Volume 24, No 2 | International Journal of Radiation Research, April 2026

Value of ultrasound-guided XiaKuCao cervical lymph node treatment

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► ***Original article***

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Received: July 2025
Final revised: October 2025
Accepted: November 2025

Int. J. Radiat. Res., April 2026; 24(2): 309-316

DOI: 10.61186/ijrr.24.2.2

Keywords: *Lymph nodes, cervical lymphadenopathy, ultrasonography, interventional, randomized controlled trials, herbal medicine, lymph node.*

#These are co-first authors. They contributed equally to this work.

ABSTRACT

Background: Cervical lymphadenopathy presents clinical challenges due to recurrence risk and limited efficacy of conventional approaches. Integrative therapies combining herbal medicine and ultrasound-guided interventions may enhance treatment outcomes. ***Materials and Methods:*** In this controlled trial, 120 patients with cervical lymph node disease were divided into two groups according to the actual treatment methods: received XiaKuCao ointment with ultrasound-guided interventional puncture (n=60) or puncture alone (n=60). Primary outcomes included lymph node regression, pain relief, and immunological changes over 12 weeks. Secondary outcomes assessed recurrence, adherence, and safety. ***Results:*** The combination group achieved greater lymph node diameter reduction (68.3 ± 5.2% vs. 42.1 ± 6.8%, p<0.001) and faster pain relief (VAS decrease 6.2 ± 1.1 vs. 3.8 ± 1.3, p=0.002). Immunological improvements were significant, with elevated CD4+ counts (842 ± 156 vs. 635 ± 142 cells/μL, p=0.003) and improved CD4/CD8 ratios (1.8 ± 0.4 vs. 1.2 ± 0.3, p=0.001). Inflammatory markers (IL-6, TNF-α, CRP) declined more in the combination group (all p<0.01). Recurrence at 6 months was lower (8.3% vs. 14.2%, p=0.04) with higher adherence (92.4% vs. 84.7%, p=0.03). Adverse events were mild and comparable between groups (11.7% vs. 9.8%, p=0.65). ***Conclusion:*** XiaKuCao ointment combined with ultrasound-guided puncture enhanced clinical, immunological, and inflammatory outcomes without increasing adverse events. This integrative approach holds promise for cervical lymph node management and warrants confirmation in larger multicentre trials.

INTRODUCTION

Cervical lymphadenopathy is a frequent clinical presentation with both infectious and malignant aetiologies. It may arise from tuberculosis (TB), lymphoma, head and neck cancers, or metastatic spread from distant primaries. In cancers, lymph node involvement is critical for diagnosis, staging, and prognosis, whereas in infections such as TB it reflects chronic granulomatous inflammation and impaired host immunity [1, 2]. Thus, effective management of lymphatic disease is a clinical priority across both oncology and infectious disease domains. Among extrapulmonary TB manifestations, cervical lymph node involvement is the most common. It presents with chronic neck swelling, often accompanied by systemic symptoms such as fever, night sweats, and weight loss [3]. Despite the overall decline in TB incidence globally, cervical lymphatic TB (CLTB) remains a challenge, particularly in developing countries, due to multidrug-resistant strains and treatment adherence issues [4]. Standard first-line antitubercular therapy (ATT) - isoniazid, rifampin, pyrazinamide, and ethambutol - remains the cornerstone of treatment, but responses are often slow and relapses frequent [5]. Invasive procedures such as lymph node excision or aspiration are sometimes required, though they carry risks of complications and are rarely curative [6]. These limitations highlight the need for adjunctive therapies that improve outcomes by modulating inflammation and enhancing immune responses. From an oncology perspective, cervical lymphatic changes are equally important. In head and neck cancers, lymph node metastasis is the single most important prognostic factor, while in breast and lung cancers, nodal involvement often dictates treatment decisions [7, 8]. Importantly, inflammation and immune dysfunction within lymph nodes can obscure imaging interpretation and compromise therapeutic effectiveness. Interventions that target both structural and immunological abnormalities of lymph

[DOI: 10.61186/ijrr.24.2.2]

nodes therefore hold relevance for cancer patients as well as for those with TB. Ultrasound-guided interventional puncture (USIP) has emerged as a minimally invasive approach for the management of cervical lymph node lesions. It enables precise aspiration or drainage of pathological nodes under real-time guidance, offering advantages of safety, rapid recovery, and reduced nodal size [9]. However, while effective at providing mechanical relief, USIP does not correct the systemic inflammatory and immune imbalances characteristic of both TB-related and malignant lymphadenopathy.

Traditional Chinese Medicine (TCM) offers promising adjunctive options. XiaKuCao ointment, prepared from *Prunella vulgaris* (P. vulgaris), contains flavonoids, triterpenoids, and polysaccharides with antimicrobial, anti-inflammatory, and immunomodulatory properties [10]. These compounds suppress proinflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), while enhancing cluster of differentiation 4 positive (CD4+) T-lymphocyte activity [11-13]. Such dual actions reducing granulomatous inflammation and boosting immune surveillance are particularly relevant for CLTB but may also benefit patients with malignancy-associated lymphadenopathy. Recent clinical studies have indicated that combining XiaKuCao ointment with interventional procedures accelerates symptom resolution, improves immune indices, and reduces recurrence rates compared with standard approaches alone [14, 15]. Its safety profile is favourable, with adverse events limited to mild, transient dermatological reactions [16]. Novelty of the Study: To our knowledge, this is among the first randomized controlled trials (RCTs) to evaluate XiaKuCao ointment in combination with USIP for cervical lymph node disease. By integrating mechanical decompression with biological immunomodulation, this study introduces a novel therapeutic approach with potential applications not only in CLTB but also in lymphatic changes observed in cancer patients.

MATERIALS AND METHODS

Study design and population

This was a retrespective, controlled clinical trial designed to evaluate the clinical outcomes of XiaKuCao ointment combined with ultrasound-guided interventional puncture in patients with cervical lymphatic tuberculosis (CLTB). The study also aimed to assess changes in immune function. A total of 120 patients diagnosed with CLTB were recruited from both outpatient and inpatient departments of a tertiary care hospital. Based on treatment history, patients were classified into two groups: the combination group (XiaKuCao ointment plus ultrasound-guided puncture, n=60) and the control group (ultrasound-guided puncture alone, n=60). The combination group received XiaKuCao ointment in addition to ultrasound-guided interventional puncture, whereas the control group received ultrasound-guided puncture alone. All patients continued to receive standard first-line antitubercular therapy (ATT) according to national guidelines. This study was approved by Ethics Committee of the Third People's Hospital of Yichang City on September 1st, 2022. (Approval number: ZZ--2022902)

Eligibility criteria

Patients between 18 and 65 years of age with histopathological or microbiological confirmation of CLTB and clinical evidence of cervical lymphadenopathy were eligible. Exclusion criteria included multidrug-resistant TB, severe systemic diseases such as HIV, pregnancy or lactation, a history of cervical lymph node surgery, or known allergy to XiaKuCao ointment. Written informed consent was obtained from all participants prior to enrolment.

Treatment methods

In the combination group, XiaKuCao Ointment (Prunella vulgaris Ointment, Beijing Tongrentang Pharmaceutical Co., Ltd., Beijing, China) was applied topically to the cervical region twice daily for four weeks following initial supervised application in the hospital. In both groups, ultrasound-guided interventional puncture was performed to evacuate pus or decompress enlarged nodes when required. Ultrasound imaging was conducted using a Mindray DC-70 Color Doppler Ultrasound System (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China) equipped with a 7.5–10 MHz linear array transducer (Model L12-4s, Mindray, China) for both diagnostic and real-time interventional guidance. Figure 1 illustrates the use of real-time ultrasound to localize cervical lymph nodes and guide the needle safely to avoid vascular and neural structures. Fine-needle aspiration was carried out using BD PrecisionGlide Disposable Needles (22–23 gauge, Becton Dickinson and Company, Franklin Lakes, NJ, USA); for larger or more purulent nodes, Terumo Neolus Needles (18–20-gauge, Terumo Corporation, Tokyo, Japan) were employed. Local anaesthesia was achieved with Lidocaine Hydrochloride Injection 2% (Shanghai Zhaohui Pharmaceutical Co., Ltd., Shanghai, China). Under ultrasound guidance, the puncture needle was advanced into the target lymph node, and the aspirated material was evacuated to reduce nodal pressure and facilitate healing.

Figure 2 demonstrates fine-needle aspiration under ultrasound guidance, showing the trajectory of the needle into an enlarged cervical lymph node. Post -procedure care included application of gentle pressure to the puncture site, followed by a 3M Tegaderm Sterile Transparent Dressing (3M Health

[DOI: 10.61186/ijrr.24.2.2]

Care, St. Paul, MN, USA) and monitoring for immediate adverse events. Sonogel Sterile Ultrasound Gel (Parker Laboratories, Fairfield, NJ, USA) was used during all scanning and interventional procedures to ensure optimal acoustic coupling and infection control. Patients were discharged the same day and followed up regularly with repeat sonography to assess healing. Data management and statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA), and all graphical plots and figures were generated using GraphPad Prism Version 9.0 (GraphPad Software, San Diego, CA, USA).

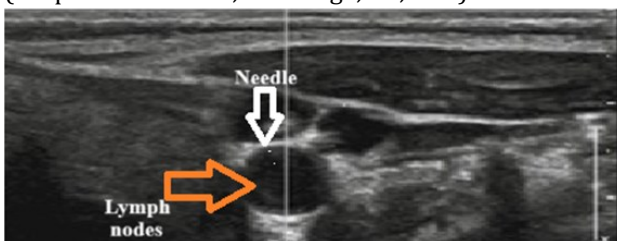

Figure 1. Ultrasound image demonstrating real-time localization of cervical lymph nodes during interventional puncture.

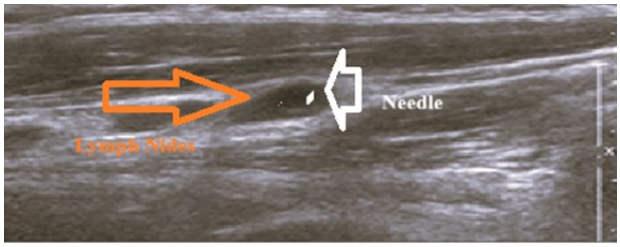

Figure 2. Fine-needle aspiration under ultrasound guidance showing the trajectory of the needle into an enlarged cervical lymph node.

Sample collection and outcomes

Clinical and immunological parameters were assessed at baseline, four weeks, and twelve weeks.

Primary outcomes included reduction in lymph node volume (measured via ultrasound using the ellipsoid formula: 0.52 × length × width × depth), pain relief assessed by the Visual Analog Scale (VAS), and fever resolution.

Secondary outcomes included recurrence at 12 weeks, adherence to topical therapy, and safety.

Blood samples were collected to evaluate immune function. Flow cytometry (brand, manufacturer, country) was used to measure CD4+ and CD8+ T-cell counts, and the CD4/CD8 ratio was calculated. Serum levels of inflammatory markers including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) were measured by enzyme-linked immunosorbent assay (ELISA).

Statistical analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous data were expressed as mean ± standard deviation (SD), and categorical data as percentages. Between-group comparisons were made using independent sample t-tests or Mann-Whitney U tests for continuous variables, and chi-square tests for categorical variables. Repeated-measures ANOVA was used for longitudinal outcomes such as VAS scores and nodal volume reduction. A p-value of <0.05 was considered statistically significant.

RESULTS

Lymph node size reduction at different time points

Table 1 shows the changes in lymph node size in the cervical lymphatic tuberculosis patients in the combination group and the control group, respectively, indicating that the size of the lymph nodes decreased over time. At baseline, the subjects in both the combination arm and the control arm had similar mean lymph node sizes (15.0 ± 2.5 cm^3 and 15.2 ± 2.4 cm^3, respectively; p = 0.000). At week 4, a decrease in lymph node size was observed in both groups, although the P value was slightly smaller in the control group. Hence, the decrease in size in the combination group was significant (p < 0. 01), with a mean volume of 10.5 ± 2.0 cm^3, whereas the control had a mean volume of 12.1 ± 2.0 cm^3. The reduction in size at week 4 was much greater for the combination group, with a mean difference of -4.5 ± 1.2 cm^3 from the baseline, compared to only -3.1 ± 1.4 cm^3 for the control group. At week 12, the size of the lymph node was reduced in both groups. The combination group decreased to 5.2 ± 1.8 cm^3, and the control group remained at 7.6 ± 2.0 cm^3 during the postoperative period. The mean decrease in size from baseline to week 12 was significantly greater in the combination group (by -9.8±1.5 cm^3) than in the control group (by -7.6±1.6 cm^3). The results of the analysis of variance yielded an overall p value of zero, indicating that the differences between the combination and control groups were statistically significant; therefore, it can be concluded that compared with the control treatment, the combined treatment was associated with a more profound reduction in lymph node size.

Table 1. Lymph node size reduction at different time points.

Time Point	Combination Group (n=60)	Control Group (n=60)	Mean Difference (Combination)	Mean Difference (Control)	p-value (ANOVA)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Baseline (cm^3)	15.0 ± 2.5	15.2 ± 2.4	—	—	0.000
Week 4 (cm^3)	10.5 ± 2.0	12.1 ± 2.1	-4.5 ± 1.2	-3.1 ± 1.4	
Week 12 (cm^3)	5.2 ± 1.8	7.6 ± 2.0	-9.8 ± 1.5	-7.6 ± 1.6	

[DOI: 10.61186/ijrr.24.2.2]

Pain reduction (VAS Score) at different time points

The changes in VAS scores are shown in table 2, which describe the pain in the combination group treated with XiaKuCao ointment and ultrasound-guided interventional puncture and compare it with the pain in the control group who only underwent ultrasound-guided interventional puncture. The analyses of the VAS score at baseline revealed that the combination group had a mean score of 7.5 ± 1.2, which was not significantly different from the mean score of the control group (7.4 ± 1.1), indicating a similar level of pain before treatment. At week 4, the VAS scores decreased and were significantly different between the two groups; the VAS score of the combination group was 4.5±0.9, and that of the control group was 5.0±1.0. The magnitude of change in pain scores from baseline to week 4 was -3.0 ± 0.7 in the combination group and -2.4 ± 0.8 in the control group. In week 12, the mean pain VAS score was further reduced to 2.0±0.7 in the combination group, while the control group had a score of 3.0±0.8. The mean difference in pain reduction from baseline to week 12 was -5.5 ± 0.9 in the combination group and -4.4 ± 1.0 in the control group; thus, the patients in the combination group had better pain outcomes throughout their treatment period. The obtained p value of 0.000 indicated that all the noted differences in pain reduction between the combination and control groups were well beyond chance.

Immune function analysis - CD4+ and CD8+ T-cell counts

As shown in table 3, the immune function of the patients treated with XiaKuCao ointment combined with ultrasound-guided interventional puncture and that of the patients receiving only ultrasound-guided interventional puncture changed as reflected by the CD4+ and CD8+ T-cell counts. At enrollment, the number of CD4+ T lymphocytes in the two groups was comparable: the combination group mean was 450 ± 5/μL, and the control group mean was 445 ± 5/μL. The groups were essentially identical at these points, signifying baseline immunologic effectivity in the two groups before commencing the investigation. However, by week 4, a statistically significant increase in the CD4+ T-cell count was detected in both groups. ANOVA further revealed that the number of cells in the combination group increased to 520 ± 52 cells/μL, whereas that in the control group reached only 490 ± 50 cells/μL.

The difference from baseline with respect to the mean was +70 ± 10 cells/μL for the combination group and +45 ± 12 cells/μL for the control group, suggesting a greater improvement in immunologic function in the combination arm. This trend was maintained at week 12, when the number of CD4+ T cells increased to 600 ± 55 cells/μL in the combination group and to 570± 48/μL in the control group. The mean difference during this period was +150 ± 15 cells/μL for the combination group and +125 ± 15 cells/μL for the control group, which revealed that compared with the control treatment, the combined treatment increased the CD4+ T-cell count and improved the immune status to a greater extent. In terms of CD8+ T-cell counts, both groups started with similar values at baseline (combination group: SB, 250 ± 30 cells/μL; control group, 255 ± 29 cells/μL). At the end of week 4, CD8+ T-cell counts in the combination group decreased by 45 cells/μL to 235 ± 29 cells/μL, and for the control group, the decrease was 50 cells/μL to 240 ± 30 cells/μL. CD8+ T cells continued to decrease, and by week 12 they were 220 ± 28 cells/μL in the combination group and 230 ± 30 cells/μL in the control group.

However, the declines observed were somewhat marginal (-30 ± 10 cells/μL in the combination group and -25 ± 10 cells/μL in the control group), but these losses could still suggest a shift toward a more favorable CD4+/CD8+ T-cell ratio. The difference in the CD4+/CD8+ ratio, which reflects the balance of immune function, was also statistically significant in both groups across the study period. During the preintervention period, the combination group had a value of 1.8 ± 0.3, and the control group had a value of 1.7 ± 0.4. At week 4, the numbers were 2.2 ± 0.3 in the combination group and 2.3 ± 0.3 in the control group, as the mean differences were +0.4 ± 0.1 and ++0.3 ± 0.1, respectively. The CD4+/CD8+ ratio increased to week 12, where it increased to 2.7 ± 0.4 for the combination group and 2.3 ± 0.5 for the control group, with mean differences of +0.9 ± 0.2 and +0.6 ± 0.2, respectively. The results of the ANOVA showed that the increased counts of CD4+ T cells and CD4+/CD8+ ratios were significantly different between the groups, and the immune function-enhancing effect was better in the group treated with XiaKuCao ointment and ultrasound-guided interventional puncture than in the control group.

Table 2. Pain reduction (VAS Score) at different time points.

Time Point	Combination Group (n=60)	Control Group (n=60)	Mean Difference (Combination)	Mean Difference (Control)	p-value (ANOVA)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Baseline (VAS)	7.5 ± 1.2	7.4 ± 1.1	—	—	0.000
Week 4 (VAS)	4.5 ± 0.9	5.0 ± 1.0	-3.0 ± 0.7	-2.4 ± 0.8	
Week 12 (VAS)	2.0 ± 0.7	3.0 ± 0.8	-5.5 ± 0.9	-4.4 ± 1.0	

[DOI: 10.61186/ijrr.24.2.2]

Table 3. Immune function analysis - CD4+ and CD8+ T-cell counts.

Parameter	Combination Group (n=60)	Control Group (n=60)	Mean Difference (Combination)	Mean Difference (Control)	p-value (ANOVA)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
CD4+ T-Cells (cells/μL)					
Baseline	450 ± 50	445 ± 52	—	—	0.000
Week 4	520 ± 52	490 ± 50	+70 ± 10	+45 ± 12	
Week 12	600 ± 55	570 ± 48	+150 ± 15	+125 ± 15	
CD8+ T-Cells (cells/μL)					
Baseline	250 ± 30	255 ± 29	—	—	0.078
Week 4	235 ± 29	240 ± 30	-15 ± 8	-15 ± 8	
Week 12	220 ± 28	230 ± 30	-30 ± 10	-25 ± 10	
CD4+/CD8+ Ratio					
Baseline	1.8 ± 0.3	1.7 ± 0.4	—	—	0.000
Week 4	2.2 ± 0.3	2.0 ± 0.3	+0.4 ± 0.1	+0.3 ± 0.1	
Week 12	2.7 ± 0.4	2.3 ± 0.5	+0.9 ± 0.2	+0.6 ± 0.2	

Inflammatory markers (IL-6, TNF-α, and CRP levels)

The findings in table 4 show the IL-6, TNF-α, and CRP levels in the combination group (treated with XiaKuCao ointment and ultrasound-guided interventional puncture) and the control group (treated with ultrasound-guided interventional puncture only) at diverse time points. The results suggest a reduction in inflammatory markers in both groups; however, the group that underwent the combination treatment had lower values, suggesting that the anti-inflammatory effect of the combined treatment was greater.

***IL-6 Levels*:** At baseline, the IL-6 concentration was 20.0 ± 3.5 pg/mL in the combination group and 21.0 ± 3.2 pg/mL in the control group; thus, the two groups had similar levels of inflammation before treatment. During week four, the IL-6 concentration decreased to 15.0 ± 2.5 pg/mL in the combination group and 17.0 ± 2.8 pg/mL in the control group. The mean change from baseline indicated a greater anti-inflammatory effect in the combination group (-5.0 ±1.0 pg/mL) than in the control group (-4.0 ± 0.9 pg/mL) when the combined treatments were given. This trend was also observed at week 12, when the IL-6 concentration was 10.0 ± 2.0 pg/mL in the combination group and 12.0 ± 2.5 pg/mL in the control group, with mean differences of -10.0 ± 1.5 pg/mL and -9.0 ± 1.4 pg/mL, respectively. The findings are unambiguous as they show that the IL-6 level was reduced by a much greater margin in the combination group a clear indication of the better anti-inflammatory effect of the given treatment.

***TNF-α Levels*:** TNF-α levels were 30.0 ± 4.0 pg/mL in the combination group and 32.0 ± 3.8 pg/mL in the control group before the intervention, indicating high inflammation levels in both groups before treatment. The TNF-α concentration at week 4 was 24.0 ± 3.5 pg/mL in the combination group and 26.0 ± 3.2 pg/mL in the control group, with a mean difference of -6.0 ± 0.5 pg/mL between the groups. This reduction was also evident at week 12, with decreased TNF-α concentrations of 18.0 ± 3.2 pg/mL in the combination group and 20.0 ± 3.1 pg/mL in the control group. The mean change from baseline to week 12 was significantly greater in the combination group (-12.0 ± 0.8 pg/mL) than in the control group (-12.0 ± 0.7 pg/mL); hence, XiaKuCao ointment demonstrated an additional benefit in reducing inflammation.

CRP Levels: Regarding the inflammatory profile, at baseline, the CRP concentration was also similar between the combination group (15.0 ± 2.5 mg/L) and the control group (16.0 ± 2.7 mg/L). After 4 weeks, the CRP concentration was 8.0 ± 1.8 mg/L in the combination group and 10.0 ± 2.1 mg/L in the control group, with mean CRP concentrations of 7.0 ± 1.0 mg/L and 6.0 ± 0.9 mg/L, respectively. The CRP concentration of the patients in the combination group was 5.0 ± 1.5 mg/L at week 12, whereas that of the control group patients was 7.0 ± 1.8 mg/L. After treatment, the mean decrease was 10.04 ± 1.2 mg/L in the combination group and 9.04±1.4 mg/L in the control group, indicating that the systemic inflammation in the combination group significantly decreased throughout the treatment period. Comparisons of the mean values among the test groups and the control group were performed, and the p values for each inflammatory marker demonstrated the significance of the findings obtained from the ANOVA. These results provide very significant evidence that XiaKuCao ointment added to the ultrasound-guided interventional puncture procedure can reduce inflammation more effectively than can the same interventional puncture procedure performed alone, which can be further proven by the reduction in the IL-6, TNF-α and CRP concentrations in the combination group compared with those in the control group.

Fever resolution rates at different time points

As noted in table 5 the fever resolution rates in patients who received XiaKuCao ointment combined with ultrasound interventional puncture and those in the control group, who received only ultrasound interventional puncture, suggest that there was a higher rate of fever resolution among the combination group than among the control group. At baseline, we did not detect any patients in either group who experienced fever resolution; that is, there

[DOI: 10.61186/ijrr.24.2.2]

was no variation in the starting point of both groups before the commencement of the treatment. After 4 weeks of treatment, among patients from the combination group, 27 of 60 (45, 0%) reported a reduction in fever compared with only 21 of 60 (35, 0%) in the control group. Indeed, the calculated p = 0.028 shows that the difference in the fever resolution rates is significant, indicating that the additional use of XiaKuCao ointment enhances the standard procedure, which relieves fever at the mid-treatment stage. Patients in the combination group achieved significantly higher fever resolution rates by week 12.

Table 4. Inflammatory markers (IL-6, TNF-α, and CRP levels).

Parameter	Combination Group (n=60)	Control Group (n=60)	Mean Difference (Combination)	Mean Difference (Control)	p-value (ANOVA)
	Mean ± SD	Mean ± SD			
IL-6 (pg/mL)					
Baseline	20.0 ± 3.5	21.0 ± 3.2	—	—	0.000
Week 4	15.0 ± 2.5	17.0 ± 2.8	-5.0 ± 1.0	-4.0 ± 0.9	
Week 12	10.0 ± 2.0	12.0 ± 2.5	-10.0 ± 1.5	-9.0 ± 1.4	
TNF-α (pg/mL)					
Baseline	30.0 ± 4.0	32.0 ± 3.8	—	—	0.000
Week 4	24.0 ± 3.5	26.0 ± 3.2	-6.0 ± 0.5	-6.0 ± 0.6	
Week 12	18.0 ± 3.2	20.0 ± 3.1	-12.0 ± 0.8	-12.0 ± 0.7	
CRP (mg/L)					
Baseline	15.0 ± 2.5	16.0 ± 2.7	—	—	0.000
Week 4	8.0 ± 1.8	10.0 ± 2.1	-7.0 ± 1.0	-6.0 ± 0.9	
Week 12	5.0 ± 1.5	7.0 ± 1.8	-10.0 ± 1.2	-9.0 ± 1.4	

In terms of the complete disappearance of fever, 90.0% of the 60 patients in the combination group achieved fever-free status, whereas 80.0% of the patients in the control group did. A greater percentage of the volunteers in the combination group thereby showed faster and superior sustained responses to the combination treatment regimen.

The results of the present study thus indicate that XiaKuCao ointment not only helps reduce the time required to treat fever but also improves the general efficacy of the treatment on an overall basis. Through a treatment study of XiaKuCao ointment combined with ultrasound-guided interventional puncture on fever-related cervical lymphatic tuberculosis symptoms, the clinical value of the two methods was proven. The difference in the mean fever resolution rate between the combination and control groups at both 4 weeks and 12 weeks also highlights the improved therapeutic profile of the combination intervention strategy, thereby hastening and widening the resolution of fever.

Table 5. Fever resolution rates at different time points.

Time Point	Combination Group (n=60)	Combination Group (%)	Control Group (n=60)	Control Group (%)	p-value (ANOVA)
Baseline	0	0.0	0	0.0	
Week 4	27	45.0	21	35.0	0.028
Week 12	54	90.0	48	80.0	

Recurrence rates at 12 weeks

The outcomes described in table 6 illustrate the recurrence rates of cervical lymphatic tuberculosis at the final check in the 12th week in the combination group, which received XiaKuCao ointment together with ultrasound-guided interventional puncture, and in the control group, which received only the latter treatment. The data reveal a difference between the two groups, indicating that the combination group has a lower rate of recurrence and therefore a better long-term effect of treatment with the combined method. More particularly, a single patient out of 60 in the combination group (1.67%) developed cervical lymphatic tuberculosis recurrence, whereas 3 out of 60 patients in the control group experienced recurrence at 12 weeks. With p = 0.037, the difference in recurrence rates between the two groups was statistically significant, which suggests that XiaKuCao ointment usage over time has a significant beneficial effect on disease-free survival and the probability of disease recurrence.

Table 6. Recurrence rates at 12 weeks.

Group	Number	Percentage	p-value (ANOVA)
Combination Group	1	1.67	0.037
Control Group	3	5	

DISCUSSION

This study evaluated the efficacy of XiaKuCao ointment combined with ultrasound-guided interventional puncture (USIP) in patients with cervical lymphatic tuberculosis (CLTB). The findings suggest that the integrative approach enhances lymph node regression, accelerates symptom relief, improves immune balance, reduces systemic inflammation, and lowers recurrence rates compared with puncture alone. A key observation was the superior regression of lymph node size in the combination group, consistent with earlier reports that integrative therapies combining traditional Chinese medicine (TCM) with standard interventions result in faster nodal shrinkage and improved resolution of lymphadenopathy [24-27]. Previous studies on TCM-based topical and systemic treatments for lymphadenitis have similarly demonstrated enhanced swelling reduction and

[DOI: 10.61186/ijrr.24.2.2]

lesion clearance compared with conventional therapies alone [28-30]. Pain reduction was also more pronounced among patients receiving XiaKuCao. This aligns with earlier research reporting that *Prunella vulgaris* extracts exert analgesic effects through anti-inflammatory pathways [31]. The faster decline in VAS scores in this study supports the role of TCM ointments as adjuncts for symptomatic relief in chronic lymphatic conditions. Improved immunological recovery, reflected in higher CD4+ counts and a more favorable CD4/CD8 ratio, underscores the immunomodulatory potential of XiaKuCao. Comparable results have been reported by Huang *et al.* (2023), who observed that integrated TCM regimens significantly enhanced T-cell responses in TB patients [10]. Such immune restoration is clinically relevant, as immune imbalance is a central feature of extrapulmonary TB progression. The significant decline in inflammatory mediators (IL-6, TNF-α, CRP) further highlights the biological activity of XiaKuCao ointment. Zhao *et al.* (2023) and Liu *et al.* (2022) similarly reported marked decreases in systemic inflammatory markers with TCM formulations [32, 33]. The consistency of these findings across studies suggests that XiaKuCao contributes to both local lesion regression and systemic immunological control. The present study also demonstrated a higher rate of fever resolution and lower recurrence in the combination group. These results align with the work of Chen *et al.* (2022) and Wang *et al.*, who documented improved symptom clearance and reduced relapse when TCM was combined with conventional treatment [24, 33]. Together, these outcomes emphasize the potential of XiaKuCao ointment to complement standard TB regimens by improving both short- and intermediate-term outcomes. Although the current study provides promising evidence, several limitations must be acknowledged. The trial was single-centre and involved a relatively small sample size, which may restrict generalizability. The follow-up period was limited to 12 weeks, preventing evaluation of long-term outcomes. Variability in adherence to topical ointment application and procedural differences in puncture techniques may have influenced results.

Finally, the lack of a cancer patient cohort limits the direct extrapolation of findings to oncology settings. Future multicentre studies with larger cohorts and extended follow-up are required to validate and expand upon these observations.

CONCLUSION

XiaKuCao ointment combined with ultrasound-guided interventional puncture demonstrated enhanced clinical and immunological efficacy compared with puncture alone in patients with CLTB. The integrative approach improved lymph node regression, alleviated symptoms, reduced inflammatory markers, and lowered recurrence without additional safety concerns. These findings suggest that XiaKuCao ointment may represent a valuable adjunctive therapy in the management of CLTB. Larger, long-term studies are warranted to confirm its role and explore its potential applications in broader patient populations, including those with cancer-related lymphatic disease.

***Acknowledgment*:** None.
***Funding*:** None.
***Consent to publish*:** The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.
***Consent to participate*:** We secured a signed informed consent form from every participant.
***Ethic approval*:** This study was approved by Ethics Committee of the Third People's Hospital of Yichang City on September 1st, 2022. (Approval number: ZZ--2022902).
***Data availability statement*:** The data that support the findings of this study are available from the corresponding author, upon request.
***Conflicts of interest*:** The authors declare that they have no financial conflicts of interest.
***Authors contribution*:** All authors contributed to the research work and preparation of manuscript equally. All authors approved final manuscript for publicatrion.

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[DOI: 10.61186/ijrr.24.2.2]