

# Postoperative Yanghe decoction regimen improves outcomes for idiopathic granulomatous mastitis

## A retrospective cohort study

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### Abstract

The etiology of idiopathic granulomatous mastitis (IGM), a rare inflammatory breast disease, is not understood. There is no consensus regarding the treatment of IGM. The purpose of this study was to determine the efficacy of surgery combined with traditional Chinese medicine for the treatment of IGM.

We retrospectively analyzed 53 patients of IGM who were treated with surgical excision at our hospital. Group A (n = 25) included patients treated with only surgery, and Group B included patients treated with surgery combined with postoperative Yanghe decoction. The clinical data were compared between the 2 groups, including demographics, clinical characteristics, and outcomes.

All patients were female with a mean age of  $34.6 \pm 5.9$  years. There were no significant differences between the groups regarding preoperative demographics or clinical characteristics. The follow-up time was comparable between the groups ( $13.2 \pm 10.0$  vs  $12.0 \pm 10.2$  months). Patients in Group B had shorter complete remission (CR) times than patients in Group A ( $76.1 \pm 15.2$  vs  $84.0 \pm 12.2$  days;  $P < .05$ ). The CR rate was higher in Group B than in Group A ( $96.4\%$  vs  $76.0\%$ ;  $P < .05$ ), and the recurrence rate was lower in Group B than in Group A ( $0\%$  vs  $16.0\%$ ;  $P < .05$ ).

The postoperative Yanghe decoction regimen was associated with more rapid recovery after IGM surgery. Surgical management combined with postoperative oral Yanghe decoction treatment yielded a higher CR rate and lower recurrence rate than surgery alone. The effect of traditional Chinese medicine in IGM treatment requires further study.

**Abbreviations:** CR = complete remission, IGM = granulomatous mastitis, TCM = Traditional Chinese medicine.

**Keywords:** granulomatous mastitis, surgery, traditional Chinese medicine

## 1. Introduction

Idiopathic granulomatous mastitis (IGM) is a rare, chronic benign inflammatory breast disease that affects women of

childbearing age and was first described by Kessler and Wolloch in 1972.<sup>[1]</sup> The etiology of the disease remains poorly understood. Factors including breast trauma, infection, and autoimmune processes may play a role.<sup>[2]</sup> At present, there is a lack of consensus and guidelines regarding surgical and medical approaches to treat IGM.<sup>[3]</sup> The primary treatments include corticosteroids, surgical intervention, and methotrexate.<sup>[4–7]</sup> Treatment with oral corticosteroids generally requires at least 2 to 3 months and can result in substantial side effects. Methotrexate is also a drug with many adverse reactions, especially when used for long periods, and is not generally used to treat IGM. Failure to respond to steroids frequently leads to surgical excision. Surgery can achieve rapid regression of IGM; however, recurrence even after a bilateral mastectomy is not rare.<sup>[2,7]</sup> Therefore, the most effective therapy with the least adverse drug reactions is worth investigating.

The role of traditional Chinese medicine (TCM) in the treatment of IGM has not been studied previously. To the best of our knowledge, this is the first study to focus on a new method using surgery combined with oral postoperative TCM in the treatment of IGM.

## 2. Materials and methods

### 2.1. Case selection

The study was conducted retrospectively in the Department of Thyroid and Breast Surgery, The Affiliated People's Hospital of Ningbo University. We analyzed the clinical data and information of 53 patients diagnosed with IGM between January 2015 and

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Informed consent was obtained from all individual participants included in the study.

The study was approved by ethics committee of The Affiliated People's Hospital of Ningbo University (NO. 2020-002, 107-W-066, January 31, 2020).

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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May 2019. All patients were female with a mean age of  $34.6 \pm 5.9$  years. Patients were divided into 2 groups: Group A ( $n=25$ ) included patients treated with only surgery and Group B included patients treated with surgery combined with postoperative Yanghe decoction. The data and information were collected from our institutional medical record electronic information system, including all data from patients who received treatment during this period. Patients were included when they met the following criteria: patients who are diagnosed with IGM as confirmed by histopathology of the surgical excision specimen, patients who underwent surgical excision, patients who received postoperative oral Yanghe decoction, and patients who were followed up at The Affiliated People's Hospital of Ningbo University. The exclusion criteria were as follows: patients who were followed up for less than 3 months or were lost to follow-up and patients who received steroids orally after surgery. Patients who were treated with surgical management only and surgical management combined with oral Yanghe decoction were included in Groups A and B, respectively. The study was approved by the hospital ethics committee (NO. 2020-002, 107-W-066, January 31, 2020).

## 2.2. Surgical management

Wide surgical excision of the lesions was performed for patients diagnosed with IGM. In some patients with disfigurement, 1-stage mammoplasty techniques were used to ensure postoperative cosmetic effects.

## 2.3. Yanghe decoction regimen

Patients were consulted by a TCM physician after the diagnosis of IGM was confirmed by pathological examination of the resected sections. Yanghe decoction was prescribed and administered daily. Patients were administered the Yanghe decoction 30 minutes after meals in the morning and evening for 3 months. TCM herbs used in the Yanghe decoction were manufactured at a standardized facility (Ningbo Yinzhou Mingbei Pharmaceutical Co Ltd, China). The ingredients in the Yanghe decoction included Radix Rehmanniae Praeparata 15g, Ephedra 2g, Colla Cornus Cervi 20g, Brassica alba Boiss 6g, Cinnamomum Cassia 3g, Raw Licorice 3g, and Rhizoma Zingiberis Praeparata 3g (Fig. 1).

## 2.4. Assessment and Follow-up

Patients were assessed every month during the first 6 months and then every 3 months for the next 6 months. Six-month follow-up was initiated at the beginning of the second year. Standard evaluations included physical examination, ultrasound, mammary radiography, magnetic resonance imaging, and core needle biopsy. Patients received all or some of these modalities based on their condition.

## 2.5. Criteria for complete remission (CR)

Complete remission (CR) was defined as the disappearance of local swelling, erythema, tenderness, and absence of any anomalies upon ultrasound examination after treatment.

## 2.6. Data collection

Patient demographics and characteristics, hospital stay, CR time, cases of CR, recurrent cases, and follow-up time were recorded.

## 2.7. Statistical analysis

SPSS 17.0 (SPSS, Inc., Chicago, IL) was used for statistical analysis. Continuous variables were recorded as mean values  $\pm$  standard deviations and were compared using independent-samples *t* tests. Chi-square tests were used to analyze categorical variables. The differences between the two groups were assessed using the Mann–Whitney *U* test. *P*-value  $<.05$  was considered statistically significant.

## 3. Results

### 3.1. Demographics and characteristics of the study cases

There were no statistically significant differences in marital status ( $P=.546$ ), lactational history ( $P=.367$ ), or preoperative treatment ( $P=.706$ ) between the groups (Table 1). There were no significant differences with respect to lesion location ( $P=.439$ ), lesion size ( $P=.761$ ), duration of illness ( $P=.752$ ), surgical methods ( $P=.552$ ), or comorbidities ( $P=.736$ ) between groups (Table 1).

### 3.2. Outcomes of the two treatments

The hospital stay and follow-up times were similar between the groups ( $P=.625$  and  $P=.896$ , respectively). Group B had shorter CR time ( $76.1 \pm 15.2$  vs  $84.0 \pm 12.2$  days,  $P=.043$ ), higher CR rate (96.4% vs 76.0%,  $P=.28$ ), and lower recurrence rate (0% vs 16.0%,  $P=.28$ ) (Table 2). No patient showed intolerance to the oral Yanghe decoction in Group B. No Yanghe decoction-related side effects were observed in Group B.

## 4. Discussion

IGM is a rare benign inflammatory disease of the breast, characterized by a recurrent disease course; morbidity due to IGM can be debilitating.<sup>[8,9]</sup> It needs to be differentiated from other tumor or tumor-like mesenchymal lesions of the breast, such as plasma cell mastitis and sarcoma.<sup>[10,11]</sup> Generally, the diagnosis can be confirmed by histopathology of core needle biopsy or excision of the lesion. The optimal treatment of patients with IGM remains uncertain, and various treatments are described in the literature. Some studies have shown that corticosteroid administration is effective, alone or in combination with surgical intervention.<sup>[3]</sup> Nevertheless, corticosteroids has a high failure rate and possible side effects associated with long-term use, including weight gain, osteoporosis, hyperglycemia, Cushing syndrome, and even life-threatening pulmonary thrombosis.<sup>[12,13]</sup> Some researchers reported that close observation was the best management for IGM.<sup>[7,14]</sup> However, observation alone can lead to a prolonged disease process and increased risk of disease exacerbation leading to ultimate skin rupture. The increased psychological pressure on patients is an issue that needs to be avoided when choosing this “wait and watch” approach. Surgical excision plays an important role in the treatment of IGM, achieving rapid remission.<sup>[10,15–17]</sup> Some have argued that excision can result in undesirable disfigurement. In our study, mammoplasty was performed to minimize this cosmetic problem. Because of the recurrent nature of IGM, the recurrence rate of the surgical intervention varied from 6.7% to 22.2%.<sup>[18–21]</sup> In particular, patients with inflammatory changes have a higher risk of recurrence and recurrences are frequent after surgical excision.<sup>[22]</sup> Although IGM is a benign disease, recurrence after



**Figure 1.** Ingredients of Yanghe decoction: (A) Colla Cornus Cervi, (B) Raw Licorice, (C) Cinnamomum Cassia, (D) Rhizoma Zingiberis Preparata, (E) Brassica alba Boiss, (F) Radix Rehmanniae Praeparata, (G) Ephedra.

surgery adds extra economic and psychological burdens on patients. Therefore, reducing postoperative recurrence is an important issue for breast surgeons. Shin et al<sup>[23]</sup> focused on oral steroids after surgery to reduce recurrence; however, the outcome was unsatisfactory. Furthermore, the optimal dose and period of treatment are unknown, and there are side effects caused by steroids.

TCM is commonly used as a complement to evidence-based therapies for illnesses; it has the unique advantages of efficacy, convenience, safety, and low cost.<sup>[24]</sup> TCM has been considered as a more “natural” method to boost human immunity and to achieve high quality of life. Patients have selected TCM, and its demand has been increasing over the past several decades, including in Western countries. Yanghe decoction was first



**Table 1****The demographical and clinical characteristics in patients with IGM between 2 groups.**

Variable	Group A (n=25)	Group B (n=28)	P
Age	35.2±7.2	34.1±4.6	.510
Gender, n (%)			—
Female	25 (100%)	28 (100%)	
Marital status			.546
Married	22 (88.0%)	26 (92.9%)	
Unmarried	3 (12.0%)	2 (7.1%)	
Lactational history, n (%)			.367
Yes	19 (76.0%)	24 (85.7%)	
No	6 (24.0%)	4 (14.3%)	
Preoperative treatment			.706
Yes	6 (24.0%)	8 (28.6%)	
No	19 (76.0%)	20 (71.4%)	
Lesion location			.439
Central area	1 (4.0%)	2 (7.1%)	
Upper outer quadrant	13 (52.0%)	16 (57.1%)	
Lower outer quadrant	6 (24.0%)	7 (25.0%)	
Upper inner quadrant	2 (8.0%)	3 (10.7%)	
Lower inner quadrant	3 (12.0%)	0	
Lesion size (T)			.761
≤ 2 cm	19 (76.0%)	23 (82.1%)	
2 cm < T ≤ 5 cm	4 (16.0%)	4 (14.3%)	
> 5 cm	2 (8.0%)	1 (3.6%)	
Duration of illness	3.0±0.7	3.0±0.4	.752
Surgical methods			.552
Wide surgical excision	22 (88.0%)	23 (82.1%)	
Wide surgical excision and mastopexy	3 (12.0%)	5 (17.9%)	
Comorbidities, n (%)			.736
Diabetes mellitus	1 (4.0%)	2 (7.1%)	
Hypertension	1 (4.0%)	1 (3.6%)	

described by Wang Hongxu during the Qing Dynasty. It consists of 6 herbs and deer-horn gelatin. According to TCM theory, Yanghe decoction warms Yang, nourishes blood, disperses cold, and activates stagnancy, and is also used for treating breast cancer.<sup>[25]</sup> Due to the safe nature of TCM, contradictions for Yanghe decoction use were not reported in the literature.<sup>[25–27]</sup> However, the role of the Yanghe decoction in the treatment of IGM has been overlooked. To the best of our knowledge, this is the first study to evaluate the effects of TCM in the treatment of IGM after surgical excision.

Treatment of IGM remains a challenge for physicians.<sup>[3]</sup> In this retrospective study, the postoperative Yanghe decoction regimen demonstrated better control after surgical excision of IGM lesions with reduced CR time, higher CR rate, and lower

recurrence rate. These findings suggest that TCM may provide a new approach to better manage this disease in the future.

There are limitations to this study. It is a retrospective and observational study in which treatment strategies may have been made according to the surgeon's preference. Selection biases may exist. Furthermore, the effective compounds in the Yanghe decoction for IGM require further study. Prospective randomized control studies are needed to investigate the value of TCM in the treatment of IGM.

In conclusion, in IGM patients, the postoperative Yanghe decoction regimen can achieve more rapid recovery after surgery. Surgical management combined with postoperative oral Yanghe decoction yields a higher CR rate and lower recurrence rate than surgery alone. It is worthwhile to investigate the effect of TCM in IGM in future studies.

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## Author contributions

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**Table 2****Outcome of IGM between 2 groups.**

Variable	Group A (n=25)	Group B (n=28)	P
Hospital stay, d	2.2±1.2	2.4±1.1	.625
Complete remission time, d	84.0±12.2	76.1±15.2	.043
Cases of complete remission, n (%)	19 (76.0%)	27 (96.4%)	.028
Recurrent cases, n (%)	4 (16.0%)	0 (0%)	.028
Follow-up time, mo	13.2±10.0	12.0±10.2	.896

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