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# Retrospective cohort study on the effects of corticosteroid combined with focused ultrasound therapy on lesion size and inflammatory markers in patients with granulomatous mastitis

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**Abstract**: To evaluate the efficacy and safety of corticosteroid therapy combined with low intensity focused ultrasound (LIFU) in treating granulomatous mastitis. A retrospective cohort study was conducted with 284 patients diagnosed with granulomatous mastitis at The Fourth Hospital of Shijiazhuang from July 2021 to October 2024. Patients were grouped into the Combination Therapy (CT) group (n = 126) and the Single Treatment (ST) group (n = 158), receiving corticosteroids only. The primary outcomes measured were lesion size, inflammatory markers (IL-6, CRP, TNF-α), and patient-reported pain levels. Baseline characteristics were similar between both groups. The CT group showed significantly higher overall effectiveness, with a recovery rate of 70.63% compared to 62.03% in the ST group ($P = 0.005$). Time to symptom resolution, including pain disappearance and lesion size reduction, was significantly shorter in the CT group ($P < 0.05$). Post-treatment, the CT group demonstrated a significant reduction in serum IL-6, CRP, and TNF-α levels compared to the ST group ($P < 0.05$ for all markers). Corticosteroids combined with LIFU therapy significantly improve clinical outcomes in patients with granulomatous mastitis, reducing lesion size, inflammatory markers, and symptom duration more effectively than corticosteroids alone.

**Keywords**: Corticosteroids; Granulomatous mastitis; Inflammatory markers; Low intensity focused ultrasound (LIFU); Non-invasive therapy; Pain management

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## INTRODUCTION

Granulomatous mastitis (GM) is a chronic inflammatory breast disease primarily affecting women of childbearing age, posing diagnostic and therapeutic challenges owing to its resemblance to breast malignancy (JM Wu and Turashvili, 2020). The etiology of granulomatous mastitis remains complex and poorly understood, involving a combination of hormonal, autoimmune, and infectious factors (Can *et al.*, 2021). This condition manifests as palpable masses within the breast, frequently accompanied by pain, erythema, and sometimes suppuration, often leading to misdiagnosis as a breast carcinoma (Bentzon *et al.*, 2021). Given the profound effect on quality of life and the potential for significant morbidity, effective management of granulomatous mastitis is paramount, yet it remains elusive (Dilaveri *et al.*, 2024).

Traditional management strategies for granulomatous mastitis have largely focused on the administration of corticosteroids, owing to their potent anti-inflammatory properties (Parperis and Theodoridou, 2025; Yin *et al.*, 2022). Corticosteroids modulate immune responses by suppressing the transcription of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) (Daetwyler *et al.*, 2024). Their usage, however, is not without drawbacks, as concerns related to adverse effects and high recurrence rates linger (Urbina *et al.*, 2024). In exploring adjunctive therapies to bolster the effects of corticosteroids and mitigate these challenges, interest has increasingly turned towards non-invasive techniques, such as focused ultrasound therapy (Scott and Klaus, 2024).

Low intensity focused ultrasound (LIFU) presents a novel, non-invasive therapeutic approach leveraging thermal and mechanical effects to target and ablate pathologic tissues (Xiao *et al.*, 2024). Focused ultrasound could theoretically enhance treatment by inducing local cellular necrosis, promoting anti-inflammatory pathways, and facilitating improved local drug uptake (Kim *et al.*, 2024). Prior studies have suggested that ultrasound mechanisms can elicit therapeutic responses by both enhancing the delivery and concentration of pharmacological agents within tissues and modulating the immune milieu through heat-induced stress responses (X Wu *et al.*, 2024). Despite this potential, empirical data evaluating the efficacy of focused ultrasound in granulomatous mastitis remains sparse.

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Given these intricate yet promising modalities, this study aims to assess the impact of combining corticosteroid therapy with focused ultrasound on lesion size and inflammatory markers in patients with granulomatous mastitis.

## MATERIALS AND METHODS

### *Case selection*

In this retrospective cohort study, we included 284 patients diagnosed with granulomatous mastitis treated at our institution from July 2021 to October 2024. We systematically gathered demographic data, general patient information, treatment effectiveness assessments, and levels of inflammatory factor expression. The data collection and processing technicians used blinding methods. Given that this retrospective study utilized only de-identified patient data, there was no potential harm or impact on the patients' medical care. Consequently, informed consent was waived. This waiver, along with the study, received approval from the Fourth Hospital of Shijiazhuang Institutional Review Board and Ethics Committee, ensuring compliance with regulatory and ethical guidelines for retrospective research.

### *Inclusion and exclusion criteria*

*Inclusion criteria*

1) Diagnosis of granulomatous mastitis (Laas *et al.*, 2015) ; 2) Non-lactating status; 3) Clinical stage classified as early to mid-stage (mass or abscess stage); 4) History of childbirth; 5) $20 \leq \text{Age} \leq 60$ years.

### *Exclusion criteria*

1) Presence of malignant breast tumors; 2) Conditions such as hyperlipidemia, obesity, diabetes, hypertension, and autoimmune diseases; 3) Drug addiction, history of allergies, or predisposition to allergies; 4) Severe liver and kidney dysfunction, hematological disorders, pulmonary insufficiency, cardiac dysfunction, or mental illness.

### *Grouping and treatment methods*

Using the PASS software for sample size estimation, we anticipate a 20% increase in the effectiveness rate, with $\alpha = 0.05$ and $\beta = 0.1$, under a two-sided test. The estimated sample size is at least 124 cases per group. In this study, the final participant count was 126 in the CT Group and 158 in the ST Group.

### *Grouping criteria*

Participants were divided into two groups based on the use of focused ultrasound therapy. The CT Group received both corticosteroids and focused ultrasound. The ST Group was treated exclusively with corticosteroids.

### *LIFU therapy*

After skin preparation, the patient was positioned in the prone position and treated using the JC Integrated Focused Ultrasound Tumor Treatment System manufactured by Chongqing Haifu Medical Technology Co., Ltd. Sedation and analgesia were employed as the anesthesia method. The treatment parameters were as follows: transducer frequency of 0.98 MHz, focal length of 151 mm, treatment power ranging from 50 to 80 W, and irradiation time between 800 and 1500 seconds.

### *Corticosteroid therapy*

Patients administered methylprednisolone tablets (manufactured by Pfizer Italia s.r.l; Import Drug Registration Certificate Number: H20150245) orally, starting with a dose of 20 mg/day for two weeks. The dosage was gradually reduced to 4 mg/day, depending on the patient's condition, with the medication being discontinued after one additional week of continuous treatment (Tan *et al.*, 2022).

### *Criteria for judging treatment efficacy*

Cure: Achieving radiological cure, defined as no residual lesions observed on imaging studies, or achieving clinical cure with no recurrence for six months.

### *Improvement*

Characterized by a significant reduction in the size of the breast lump, alleviation of pain, and a decrease in the inflammatory response.

### *Invalid outcome*

Occurs when there is no reduction, or an increase, in the size of the lump, no relief from pain, and no change or worsening of the inflammatory response (Yildirim *et al.*, 2021).

### *Measurement of breast mass size*

Breast mass size was assessed by measuring the largest diameter of the palpable mass. This was done every 3 days during the first month and every 7 days during the second month of treatment. The boundaries of the mass were determined by palpation and corroborated with ultrasound imaging. The maximum diameter reduction rate during the second month of treatment was calculated for each patient using the formula: Reduction rate = (Initial size - Post-treatment size) / Initial size. Only the largest reduction rate was recorded for each patient.

### *Visual analogue scale (VAS)*

We assessed patients' pain levels using the Visual Analog Scale (VAS). The primary evaluation method involved the physician drawing a 10 cm horizontal line on paper, with the endpoints marked as 0 and 10, representing 'no pain' and 'severe pain, ' respectively. Patients were instructed to mark a point on the line that corresponded to their perceived level of pain. Scores were assigned based on this marking: 1-3 points indicated mild pain, 4-6 points indicated moderate pain, and 7-10 points indicated severe pain. A higher score reflected more intense pain. The reliability of the VAS score was measured at 0.94 (Naunheim *et al.*, 2020).

***Inflammatory cytokine level expression***

Before and after treatment, 5 mL of fasting venous blood was collected from the patient's elbow in the morning. Enzyme linked immunosorbent assay (ELISA) was used to detect the levels of IL-6 (Item number: EH2IL6, Thermo Fisher Scientific Inc., USA.), CRP (Item number: KHA0031, Thermo Fisher Scientific Inc., USA.), and tumor necrosis factor-α (TNF-α, Item number: 88-7346-88, Thermo Fisher Scientific Inc., USA.) in the patient's serum.

***Statistical analysis***

Data analysis was conducted using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as [n (%)]. When the sample size was ≥40 and the expected frequency T was ≥5, the chi-square test was utilized based on standard formulas. For a sample size of ≥40 but expected frequency 1≤T < 5, a corrected chi-square test was applied. In cases where the sample size was < 40 or the expected frequency was T < 1, the Fisher's exact test was used for statistical analysis. The Shapiro-Wilk test was employed to assess the normality of continuous variables. Continuous variables following a normal distribution were represented as (Mean ± SD) and analyzed using the corrected variance t-test. A two-sided P-value of < 0.05 was considered statistically significant.

## RESULTS

***Baseline characteristics***

In this retrospective cohort study, we evaluated the effects of corticosteroid combined with focused ultrasound therapy on lesion size and inflammatory markers in patients with granulomatous mastitis (Table 1). The baseline characteristics between the CT group (combination therapy) and the ST group (standard treatment) were comparable, with no significant differences observed. The mean age was 36.56 ± 6.34 years in the CT group and 37.52 ± 6.10 years in the ST group ($P$ = 0.200). Body mass index (BMI) was similar between groups, with the CT group at 22.18 ± 3.46 kg/m² and the ST group at 21.95 ± 3.54 kg/m² ($P$ = 0.590). Education level, marital status, breastfeeding history, presence of inverted nipples, and number of births did not significantly differ between groups ($P$ > 0.05 for all). The causes of onset, whether gestational, lactational disorders, bacterial infection, or otherwise, were similar between the two groups ($P$ = 0.230). Disease duration was nearly identical, with an average of 75.21 ± 2.38 days in the CT group and 75.56 ± 2.79 days in the ST group ($P$ = 0.230). Furthermore, medical history regarding initial onset versus recrudescence and clinical stages, lump versus abscess, showed no significant disparity ($P$ > 0.05). These results indicate that baseline characteristics did not influence the comparability of the two groups for subsequent clinical outcome analysis.

***Clinical efficacy***

The overall effectiveness was notably higher in the CT group compared to the ST group ($P$ = 0.005) (Table 2). Specifically, 89 patients (70.63%) in the CT group achieved recovery, versus 98 patients (62.03%) in the ST group. The number of cases classified as effective was 32 (25.40%) in the CT group and 35 (22.15%) in the ST group. Importantly, the CT group experienced a significantly lower rate of ineffective treatment, with only 5 patients (3.97%) deemed as invalid compared to 25 patients (15.82%) in the ST group. These results suggest that the addition of corticosteroid and focused ultrasound therapy may enhance treatment outcomes for patients with granulomatous mastitis.

***Improve time and treatment duration***

The time to disappearance of pain was reduced in the CT group (7.64 ± 2.13 days) compared to the ST group (8.36 ± 2.58 days), with a statistically significant difference ($P$ = 0.017) (Fig. 1A). Similarly, the time required for redness and swelling to diminish was shorter in the CT group (8.66 ± 1.72 days) versus the ST group (9.12 ± 1.54 days), also reaching statistical significance ($P$ = 0.017) (Fig. 1B). Furthermore, the tumor disappearance time was significantly less in the CT group at 17.35 ± 3.26 days compared to 18.39 ± 3.45 days in the ST group ($P$ = 0.010) (Fig. 1C). The overall treatment duration was similarly shorter in the CT group, averaging 30.56 ± 4.65 days, compared to 31.64 ± 4.27 days in the ST group, with this difference achieving statistical significance ($P$ = 0.043) (Fig. 1D). These results suggest that the CT may expedite clinical recovery in patients with granulomatous mastitis.

***Breast pain severity and lesion size***

Prior to treatment, there was no significant difference in VAS scores for pain between the CT group (5.24 ± 1.07) and the ST group (5.16 ± 1.24, $P$ = 0.588) (Table 3). However, post-treatment, the CT group exhibited a significantly lower VAS score (1.92 ± 0.32) than the ST group (2.02 ± 0.33, $P$ = 0.017), indicating better pain relief. Regarding lesion size, no significant difference was observed before treatment between the groups (CT: 7.32 ± 1.56 cm, ST: 7.35 ± 1.26 cm, $P$ = 0.876). After treatment, the CT group had a statistically smaller lesion size (1.98 ± 0.27 cm) compared to the ST group (2.05 ± 0.31 cm, $P$ = 0.035). These results suggest that the CT was more effective in reducing both pain severity and lesion size in this patient population.

***Pre-treatment serum inflammatory cytokine expression levels***

The levels of IL-6 were 151.34 ± 9.62 ng/mL in the CT group and 150.36 ± 8.59 ng/mL in the ST group ($P$ = 0.366) (Table 4). Similarly, the CRP levels were 24.38 ± 3.26 mg/mL in the CT group and 24.15 ± 3.57 mg/mL in the ST group ($P$ = 0.564). TNF-α levels were 93.45 ± 7.14 ng/mL in the CT group compared to 92.64 ± 7.03 ng/mL in the ST group ($P$ = 0.337). These findings indicate comparable baseline cytokine expression levels across both treatment groups.

**Table 1**: Baseline Characteristics of Participants

| Parameters | CT Group (n = 126) | ST group (n = 158) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Age (years) | 36.56 ± 6.34 | 37.52 ± 6.10 | 1.284 | 0.200 |
| Body Mass Index (kg/m²) | 22.18 ± 3.46 | 21.95 ± 3.54 | 0.540 | 0.590 |
| Education Level [n/ (%)] | | | 0.006 | 0.997 |
| Primary school and below | 12 (9.52%) | 15 (9.49%) | | |
| Middle school | 29 (23.02%) | 37 (23.42%) | | |
| College and above | 85 (67.46%) | 106 (67.09%) | | |
| Marital status [n/ (%)] | | | 0.642 | 0.887 |
| Married | 112 (88.89%) | 142 (89.87%) | | |
| Divorced | 6 (4.76%) | 8 (5.06%) | | |
| Widowed | 6 (3.17%) | 7 (3.16%) | | |
| Unmarried | 2 (3.17%) | 1 (1.90%) | | |
| Breastfeeding history | 107 (84.92%) | 134 (84.81%) | 0.001 | 0.979 |
| Inverted nipple | 25 (19.84%) | 28 (17.72%) | 0.208 | 0.649 |
| Number of births [n/ (%)] | | | 1.240 | 0.265 |
| 1 | 90 (71.43%) | 122 (77.22%) | | |
| > 1 | 36 (28.57%) | 36 (22.78%) | | |
| Cause of onset [n/ (%)] | | | 4.309 | 0.230 |
| Gestation | 64 (50.79%) | 87 (55.06%) | | |
| Lactational disorders | 50 (39.68%) | 65 (41.14%) | | |
| Bacterial infection | 6 (4.76%) | 4 (2.53%) | | |
| Others | 6 (4.76%) | 2 (1.27%) | | |
| Onset quadrant [n/ (%)] | | | 0.677 | 0.411 |
| Single quadrant | 66 (52.38%) | 75 (47.47%) | | |
| Multiple quadrants | 60 (47.62%) | 83 (52.53%) | | |
| Disease duration (d) | 75.21 ± 2.38 | 75.56 ± 2.79 | 1.204 | 0.230 |
| Medical history [n/ (%)] | | | 0.119 | 0.730 |
| Initial onset | 62 (49.21%) | 81 (51.27%) | | |
| Recrudescence | 64 (50.79%) | 77 (48.73%) | | |
| Clinical stages [n/ (%)] | | | 0.657 | 0.418 |
| Lump stage | 87 (69.05%) | 116 (73.42%) | | |
| Abscess stage | 39 (30.95%) | 42 (26.58%) | | |

**Table 2**: Comparison of clinical efficacy

| Parameters | CT Group (n = 126) | ST group (n = 158) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Overall effective | | | 10.428 | 0.005 |
| Recovery | 89 (70.63%) | 98 (62.03%) | | |
| Effective | 32 (25.40%) | 35 (22.15%) | | |
| Invalid | 5 (3.97%) | 25 (15.82%) | | |

**Table 3**: Comparison of breast pain severity and lesion size

| Parameters | CT Group (n = 126) | ST group (n = 158) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Score of VAS before treatment | 5.24 ± 1.07 | 5.16 ± 1.24 | 0.543 | 0.588 |
| Score of VAS after treatment | 1.92 ± 0.32 | 2.02 ± 0.33 | 2.408 | 0.017 |
| lesion size (cm) before treatment | 7.32 ± 1.56 | 7.35 ± 1.26 | 0.157 | 0.876 |
| lesion size (cm) after treatment | 1.98 ± 0.27 | 2.05 ± 0.31 | 2.115 | 0.035 |

Note: VAS: Visual Analogue Scale.

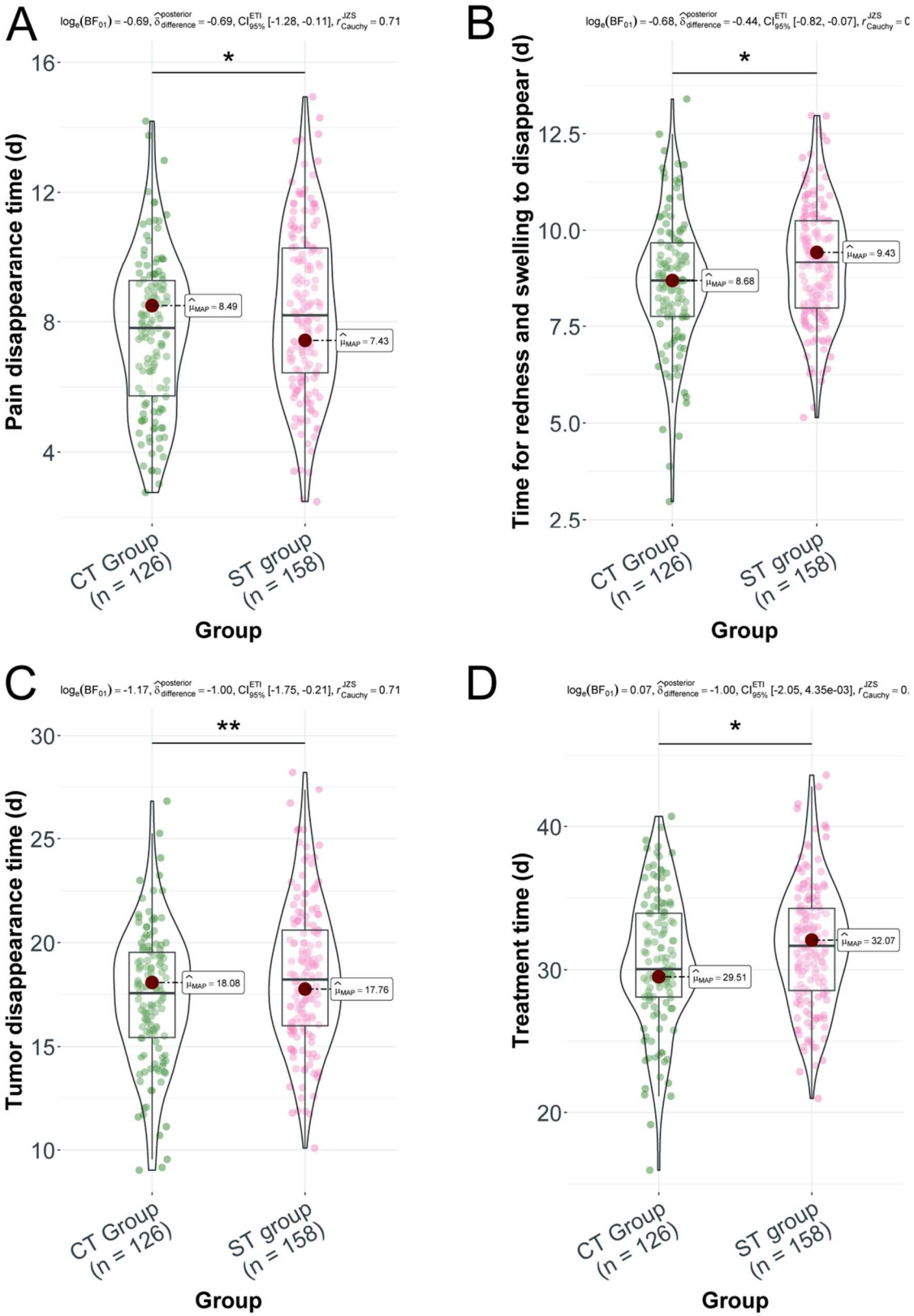


**Fig. 1**: Improve time and treatment duration (Note: A. Comparison of pain disappearance time between the CT group and the ST group; B. Comparison of time for redness and swelling to disappear between the CT group and the ST group; C. Comparison of tumor disappearance time between the CT group and the ST group; D. Comparison of treatment time between the CT group and the ST group).

**Table 4**: Pre-treatment serum inflammatory cytokine expression levels

| Parameters | CT Group (n = 126) | ST group (n = 158) | $t/\chi^2$ | P |
|---|---|---|---|---|
| IL-6 (ng/L) | 81.63 ± 98.63 | 82.06 ± 8.06 | 0.869 | 0.254 |
| CRP (mg/L) | 24.38 ± 3.26 | 24.15 ± 3.57 | 0.613 | 0.556 |
| TNF-α (μg/L) | 55.34 ± 6.18 | 54.38 ± 6.89 | 0.851 | 0.315 |

Note: IL-6: Interleukin-6; CRP: C-Reactive Protein; TNF-α: Tumor Necrosis Factor.

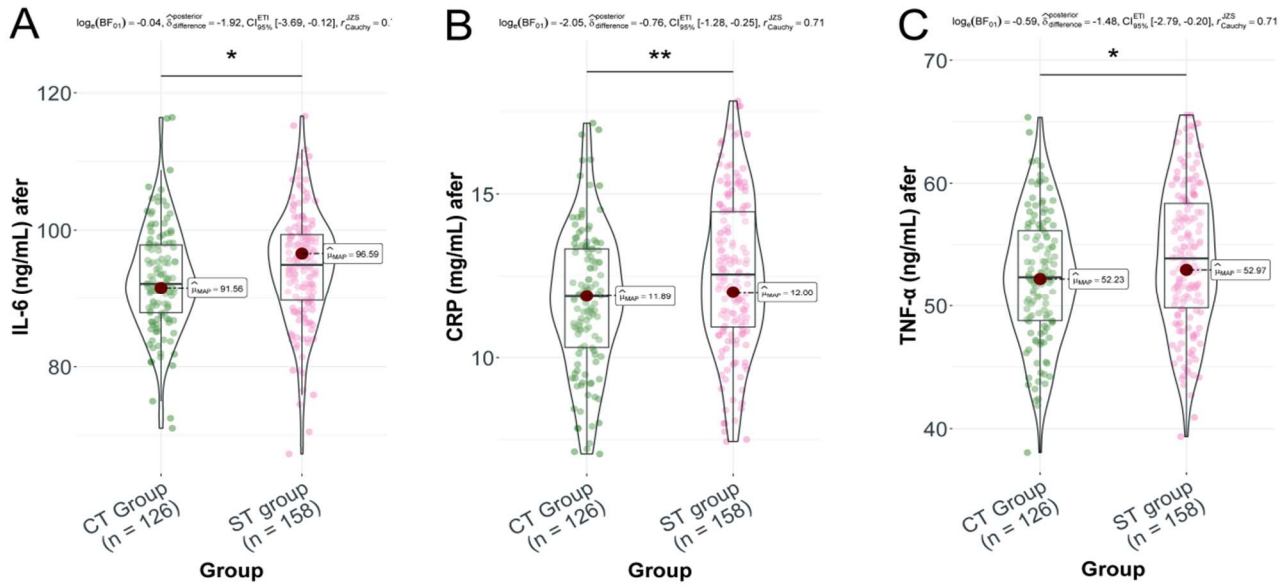


**Fig. 2**: Post-treatment serum inflammatory cytokine expression levels (Note:A. Comparison of IL-6 between the CT group and the ST group; B. Comparison of CRP between the CT group and the ST group; C. Comparison of TNF-α between the CT group and the ST group).

Note: IL-6: Interleukin-6; CRP: C-Reactive Protein; TNF-α: Tumor Necrosis Factor.

***Post-treatment serum inflammatory cytokine expression levels***

IL-6 levels were significantly reduced in the CT group, with mean levels of 92.69 ± 7.63 ng/mL compared to 94.68 ± 8.24 ng/mL in the ST group ($P = 0.037$) (Fig. 2A). CRP levels exhibited a more pronounced reduction in the CT group (11.76 ± 2.15 mg/mL) than in the ST group (12.56 ± 2.34 mg/mL), achieving statistical significance ($P = 0.004$) (Fig. 2B). Additionally, TNF-α levels were significantly lower in the CT group, recorded at 52.32 ± 5.21 ng/mL, compared to 53.87 ± 5.78 ng/mL in the ST group ($P = 0.019$) (Fig. 2C). These results indicate that the combination of corticosteroid and focused ultrasound therapy more effectively reduces inflammation, as evidenced by the levels of these cytokines.

## DISCUSSION

In this retrospective cohort study, we examined the therapeutic effects of combining corticosteroids with focused ultrasound therapy in the management of granulomatous mastitis, focusing on changes in lesion size and inflammatory markers.

GM is a chronic inflammatory breast disease predominantly affecting young women, often presenting as a painful breast mass that can be mistaken for malignancy (Coombe and Hamed, 2021; Omranipour and Vasigh, 2020). The etiology of granulomatous mastitis is multifaceted, potentially involving hormonal influences, autoimmune reactions, and infectious agents (Schmitt *et al.*, 2022; Yuan *et al.*, 2022). Treatment strategies have historically been varied, reflecting the complexity and enigmatic nature of this condition (Wolfrum *et al.*, 2018). Corticosteroids have been a mainstay of treatment, owing to their potent anti-inflammatory effects, but relapse rates and side effects remain a concern (Thompson *et al.*, 2021). Our study introduces focused ultrasound therapy as a complementary modality, potentially overcoming some limitations of conventional treatment.

The CT demonstrated a superior overall effectiveness than corticosteroids alone, attributable to several underlying mechanisms. Corticosteroids, such as methylprednisolone, function by downregulating pro-inflammatory gene expression, thereby decreasing the synthesis of inflammatory cytokines, including TNF-α, IL-6, and CRP (Pappas *et al.*, 2022; Zhang *et al.*, 2020). These cytokines were identified in our study as elevated in granulomatous mastitis, and their marked reduction post-treatment in the

CT group affirms the enhanced anti-inflammatory effect. Focused ultrasound potentially augments this effect through thermal and mechanical mechanisms. The LIFU induces localized thermal ablation, leading to cellular necrosis of fibrotic tissue, and stimulates heat shock proteins, which can promote wound healing and further modulate the immune response (Co *et al.*, 2022; de Maar *et al.*, 2020). Mechanical disruption of tissue by ultrasound may also enhance steroid penetration, ensuring more concentrated delivery to affected areas (Hong *et al.*, 2023; Zhu *et al.*, 2024).

Furthermore, several studies have highlighted the potential of focused ultrasound in reducing local inflammation and edema in chronic inflammatory conditions, including granulomatous mastitis (Zanos *et al.*, 2023). The ability of ultrasound to remodel fibrotic tissue and improve local blood flow creates an environment conducive to recovery, as demonstrated in recent trials where ultrasound therapy significantly reduced lesion sizes and improved symptom resolution (Pham *et al.*, 2024) This is consistent with our findings, where the combination therapy led to faster symptom relief and a greater reduction in inflammatory markers compared to corticosteroids alone.

The observed improvement in clinical efficacy and expedited resolution of symptoms in the CT group aligns with these proposed mechanisms. The accelerated pain relief and reduction in lesion size could be partly due to the rapid resolution of inflammatory edema and lower mechanical stress on surrounding tissues provided by both corticosteroid-induced cytokine imbibing and ultrasound-induced tissue remodeling (Dutra *et al.*, 2023; X Wu *et al.*, 2023). The synergy between therapies underlines the potential of a multi-pronged approach that mitigates inflammation while simultaneously addressing structural aspects of granulomatous inflammation.

Another critical observation from our study was the significant disparity in treatment outcomes in favor of CT concerning the time to symptom resolution, including the time to pain disappearance, redness, swelling, and tumor regression. These outcomes suggest an enhanced healing process, possibly linked to improved local circulation and immune cell activity modulated by thermal effects from ultrasound. This CT leverages not just the potency of corticosteroids in modulating immune pathways but likely optimizes local physiological conditions conducive to recovery.

Further, the CT group's more significant reduction in post-treatment inflammatory cytokine levels lends credence to the hypothesis of a robust systemic immune-modulatory impact, beyond localized breast tissue effects. This reduction in systemic inflammation could also account for quicker resolution times across multiple clinical markers, reflecting a hastened return to homeostasis.

Our findings also prompt a consideration of focused ultrasound's role in enhancing drug delivery and tissue absorption. The mechanical and thermal impact of ultrasound may transiently disrupt cellular membranes, enhancing permeability and absorption of administered corticosteroids, resulting in higher localized drug concentrations and, consequently, better therapeutic outcomes. This aligns with previous studies demonstrating that focused ultrasound enhances chemotherapy and anti-inflammatory drug delivery by disrupting interstitial barriers (McMahon D *et al*., 2023), improving tissue penetration, further validating its potential in granulomatous mastitis management.

Moreover, the CT 's ability to achieve these results without additional health complications or adversities emphasizes the safety and tolerability of incorporating focused ultrasound into existing protocols. However, it's essential to note that while focused ultrasound is promising, its mechanistic action could raise concerns about potential off-target tissue effects over time, necessitating further long-term studies.

Interestingly, demographic parameters and baseline characteristics did not significantly differ between groups, thereby ruling out these factors as confounders and affirming the reliability of our findings. It speaks to the intrinsic efficacy of the therapeutic approach rather than any systemic bias.

While our study provides valuable insights into the therapeutic advantages of combining corticosteroids with focused ultrasound for treating granulomatous mastitis, it is not without limitations. As a retrospective cohort study, it is inherently subject to selection bias, as the allocation to treatment groups was not randomized, potentially influencing the comparability between cohorts. Additionally, the reliance on previously recorded data may lead to incomplete or inconsistent information, affecting the robustness of our findings. Another limitation is the relatively small sample size, which may not fully capture the variability in patient responses and could limit the generalizability of our results. Furthermore, the study lacks long-term follow-up data, which would be crucial to assess the durability of treatment benefits and potential late-emerging side effects. Finally, while we observed significant improvements in cytokine levels and clinical outcomes, the precise biological mechanisms underlying the synergistic effects of focused ultrasound and corticosteroids were not directly investigated, warranting further experimental studies to elucidate these pathways.

## CONCLUSION

In conclusion, the incorporation of focused ultrasound with corticosteroids represents a promising advancement in the management of granulomatous mastitis, offering a

substantial improvement in reducing lesion size, inflammatory markers, and symptom resolution time compared to corticosteroid monotherapy. The study is not randomized. This can cause bias and make the results less trustworthy. But the findings provide a compelling argument for further exploration through randomized controlled trials to validate these observed benefits and to uncover more precise elucidations of the underlying mechanisms. Our study lays a foundational basis for these advances and heralds new avenues for managing a condition that poses considerable challenges to both patients and healthcare providers.

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***Authors' contributions***
Haixing Wang, Hongyan Wang: Edited and refined the manuscript with a focus on critical intellectual contributions.
Wenjie Ning, Ge Zhang: Participated in collecting, assessing, and interpreting the date.
QingGuo, Kai Li: Made significant contributions to date interpretation and manuscript preparation.
All authors have read and approved the final manuscript.
#These authors contributed equally to this work as co-first authors.

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***Data availability statement***
The data that support the findings of this study are available from the corresponding author upon request.

***Ethical approval***
The study received approval from the Fourth Hospital of Shijiazhuang Institutional Review Board and Ethics Committee (Ethics Code No.: 20220135).

***Conflicts of interest***
The authors declare that they have no financial conflicts of interest.

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