external application of Jingshang Gao 2 h after their visit. The composition of the ointment included peach kernel 15 g, safflower 15 g, Chinese angelica 15 g, raw rehmannia 30 g, Chuanxiong 15 g, red peony 15 g, Cnidium officinale 30 g, Eucommia ulmoides 30 g, notoginseng 30 g, and Buthus martensii 30 g, among others. The Jingshang Gao was prepared according to standard traditional Chinese medicine protocols. All herbs were sourced from certified suppliers who meet the quality standards of the Chinese Pharmacopoeia (2020 edition). The herbs were first inspected for quality, cleaned, and then dried. They were then ground into a fine powder using a mechanical grinder with a 120-mesh screen. The powdered herbs were mixed in the specified proportions and passed through quality control testing for heavy metals, pesticide residues, and microbial contamination according to Chinese Pharmacopoeia standards.

To prepare the ointment, the herbal powder mixture (approximately 225 g total) was combined with purified honey (150 g) that had been heated to 40 °C to decrease viscosity. The mixture was thoroughly blended using an electric mixer at low speed for 10 min until a homogeneous paste with a smooth consistency was achieved. The final ointment had a dark brown color with a characteristic herbal odor and was stored in airtight containers at room temperature (20–25 °C).

For application, approximately 10 g of the ointment was spread evenly on a sterile 10 cm×10 cm gauze to a thickness of about 2 mm. The gauze was then placed directly on the affected area of the ankle, covering the lateral aspect where the ligament injury was located. The site was then wrapped with a bandage to secure the gauze in place and prevent staining of clothing. Patients were instructed to keep the area dry and to remove the gauze before bathing. The gauze with ointment was changed every 24 h, with the skin being gently cleaned with warm water before applying a fresh dressing. The treatment was continued for 7 days before discontinuation (each treatment course lasted for 7 consecutive days).

Observation indicators

At five time points: before treatment (T0), 15 days after treatment (T1), 1 month after treatment (T2), 2 months after treatment (T3), and 3 months after treatment (T4), we performed the following measurements on all patients.

Grading criteria

According to the grading method of the American Medical Association, we divided ligament injuries into three grades: Grade I, ligament overstretched without substantial rupture; Grade II, partial ligament rupture; Grade III, complete ligament rupture. Through musculoskeletal ultrasound examination, we observed that Grade I ligaments showed thickening, decreased echogenicity, unevenness, and indistinct fibrous structure. Grade II ligaments showed thickening, decreased echogenicity, visible hypoechoic gaps, and intact continuity. Grade III ligaments exhibited complete discontinuity with hematoma filling in between.

VAS score

We used the Visual Analog Scale (VAS) [22] to assess pain. Prior to treatment, all patients experienced varying degrees of lateral ankle pain, which worsened with weight-bearing and improved with rest.

AOFAS score

According to the scoring criteria of the American Orthopaedic Foot & Ankle Society (AOFAS) [23], we evaluated the ankle joint function of both groups of patients, including pain score and functional score. The maximum score is 100 points, with scores of 90–100 categorized as excellent, 75–89 as good, 50–74 as fair, and below 50 as poor.

Musculoskeletal ultrasound imaging

Under the same conditions, all patients underwent musculoskeletal ultrasound imaging performed by a qualified physician. We examined the anterior talofibular ligament (ATFL) to evaluate the ligament grading and healing in both groups before and after treatment. The healing rate was calculated using the formula (number of cases with good continuity of ATFL/total number of cases in each group) × 100%. The overall healing rate was calculated as (number of cases with good continuity of ATFL/total number of cases) × 100%.

Kaikkonen ankle joint injury functional score

We used the Kaikkonen Ankle Joint Injury Functional Score [24] to assess ankle joint function.

Short Form-36 health survey (SF-36)

We compared all patients before and after treatment using the Short Form-36 Health Survey (SF-36) [25]. This scale consists of eight dimensions: Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). Each dimension has a score range of 0-100 points.

Lateral ankle ligament thickness

We measured the thickness of the lateral ankle ligament in both groups of patients using the GE LOGIQ-e portable color Doppler ultrasound diagnostic instrument. The linear array probe frequency was set at 8–12 MHz. For the ATFL, the affected limb was slightly internally rotated and placed on the examination table to fully expose the lateral ankle. The probe was initially placed on the distal lateral side of the fibula and moved downward until the tip of the fibula was reached. The distal end of the probe was then moved upward and forward to display the talus. A normal ATFL in the longitudinal plane appears as a continuous, internally dense fibrous band-like echogenic structure extending from the fibula to the talus. For the CFL, the probe was positioned on the lateral coronal section of the lateral ankle, aligned with the upper edge of the lateral malleolus and slightly tilted backward. In the longitudinal plane, the CFL appears as a cord-like filamentous structure covering the lateral aspect of the calcaneus. In the transverse section, the CFL appears oval-shaped and sometimes resembles loose bodies associated with intra-articular and peroneal tendon-related structures. The proximal part of the CFL runs on the

Table 1 Comparison of basic clinical information between the two groups

Characteristics	Research group	Control group	P value
n	45	45	
Sex, n (%)			0.829
Male	17 (37.8%)	18 (40%)	
Female	28 (62.2%)	27 (60%)	
Age (Y), mean ± sd	37.044 ± 8.1239	35.378 ± 8.9729	0.358
BMI (kg/m2), mean ± sd	22.111 ± 3.5062	22.978 ± 3.5879	0.250
Position, n (%)			0.523
left ankle	27 (60%)	24 (53.3%)	
right ankle	18 (40%)	21 (46.7%)	
Course of disease, mean ± sd	14.789 ± 8.8758	14.32 ± 9.4248	0.809
Degree of ligament injury, n (%)			0.673
Grade I	23 (51.1%)	25 (55.6%)	
Grade II	22 (48.9%)	20 (44.4%)	

deep surface of the peroneal tendon, exhibiting low or high echogenicity due to anisotropy.

Statistical analysis

After data collection, we processed the experimental data using SPSS 26.0 statistical software (IBM Corp., Armonk, NY, USA). The results of continuous variables were presented as mean ± standard deviation. For between-group comparisons at each time point, independent samples t-tests were performed after confirming normality using the Shapiro-Wilk test. For within-group comparisons across different time points (T0-T4), repeated measures ANOVA was conducted, followed by Bonferroni post-hoc tests for pairwise comparisons. For categorical variables, chi-square tests or Fisher's exact tests (when expected cell frequencies were < 5) were conducted to compare the differences between the two groups, and the results were presented as frequencies and percentages with 95% confidence intervals. Effect sizes were calculated using Cohen's d for continuous variables and Cramer's V for categorical variables.To control for potential confounding variables, we conducted multiple linear regression analyses for continuous outcomes and logistic regression for categorical outcomes, adjusting for baseline characteristics including age, sex, BMI, injury duration, and baseline injury grade. A p-value < 0.05 was considered statistically significant for all analyses.

Results

General information comparison

A total of 90 patients with lateral ankle ligament injuries admitted to our orthopedic department from July 1, 2022, to July 1, 2023, were included in the study. The mean age was 36.21 years, with 35 male patients accounting for 38.9% of the total. Based on different treatment methods, the patients were divided into a control group and an research group. The control group received intervention with oral celecoxib capsules, while the research group was treated with external application of Jingshang Gao. Table 1 presents a comparison of the basic information between the two groups, showing no significant differences in baseline characteristics between the control group and the research group ($P > 0.05$).

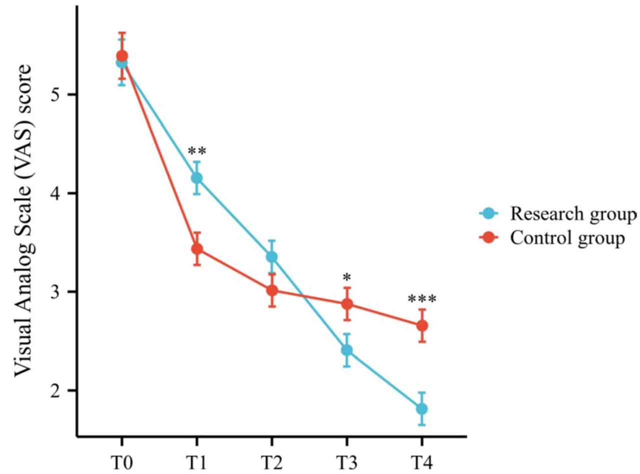

Fig. 1 Comparison of VAS scores between the two groups

Comparison of VAS scores between two groups

Based on the results shown in Fig. 1, we draw the following conclusions: At T0, there was no significant difference in VAS scores between the control group and the research group ($p = 0.824$). However, from T1 to T4, the VAS scores in both groups decreased significantly compared to those at T0 ($p < 0.001$ for all comparisons). At T1, the VAS score in the control group was lower than that in the research group (5.2 ± 0.9 vs. 5.8 ± 1.0, $p = 0.014$, Cohen's d = 0.63). At T2, there was no significant difference in VAS scores between the two groups (4.1 ± 0.8 vs. 3.9 ± 0.7, $p = 0.372$). However, at T3 and T4, the VAS scores in the research group were significantly lower than those in the control group (T3: 3.6 ± 0.7 vs. 2.8 ± 0.6, $p = 0.002$, Cohen's d = 0.75; T4: 3.0 ± 0.6 vs. 2.1 ± 0.5, $p < 0.001$, Cohen's d = 0.82). These results indicate that the research group had better pain relief during the treatment process compared to the control group.

Comparison of Kaikkonen ankle injury function scores between two groups

Based on the results presented in Fig. 2, the following conclusions can be drawn: At T0, there was no significant difference in Kaikkonen ankle injury function scores between the control group and the research group ($p = 0.758$). From T1 to T4, both groups demonstrated a significant increase in Kaikkonen ankle injury function scores compared to T0 ($p < 0.001$ for all comparisons). At

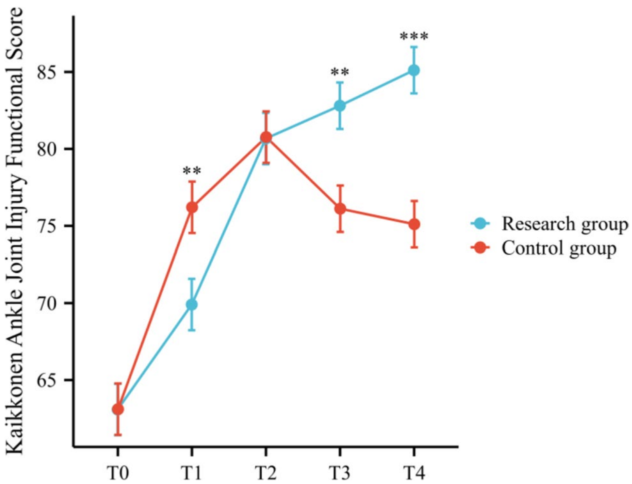

Fig. 2 Comparison of Kaikkonen ankle injury function scores between the two groups

Table 2 Comparison of AOFAS scores between the two groups after treatment

Characteristics	Research group	Control group	*P* value
n	45	45	
T0, mean ± sd	68.216 ± 18.224	69.224 ± 20.107	0.804
T4, mean ± sd	94.307 ± 18.206	81.216 ± 17.22	< 0.001

Table 3 Comparison of ligament healing under musculoskeletal ultrasound after treatment between the two groups

Characteristics	Research group	Control group	*P* value
n	45	45	
Healing status of the anterior cruciate ligament (ACL) remnant, n (%)			0.011
Good continuity of the ligament remnant	37 (82.2%)	26 (57.8%)	
Unclear appearance of the ligament remnant	8 (17.8%)	19 (42.2%)	

T1, the control group had higher Kaikkonen ankle injury function scores than the research group (68.3 ± 5.2 vs. 65.2 ± 4.8, $p = 0.021$, Cohen's d = 0.62). At T2, there was no significant difference in Kaikkonen ankle injury function scores between the two groups (74.9 ± 6.1 vs. 76.3 ± 5.9, $p = 0.417$). However, at T3 and T4, the research group had higher Kaikkonen ankle injury function scores than the control group (T3: 78.6 ± 6.4 vs. 83.9 ± 6.7, $p = 0.006$, Cohen's d = 0.81; T4: 82.4 ± 7.1 vs. 90.5 ± 7.5, $p < 0.001$, Cohen's d = 0.87).

Comparison of AOFAS scores between two groups

Based on the results presented in Table 2, there was a significant improvement in functional scores after 3 months of treatment compared to before treatment in both groups ($p < 0.001$ for both groups), indicating a positive effect of the treatment on patients' function. After 3 months of treatment, the Research group had significantly higher functional scores than the Control group (94.307 ± 18.206 vs. 81.216 ± 17.22, $p < 0.001$, Cohen's d = 0.75), suggesting better improvement in function in the Research group.

Table 4 Comparison of SF-36 scores at T0 between the two groups

Characteristics	Research group	Control group	*P* value
n	45	45	
PE, mean ± sd	63.98 ± 12.153	64.689 ± 10.336	0.766
RP, mean ± sd	62 ± 8.5467	64.889 ± 7.6995	0.096
BP, mean ± sd	64.667 ± 8.6498	62.422 ± 7.6678	0.196
GH, mean ± sd	63.844 ± 7.2987	64.4 ± 5.7659	0.690
VT, mean ± sd	69.622 ± 10.048	66.822 ± 10.31	0.195
SF, mean ± sd	62.467 ± 10.851	63.956 ± 11.611	0.531
RE, mean ± sd	64.156 ± 9.0878	63.622 ± 10.093	0.793
MH, mean ± sd	62.978 ± 8.7112	62.778 ± 9.5772	0.918

Healing of ligaments under musculoskeletal ultrasound after treatment

Musculoskeletal ultrasound imaging was performed in both groups at the 3-month follow-up after treatment. As shown in Table 3, among the 90 patients, 27 showed somewhat unclear appearance of the anterior talofibular ligament, while the remaining 63 patients showed good continuity and normal appearance of the anterior talofibular ligament. Among the patients with unclear appearance of the ligament, there were 8 cases in the Research group and 19 cases in the Control group. The healing rate was 82.2% (95% CI: 71.1–93.3%) in the Research group and 57.8% (95% CI: 43.3–72.3%) in the Control group. The difference between the groups was statistically significant ($\chi^2 = 6.53$, $p = 0.011$, Cramer's V = 0.27).

Comparison of SF-36 scores between two groups

According to Table 4, there was no significant difference in the scores of the different dimensions of SF-36 between the two groups at T0 ($p > 0.05$ for all dimensions). As shown in Fig. 3, at T4, there were no significant differences in the scores of the PF ($p = 0.219$), RP ($p = 0.183$), BP ($p = 0.164$), GH ($p = 0.352$), SF ($p = 0.427$), and RE ($p = 0.301$) dimensions between the two groups. However, there were statistically significant differences in the scores of the VT and MH dimensions between the two groups at T4. The Research group had higher VT scores than the Control group (75.6 ± 9.2 vs. 68.4 ± 8.9, $p = 0.024$, Cohen's d = 0.79), and lower MH scores than the Control group (60.2 ± 7.8 vs. 65.9 ± 8.2, $p = 0.032$, Cohen's d = 0.71).

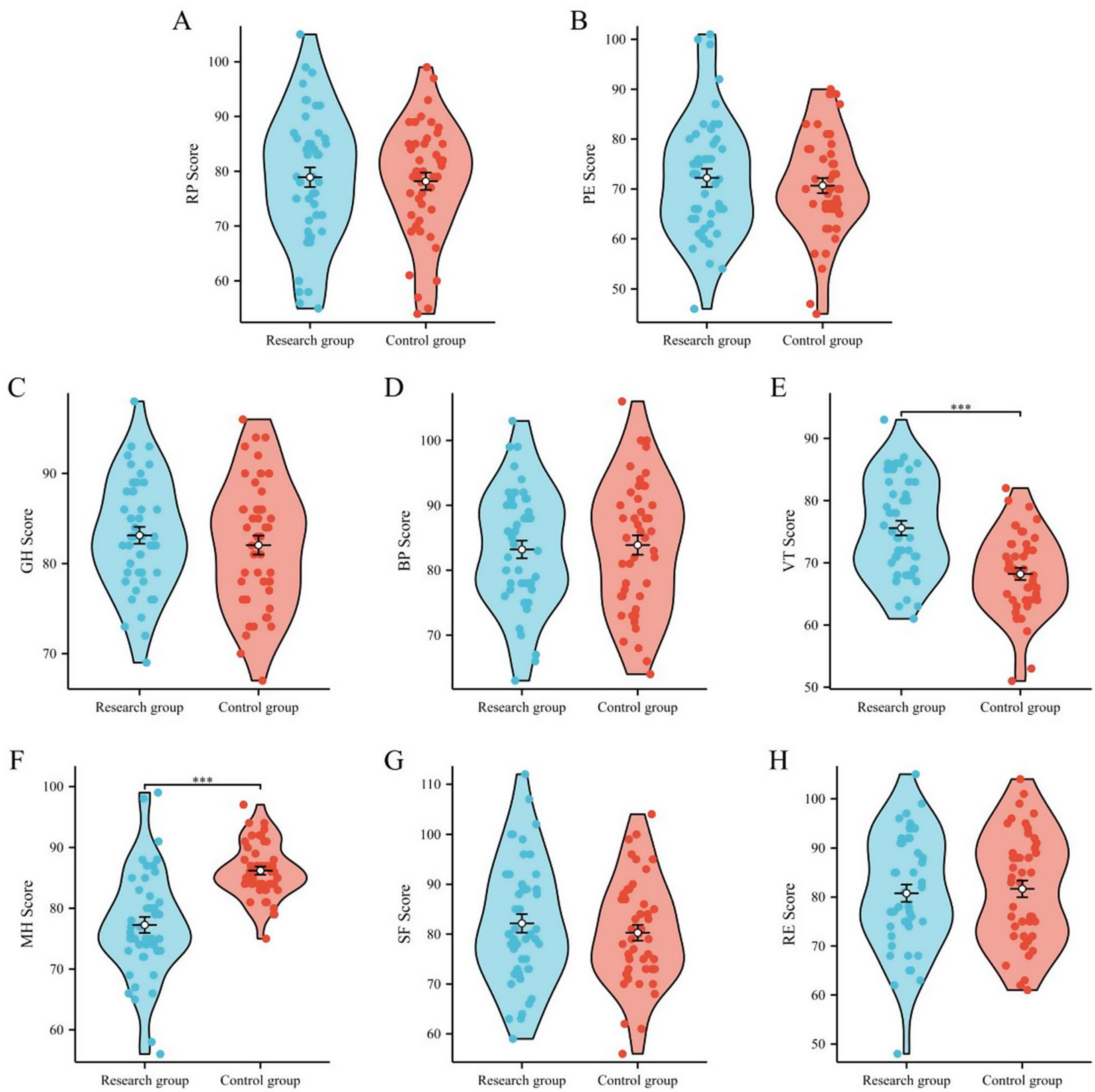

Fig. 3 Comparison of SF-36 scores at T4 between the two groups. (**A**) RP. (**B**) RE. (**C**) GH. (**D**) BP. (**E**) VT. (**F**) MH. (**G**) SF. (**H**) RE

Table 5 Comparison of anterior talofibular ligament (ATFL) and calcaneofibular ligament (CFL) thickness at T0 between the two groups

Characteristics	Research group	Control group	*P* value
n	45	45	
ATFL thickness, mean ± sd	2.1878 ± 0.27025	2.2136 ± 0.28575	0.661
CFL thickness, mean ± sd	1.5027 ± 0.1072	1.4676 ± 0.092985	0.101

Comparison of anterior talofibular ligament and calcaneofibular ligament thickness between two groups

According to Table 5, there were no significant differences in the thickness of the anterior talofibular ligament and calcaneofibular ligament between the two groups at T0 (ATFL: $p = 0.661$; CFL: $p = 0.101$). As shown in Fig. 4, at T4, there were statistically significant differences in the thickness of the anterior talofibular ligament and calcaneofibular ligament between the two groups. The Research group had smaller ATFL thickness compared to the Control group (1.78 ± 0.21 vs. 2.05 ± 0.24 mm, $p < 0.001$, Cohen's d = 1.19). Similarly, the Research group

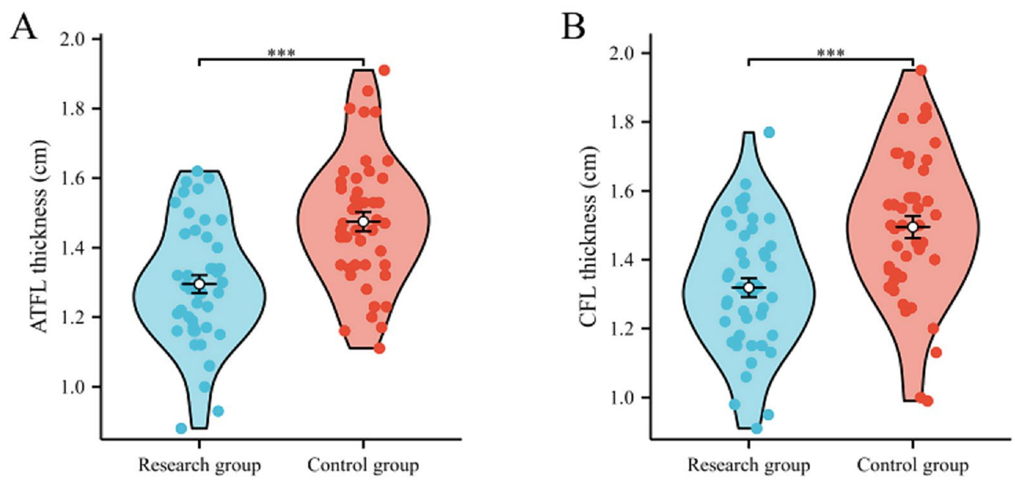

Fig. 4 Comparison of ATFL and CFL thickness at T4 between the two groups. (**A**) ATFL thickness. (**B**) CFL thickness

had smaller CFL thickness compared to the Control group (1.32 ± 0.09 vs. 1.41 ± 0.08 mm, $p < 0.001$, Cohen's d = 1.06).

Discussion

Lateral ligament injury of the ankle is a common orthopedic condition, and various treatment approaches including cold compress therapy and traditional Chinese medicine techniques are widely used in clinical practice [26, 27]. The lateral collateral ligament of the ankle is an important component for stabilizing the ankle joint, connecting the fibula and talus bone, and restricting inversion and anterior movement of the ankle joint. Damage to the lateral collateral ligament can lead to ankle joint instability, thereby affecting normal ankle function. Therefore, protecting and restoring the function of the lateral collateral ligament is crucial for ankle stability and normal movement.

The correlation between pain relief (as measured by VAS scores) and ligament healing (as observed through ultrasound) is an important finding in our study. The significant reduction in pain scores at T3 and T4 in the research group corresponds with the higher healing rate observed in musculoskeletal ultrasound imaging (82.2% vs. 57.8%). This suggests that Jingshang Gao not only provides symptomatic relief but also promotes structural healing of the damaged ligaments. The active ingredients in Jingshang Gao likely facilitate both processes simultaneously by improving local blood circulation, reducing inflammation, and supporting tissue repair mechanisms. As the ligament structure heals, the mechanical stress on surrounding tissues decreases, which further contributes to pain reduction. This bidirectional relationship between structural healing and pain relief demonstrates the comprehensive therapeutic effect of Jingshang Gao. Our results showed an interesting pattern in the VAS scores across the treatment timeline. At T1 (15 days after treatment), the control group had lower VAS scores than the research group, indicating that celecoxib provided more rapid initial pain relief. This can be attributed to the direct and immediate anti-inflammatory action of celecoxib, which inhibits COX-2 enzymes and rapidly reduces pain and inflammation [28]. In contrast, the therapeutic effects of Jingshang Gao appear to develop more gradually, with pain relief becoming more pronounced at later time points (T3 and T4). This delayed but more sustained improvement suggests that Jingshang Gao works by addressing the underlying pathology rather than merely suppressing pain symptoms. The herbal components need time to penetrate tissues, promote blood circulation, and stimulate the body's repair mechanisms. This finding aligns with traditional Chinese medicine philosophy, which often emphasizes gradual restoration of balance and function rather than rapid symptomatic relief.

The distal position of the fibula is lower than that of the tibia and the strength of the anterior talofibular ligament is relatively weak. According to literature reports [29], the anterior talofibular ligament can only withstand a load of 139 N, while the medial deltoid ligament can withstand 714 N, which is why inversion ankle sprains frequently occur and are prone to ligament damage. When the ankle joint is in a state of inversion and dorsiflexion, the anterior talofibular ligament is tense and the ligament alignment is parallel to the long axis of the bone. When twisting or local stress increases, the anterior talofibular ligament is the first to be affected and damaged. The main causes of lateral collateral ligament injuries of the ankle include sports injuries, sprains, falls, and other external forces. These external forces can result in stretching or tearing of the lateral collateral ligament, leading to ankle joint instability. Conservative treatment is chosen because lateral collateral ligament injuries of the ankle are generally mild or moderate, without obvious fractures or joint dislocations, and therefore do not require surgical treatment. Conservative treatment can alleviate pain, reduce inflammation, promote ligament healing, and avoid the trauma and complications associated with surgery. According to literature reports, satisfactory therapeutic effects can be achieved through conservative treatment for most anterior talofibular ligament injuries [30], but 10–30% of patients still have residual symptoms after conservative treatment, including persistent pain and ankle stiffness, leading to secondary chronic ankle instability [31]. For patients with chronic mechanical instability after injury, surgery is often required to resolve the problem. Additionally, in patients with lateral collateral ligament injuries of the ankle, some may also experience talar cartilage damage. Studies conducted in vitro and in vivo have shown that talar tilt occurring during ankle sprains and fractures can lead to talar cartilage damage [32, 33]. Once talar cartilage damage occurs, satisfactory treatment outcomes are often not achieved through conservative treatment, and surgery is required. Therefore, improving the healing rate of lateral collateral ligament injuries of the ankle and preventing the occurrence of chronic ankle instability are important treatment goals in clinical practice. This study demonstrates that Jingshang Gao treatment significantly improves patient outcomes in terms of pain scores and ankle stability compared to the control group.

Celecoxib, a COX-2 inhibitor, is a commonly used nonsteroidal anti-inflammatory drug that possesses anti-inflammatory, analgesic, and antipyretic effects [28]. Its oral form works by inhibiting the synthesis and release of inflammatory mediators, thereby relieving joint pain and improving inflammatory tissue. However, long-term use of oral celecoxib may lead to gastrointestinal adverse reactions, such as gastric ulcers and bleeding [34, 35]. Additionally, celecoxib may also increase the risk of cardiovascular events, therefore caution is required during its use. Traditional Chinese medicine (TCM) is widely applied in the treatment of sports injuries and emphasizes overall regulation to improve the body's overall condition and enhance self-healing ability. TCM has good safety and tolerability, and does not cause significant adverse reactions. TCM can exert its effects through various means, such as medication, acupuncture, and massage, with better overall treatment effects. Compared to oral Western medicine, TCM has certain advantages in the treatment of sports injuries, as it can comprehensively regulate the body, promote healing and functional recovery of the injured site.

Jingshang Gao is a traditional Chinese medicine preparation, and its ingredients include peach kernel, safflower, Chinese angelica, raw rehmannia, chuanxiong, red peony, threelobe, curcuma, notoginseng, and whole scorpion. These ingredients have specific therapeutic functions based on both traditional use and modern pharmacological research. Peach kernel (Prunus persica) and safflower (Carthamus tinctorius) contain active compounds that promote blood circulation and dissolve stasis by inhibiting platelet aggregation and improving microcirculation, which accelerates the blood flow to damaged tissues and speeds up the repair and healing of ligaments [36, 37]. Studies have shown that safflower extract contains hydroxysafflor yellow A, which exhibits anti-inflammatory effects by suppressing pro-inflammatory cytokine production and reducing vascular permeability [38].

Red peony (Paeonia lactiflora) and threelobe (Stephania tetrandra) have anti-inflammatory and analgesic effects that can alleviate pain and inflammatory reactions. Paeoniflorin from red peony has been shown to inhibit the production of nitric oxide, TNF-α, and IL-1β in activated macrophages [39]. Stephania tetrandra contains tetrandrine, which exhibits potent anti-inflammatory activity through the inhibition of NF-κB signaling pathways [40].

Chinese angelica (Angelica sinensis) and raw rehmannia (Rehmannia glutinosa) can promote tissue repair and regeneration, accelerating the healing process of ligaments. Research has demonstrated that polysaccharides from Angelica sinensis stimulate fibroblast proliferation and collagen synthesis, essential processes for ligament healing [41]. Rehmannia glutinosa contains catalpol and other iridoid glycosides that exhibit tissue-protective effects through antioxidant mechanisms and promotion of angiogenesis [42].

Notoginseng (Panax notoginseng) is particularly important for treating injuries, as it helps stop bleeding and promotes tissue healing. Its saponins have been shown to enhance the proliferation and migration of vascular endothelial cells, contributing to improved blood vessel formation during the healing process [43]. Whole scorpion (Buthus martensii) contains peptides with analgesic properties that act on pain receptors to provide relief from acute and chronic pain [44].

The functional improvement observed in our study, as indicated by the Kaikkonen ankle injury function scores and AOFAS scores, shows a clear relationship with the structural changes measured through ultrasound. The significantly higher functional scores in the research group at T3 and T4 correspond directly with the reduced ligament thickness measurements (ATFL and CFL). A thinner ligament indicates better resolution of inflammation and more complete structural healing, which translates to improved functional capacity. The normal, non-injured ATFL typically measures approximately 1.5–2.0 mm in thickness, and our results show that the research group's ATFL thickness (1.78 ± 0.21 mm) approached this normal range more closely than the control group (2.05 ± 0.24 mm). This structural improvement directly contributes to better ankle joint stability and function, as reflected in the higher Kaikkonen and AOFAS scores. The mechanical properties of a healed ligament with normal thickness allow for more optimal force transmission and joint stability during movement, resulting in improved functional outcomes.

The SF-36 results provide interesting insights into the broader impacts of treatment on patients' quality of life. The research group showed significantly higher Vitality (VT) scores, indicating greater energy levels and reduced fatigue compared to the control group. This improvement may be related to better pain control and functional recovery, allowing patients to engage more actively in daily activities. However, the research group also displayed lower Mental Health (MH) scores. This somewhat unexpected finding might be related to several factors. Traditional Chinese medicine treatments often require greater patient involvement and adherence to specific protocols, which could potentially increase treatment-related anxiety or stress. Additionally, while Jingshang Gao provided better long-term outcomes, the initially slower improvement in pain (as seen at T1) might have caused some psychological impact. The complex relationship between physical recovery and mental health in injury rehabilitation warrants further investigation, and future studies should consider incorporating more comprehensive psychological assessments.

Potential side effects associated with Jingshang Gao include mild skin irritation (redness, itching) at the application site in some patients, which usually resolves shortly after discontinuation. Some patients may experience a warming or tingling sensation upon application, which is considered part of the therapeutic effect rather than an adverse reaction. Allergic reactions to specific herbal components are possible but rare. In our study, no serious adverse events were reported, and mild skin irritation occurred in only 3 patients (6.7%), all of which resolved without intervention within 24–48 h. Compared to the potential systemic side effects of oral celecoxib, including gastrointestinal issues and cardiovascular risks, the topical application of Jingshang Gao appears to have a favorable safety profile.

The influence of demographic characteristics on treatment outcomes is an important consideration. In our study, age, sex, BMI, and baseline injury characteristics were similar between groups, minimizing their potential confounding effects. However, these factors may influence treatment response. Younger patients typically demonstrate faster healing due to higher metabolic rates and better tissue regeneration capacity. Female patients might respond differently to treatments due to hormonal influences on inflammation and tissue repair processes. Higher BMI could impact weight-bearing stress on the injured ankle and potentially delay healing. The severity and chronicity of the injury at baseline also significantly affect prognosis. While our regression analyses controlling for these factors maintained the significance of our primary findings, larger studies stratified by these characteristics would provide more specific insights into which patient populations might benefit most from Jingshang Gao treatment.

According to our research findings, the research group demonstrated better outcomes in pain relief during the treatment process compared to the control group. At T1, the VAS scores of the research group were lower than those of the control group, and at T3 and T4, the VAS scores of the research group remained lower. This indicates that Jingshang Gao treatment can effectively alleviate pain symptoms in patients with lateral ankle ligament injury. Furthermore, the Kaikkonen ankle injury function scores of the research group were higher than those of the control group during the treatment process, suggesting that Jingshang Gao treatment can improve ankle function and enhance patients' mobility and quality of life. The research group exhibited better functional improvement, with significantly higher functional scores than the control group, further confirming the therapeutic effects of Jingshang Gao treatment on lateral ankle ligament injury in promoting patient recovery and functional restoration. The ligament healing rate was 82.2% in the research group compared to 57.8% in the control group, indicating that Jingshang Gao treatment can promote the healing of lateral ankle ligaments and improve the cure rate. Musculoskeletal ultrasound reexamination results further support the effectiveness of Jingshang Gao treatment. At T4, the VT scores of the research group were higher than those of the control group, while the MH scores of the research group were lower. This suggests that Jingshang Gao treatment can increase patients' physical activity level, but its impact on mental health may be limited. The ATFL and CFL thicknesses in the research group were both smaller than those in the control group, which may imply that Jingshang Gao treatment can reduce ligament swelling and thickening caused by lateral ankle ligament injury, promoting ligament recovery and repair. Our research findings are consistent with relevant studies in the literature. One study found that traditional Chinese medicine ingredients such as peach kernel and safflower have anti-inflammatory and analgesic effects, which can alleviate inflammatory reactions and pain symptoms [36]. Another study found that ingredients such as Angelica sinensis and Panax notoginseng can promote tissue repair and healing [37]. These research findings mutually corroborate with our results, supporting the effectiveness of Jingshang Gao treatment for lateral ankle ligament injury.

This study has several limitations that should be acknowledged. First, this was not a randomized controlled trial, which introduces potential selection bias and limits causal inference. The lack of randomization means that unknown confounding factors might have influenced our results despite our attempts to control for baseline differences. Second, neither patients nor researchers were blinded to the treatment allocation, which could have introduced performance and detection bias. Future studies should implement double-blind designs, perhaps using a placebo ointment with similar appearance and sensation but without active ingredients.

Third, our sample size was relatively small ($n = 90$), which limits statistical power for subgroup analyses and generalizability to broader populations. Fourth, while we followed patients for three months post-treatment, longer follow-up periods would be valuable to assess the durability of treatment effects and long-term outcomes such as recurrence rates and chronic ankle instability. Fifth, we did not collect data on patient compliance with the treatment protocols, which could have influenced outcomes. Finally, we focused primarily on structural and functional outcomes, with limited assessment of physiological mechanisms. Future research should incorporate biomarker analysis to better understand the biological mechanisms underlying the observed effects.

Despite these limitations, our study provides promising evidence for the potential benefits of Jingshang Gao in treating lateral ankle sprains. The findings warrant further investigation through more rigorous randomized controlled trials with larger sample sizes, longer follow-up periods, and more comprehensive outcome measures.

Conclusion

In this study, we investigated the efficacy of Jingshang Gao, a traditional Chinese medicine preparation, in the treatment of lateral ankle sprains through musculoskeletal ultrasound observation. Our findings indicate that Jingshang Gao treatment shows promising results in relieving pain, improving ankle function, and promoting ligament healing compared to conventional treatment with oral celecoxib.

The research group demonstrated significantly lower VAS scores at later time points (T3 and T4), higher Kaikkonen ankle injury function scores, and higher AOFAS functional scores. Musculoskeletal ultrasound imaging revealed a higher healing rate of 82.2% in the research group compared to 57.8% in the control group. Additionally, the research group showed reduced ligament thickness measurements, suggesting better resolution of inflammation and more complete structural healing.

While these results are encouraging, it is important to recognize the limitations of our non-randomized study design. The observed benefits of Jingshang Gao require confirmation through randomized controlled trials before definitive claims about efficacy can be made. Future research should also explore the long-term effects of this treatment approach and identify which patient populations might benefit most from its use.Nonetheless, this study provides preliminary evidence supporting the integration of traditional Chinese medicine approaches like Jingshang Gao into the management of lateral ankle sprains. The combination of subjective functional improvements and objective structural changes observed through ultrasound suggests that this treatment modality warrants further investigation as a complementary approach in the conservative management of ankle ligament injuries.

Acknowledgements
We thank all researchers who participated in the experiments and data processing.

Author contributions
LXY, and JS designed the study. LXY, JS and XLL Experiment and data processing. SW and XLL performed the data analysis.LXY and JS wrote the manuscript. LHL revised the manuscript. LHL and SW modified the language. All authors have read and approved the final manuscript.

Funding
Jiuquan City Science and Technology Plan Project (2022MB1034).

Data availability
The data used to support the findings of this study are available online or from the corresponding author upon request.

Declarations

Ethical approval
The study was approved by the Ethics Committee of Jiuquan Traditional Chinese Medicine Hospital(Approval Number: xxx, dated June xxx).
The study strictly adheres to the Declaration of Helsinki (2013 revision).

Consent to participate
All patients have signed written informed consent.

Consent for publication
All authors provide consent for publication.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Ultrasound, Jiuquan Traditional Chinese Medicine Hospital, Jiuquan 735000, China
[2]Department of Pharmacy, Jiuquan Traditional Chinese Medicine Hospital, Jiuquan 735000, China
[3]Department of Spinal Orthopedics, Jiuquan Traditional Chinese Medicine Hospital, Jiuquan 735000, China
[4]Functional of General Medicine, The Second People's Hospital of Jiuquan City, No. 89 Youdian Street, Jiuquan, Jiuquan 735000, P.R. China

Received: 13 January 2025 / Accepted: 28 March 2025
Published online: 05 April 2025

References
1. Al-Janabi MM, Apostolides M, Southgate C, et al. Early mobilization following elective ankle lateral collateral ligament reconstruction in adults. Foot (Edinb). 2023;55:101988.
2. Guelfi M, Vega J, Malagelada F, et al. The arthroscopic all-inside ankle lateral collateral ligament repair is a safe and reproducible technique. Knee Surg Sports Traumatol Arthrosc. 2020;28(1):63–9.

3. Tang KL. [Recognition of ankle sprain: not only lateral collateral ligament injury]. Zhonghua Yi Xue Za Zhi. 2021;101(37):2930–3.
4. Wang Y, Zhu JX. Arthroscopic anatomical reconstruction of lateral collateral ligaments with ligament advanced reinforcement system artificial ligament for chronic ankle instability. World J Clin Cases. 2022;10(25):8893–905.
5. Vega J, Malagelada F, Manzanares Céspedes MC, et al. The lateral fibulotalocalcaneal ligament complex: an ankle stabilizing isometric structure. Knee Surg Sports Traumatol Arthrosc. 2020;28(1):8–17.
6. Rochelle DC, Herbert A, Ktistakis I, et al. Mechanical characterisation of the lateral collateral ligament complex of the ankle at realistic sprain-like strain rates. J Mech Behav Biomed Mater. 2020;102:103473.
7. Colin F, Barbier O, Cordier G. Role of surgery in the management of lesions of the medial collateral ligament of the ankle. Orthop Traumatol Surg Res. 2020;106(8s):S195–9.
8. Vasta S, Papalia R, Albo E, Maffulli N, Denaro V. Top orthopedic sports medicine procedures. J Orthop Surg Res. 2018;13(1):190.
9. Vega J, Guelfi M. Arthroscopic assessment and treatment of medial collateral ligament complex. Foot Ankle Clin. 2021;26(2):305–13.
10. Mansur NSB, Lemos A, Baumfeld DS, et al. Medial and lateral combined ligament arthroscopic repair for multidirectional ankle instability. Foot Ankle Orthop. 2021;6(1):2473011420986150.
11. Chanlalit C, Mahasupachai N, Sakdapanichkul C. Arthroscopic lateral collateral ligament imbrication for treatment of atraumatic posterolateral rotatory instability. J Orthop Surg (Hong Kong). 2022;30(2):10225536221113243.
12. Kohlprath R, Vuylsteke K, Van Riet R. Arthroscopic lateral collateral ligament imbrication of the elbow: short-term clinical results. J Shoulder Elb Surg. 2022;31(11):2316–21.
13. Hong CC, Calder J. Ability to return to sports after early lateral ligament repair of the ankle in 147 elite athletes. Knee Surg Sports Traumatol Arthrosc. 2023;31(10):4519–25.
14. Aicale R, Tarantino D, Maffulli N. Overuse injuries in sport: a comprehensive overview. J Orthop Surg Res. 2018;13(1):309.
15. Hou H, Zhou M, Zhou X, et al. Comparison arthroscopic reconstruction and percutaneous reconstruction of ankle lateral ligament for chronic ankle lateral instability: A protocol for a meta-analysis of comparative studies. Med (Baltim). 2022;101(45):e31926.
16. Huang L, Li M, Deng C et al. Potential therapeutic strategies for skeletal muscle atrophy. Antioxid (Basel), 2022, 12(1).
17. Zhao D, Liang GH, Pan JK, et al. Risk factors for postoperative surgical site infections after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Br J Sports Med. 2023;57(2):118–28.
18. Li Q, Tu Y, Chen J, et al. Reverse anterolateral drawer test is more sensitive and accurate for diagnosing chronic anterior talofibular ligament injury. Knee Surg Sports Traumatol Arthrosc. 2020;28(1):55–62.
19. Sowa C, Annett S. Musculoskeletal sports ultrasound. Curr Sports Med Rep. 2021;20(6):277–8.
20. Gitto S, Messina C, Vitale N, et al. Quantitative musculoskeletal ultrasound. Semin Musculoskelet Radiol. 2020;24(4):367–74.
21. Perone MV, Yablon CM. Musculoskeletal ultrasound in the emergency department: is there a role??. Semin Roentgenol. 2021;56(1):115–23.
22. Ding SL, Ji LF, Zhang MZ, et al. Safety and efficacy of intra-articular injection of platelet-rich plasma for the treatment of ankle osteoarthritis: a systematic review and meta-analysis. Int Orthop. 2023;47(8):1963–74.
23. Lau JT, Mahomed NM, Schon LC. Results of an internet survey determining the most frequently used ankle scores by AOFAS members. Foot Ankle Int. 2005;26(6):479–82.
24. Yin Q, Rui Y, Wu Y, et al. Surgical treatment of avulsion fracture around joints of extremities using Hook plate fixation. BMC Musculoskelet Disord. 2019;20(1):200.
25. Al-Ibrahimy AS, Rabea IS. Evaluation of general health status in diabetic patients using short form health survey (SF-36). Curr Diabetes Rev. 2023;19(9):e081420184858.
26. Drakos M, Hansen O, Kukadia S. Ankle instability. Foot Ankle Clin. 2022;27(2):371–84.
27. Chang SH, Morris BL, Saengsin J, et al. Diagnosis and treatment of chronic lateral ankle instability: review of our Biomechanical evidence. J Am Acad Orthop Surg. 2021;29(1):3–16.
28. Krasselt M, Baerwald C. Celecoxib for the treatment of musculoskeletal arthritis. Expert Opin Pharmacother. 2019;20(14):1689–702.
29. Wire J, Hermena S, Slane VH. Ankle Fractures [M]. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Shady Hermena declares no relevant financial relationships with ineligible companies. Disclosure: Valori Slane declares no relevant financial relationships with ineligible companies; StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC. 2023.
30. Corte-Real N, Caetano J. Ankle and syndesmosis instability: consensus and controversies. EFORT Open Rev. 2021;6(6):420–31.
31. Kim JS, Kim MS, Kim DK, et al. Magnetic resonance imaging characteristics of a lateral ligament injury in acute ankle sprains among athletes. Orthop J Sports Med. 2023;11(11):23259671231207688.
32. Jeon JY. [Diagnosis of lateral ankle ligament injury in the evaluation of chronic lateral ankle instability]. Taehan Yongsang Uihakhoe Chi. 2021;82(6):1402–12.
33. Brun OL, Stødle AH, Molund M et al. [Lateral ankle ligament injuries]. Tidsskr nor Laegeforen, 2023, 143(6).
34. Puljak L, Marin A, Vrdoljak D, et al. Celecoxib for osteoarthritis. Cochrane Database Syst Rev. 2017;5(5):Cd009865.
35. Bąk U, Krupa A. Challenges and opportunities for celecoxib repurposing. Pharm Res. 2023;40(10):2329–45.
36. Elshamy AI, Abdallah HMI, El Gendy AE, G, et al. Evaluation of Anti-inflammatory, antinociceptive, and antipyretic activities of Prunus persica Var. Nucipersica (Nectarine) kernel. Planta Med. 2019;85(11–12):1016–23.
37. Nai J, Zhang C, Shao H, et al. Extraction, structure, Pharmacological activities and drug carrier applications of Angelica sinensis polysaccharide. Int J Biol Macromol. 2021;183:2337–53.
38. Wei X, Liu H, Sun X, et al. Hydroxysafflor yellow A protects rat brains against ischemia-reperfusion injury by antioxidant action. Neurosci Lett. 2005;386(1):58–62.
39. Wu D, Chen J, Zhu B, et al. Paeoniflorin inhibits inflammatory responses in mice with allergic contact dermatitis by regulating the balance between inflammatory and anti-inflammatory cytokines. Inflamm Res. 2013;62(12):1035–44.
40. Choi HS, Kim HS, Min KR, et al. Anti-inflammatory effects of Fangchinoline and tetrandrine. J Ethnopharmacol. 2000;69(2):173–9.
41. Tang C, Zhou R, Cao K, et al. Current progress in the hypoglycemic mechanisms of natural polysaccharides. Food Funct. 2023;14(10):4490–506.
42. Ren H, Li Z, Gao R, et al. Structural characteristics of Rehmannia glutinosa polysaccharides treated using different decolorization processes and their antioxidant effects in intestinal epithelial cells. Foods. 2022;11(21):3449.
43. Hong SJ, Wan JB, Zhang Y, et al. Angiogenic effect of saponin extract from Panax Notoginseng on HUVECs in vitro and zebrafish in vivo. Phytother Res. 2009;23(5):677–86.
44. Guan R, Wang M, Wu J, et al. Advances in the studies of roles of Rho/Rho-kinase in diseases and the development of its inhibitors. Eur J Med Chem. 2013;70:613–22.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.