


# The role of clinical and radiological risk factors and triglyceride-glucose index in predicting recurrence of idiopathic granulomatous mastitis

 Semih Sağlık

Department of Radiology, Siirt Training and Research Hospital, Siirt, Turkiye

**Cite this article as:** Sağlık S. The role of clinical and radiological risk factors and triglyceride-glucose index in predicting recurrence of idiopathic granulomatous mastitis. *J Med Palliat Care.* 2024;5(5):247-255.

Received: 26.08.2024

Accepted: 28.09.2024

Published: 26.10.2024

## ABSTRACT

**Aims:** Idiopathic granulomatous mastitis (IGM) is a rare breast disease characterised by granulomatous inflammation that is clinically and radiologically similar to breast cancer. The main challenge in treating IGM is the development of treatment resistance and recurrence. Many studies have been carried out in the literature to identify markers of recurrence in this disease, but no satisfactory results have been obtained. The aim of this study was to determine the role of clinical, radiological and laboratory parameters in predicting recurrence in patients with IGM and to evaluate the relationship between the triglyceride-glucose (TyG) index and IGM recurrence.

**Methods:** In this study, the electronic medical records of 92 patients who were histopathologically diagnosed with IGM between January 2016 and February 2024 were retrospectively reviewed. Patients were divided into two groups according to recurrence status. Clinical, radiological and laboratory parameters were compared between groups.

**Results:** Recurrence was detected in 26.1% of the patients included in the study and the average follow-up period was 27.6±4.6 months. No statistically significant difference was found between the two groups with regard to age, follow-up time, menopausal status, breastfeeding, oral contraceptive use, smoking history, parity and pathological diagnosis ( $p>0.05$  for all). In univariate analysis, axillary lymphadenopathy, long duration of breastfeeding, low serum albumin globulin ratio and high TyG index were identified as risk factors for IGM recurrence. In multivariate regression analysis, long duration of breastfeeding ( $p=0.042$ , OR: 4.12; 95% confidence interval (CI), 1.05-16.11) and high TyG index ( $p=0.005$ , OR: 5.75; 95% confidence interval (CI), 1.69-19.54) were found to be independent risk factors for recurrence.

**Conclusion:** Study results suggest that a high TyG index at initial presentation and long duration of breastfeeding increase the risk of recurrence in IGM patients. Therefore, questioning the breastfeeding history at the time of admission and determining and analyzing the TyG index can identify patients at high risk for recurrence.

**Keywords:** Idiopathic granulomatous mastitis, recurrence, ultrasonography, triglyceride-glucose index, axillary lymphadenopathy, breastfeeding duration

## INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a granulomatous inflammatory disease of the breast that is clinically and radiologically similar to breast cancer.<sup>1</sup> It is most common in premenopausal women and causes clinical symptoms such as pain, palpable mass, edema and ulceration.<sup>2</sup> As clinical and radiological findings can be confused with breast cancer, histopathological samples are required for differential diagnosis.<sup>1,2</sup> The main challenge in treating IGM patients is the development of treatment resistance and recurrence. There are studies suggesting that some factors such as smoking, pregnancy status, breastfeeding and secondary infections increase the likelihood of recurrence.<sup>3-5</sup> Anti-inflammatory agents, corticosteroids and surgical excision are included in the treatment of the disease and in preventing recurrences.<sup>6,7</sup>

Although surgical excision is the mainstay of treatment, recurrence rates of 5% to 50% have been reported despite wide surgical excision.<sup>3,6</sup> Therefore, identifying patients who are likely to develop a recurrence will help clinicians determine the type of treatment and follow-up period. Many studies have been conducted in the literature to determine the markers of recurrence in IGM patients, but no satisfactory results have been obtained.<sup>2,3,7</sup>

Insulin resistance (IR) is a pathological condition that plays an important role in the development of chronic metabolic disorders, often associated with diabetes. The gold standard for detecting IR is the euglycaemic hyperinsulinemic clamp test. However, as this method is time-consuming and expensive, the triglyceride-glucose (TyG) index, which is a good indicator of

**Corresponding Author:** Semih Sağlık, drsmhsglk@gmail.com



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insulin resistance, has become a valuable indicator. The TyG index is closely related to systemic inflammation and has been shown to play an important role in determining the severity and prognosis of many diseases.<sup>8-16</sup> A few studies have examined the relationship between the TyG index and breast cancer and have shown that the TyG index is associated with breast cancer risk.<sup>17-19</sup> However, the relationship between the TyG index and IGM is not yet known.

The aim of this study was to determine the role of clinical, radiological and laboratory parameters in predicting recurrence in patients with idiopathic granulomatous mastitis and to evaluate the relationship between the TyG index and IGM recurrence.

## METHODS

### Study Participants

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics Committee Approval was obtained from the Siirt University Non-Invasive Ethics Committee (Date: 22.02.2024, Decision No: 101661).

In this single-centre retrospective study, the electronic medical records of patients with a histopathological diagnosis of idiopathic granulomatous mastitis between January 2016 and May 2024 were retrospectively reviewed. Patients diagnosed with granulomatous mastitis due to secondary causes (tuberculosis, granulomatous polyangiitis, sarcoidosis, etc.) or foreign bodies, patients with a history of malignancy, chronic liver or kidney disease, patients with missing fasting blood glucose or fasting triglyceride data, patients with conditions such as diabetes mellitus or pancreatitis, patients using lipid-lowering drugs, patients without adequate medical record data or follow-up information were excluded.

### Study Data

Definitive diagnostic methods included fine needle aspiration biopsy (FNAB), tru-cut biopsy, or surgical excision. On microscopic examination, the presence of non-caseous granulomatous inflammation of the breast lobules was a pathological diagnostic criterion. Data on clinical and demographic characteristics of all patients, such as age, body mass index (BMI), parity, breastfeeding status, duration of breastfeeding, smoking history, menopausal status and history of oral contraceptive use were collected and recorded. When determining the breastfeeding duration of patients who had given birth more than once, after determining the breastfeeding duration for each child, the total breastfeeding duration was divided by the number of children and the average was taken. Triglyceride (TG), blood glucose, serum albumin, total protein, sedimentation (ESR), C-reactive protein (CRP), haematological parameters (Hb, neutrophil, lymphocyte, platelet and leukocyte levels), serum neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and albumin-to-globulin ratio (AGR) were recorded from the laboratory information system. AGR, NLR and PLR were obtained by dividing the relevant parameters by each other. Globulin values were obtained by subtracting albumin from total protein. TyG index was calculated as follows:  $TyG\ index = Ln\ [fasting\ TG\ (mg/dL) \times fasting\ glucose\ (mg/dL) / 2]$ .<sup>20</sup>

### Radiological Findings

Ultrasonography (USG) reports of all patients were accessed from the electronic medical record system and data on radiological imaging features of the disease were obtained. Patients without a USG report in the system were excluded from the study. In accordance with the information obtained from the USG reports, the findings were evaluated as follows; irregularly circumscribed, heterogeneous lesions and interrelated tubular collections, fluid collections compatible with abscess, irregularly circumscribed mass-like lesions, multiple millimetric hypoechoic lesions, heterogeneous thickened breast parenchyma, fistulisation to the skin and axillary lymphadenopathy. Axillary lymphadenopathy characteristics detected from USG reports were recorded in the registry. While lymph nodes with oval, thin cortex and wide fatty hilus were evaluated in favor of normal lymph nodes, cortical thickening, reduction or absence of fatty hilus, change in shape, disappearance of ovoid form and abnormal vascularization were evaluated in favor of lymphadenopathy.<sup>21</sup> (Figure 1).

### Definition of Remission and Recurrence

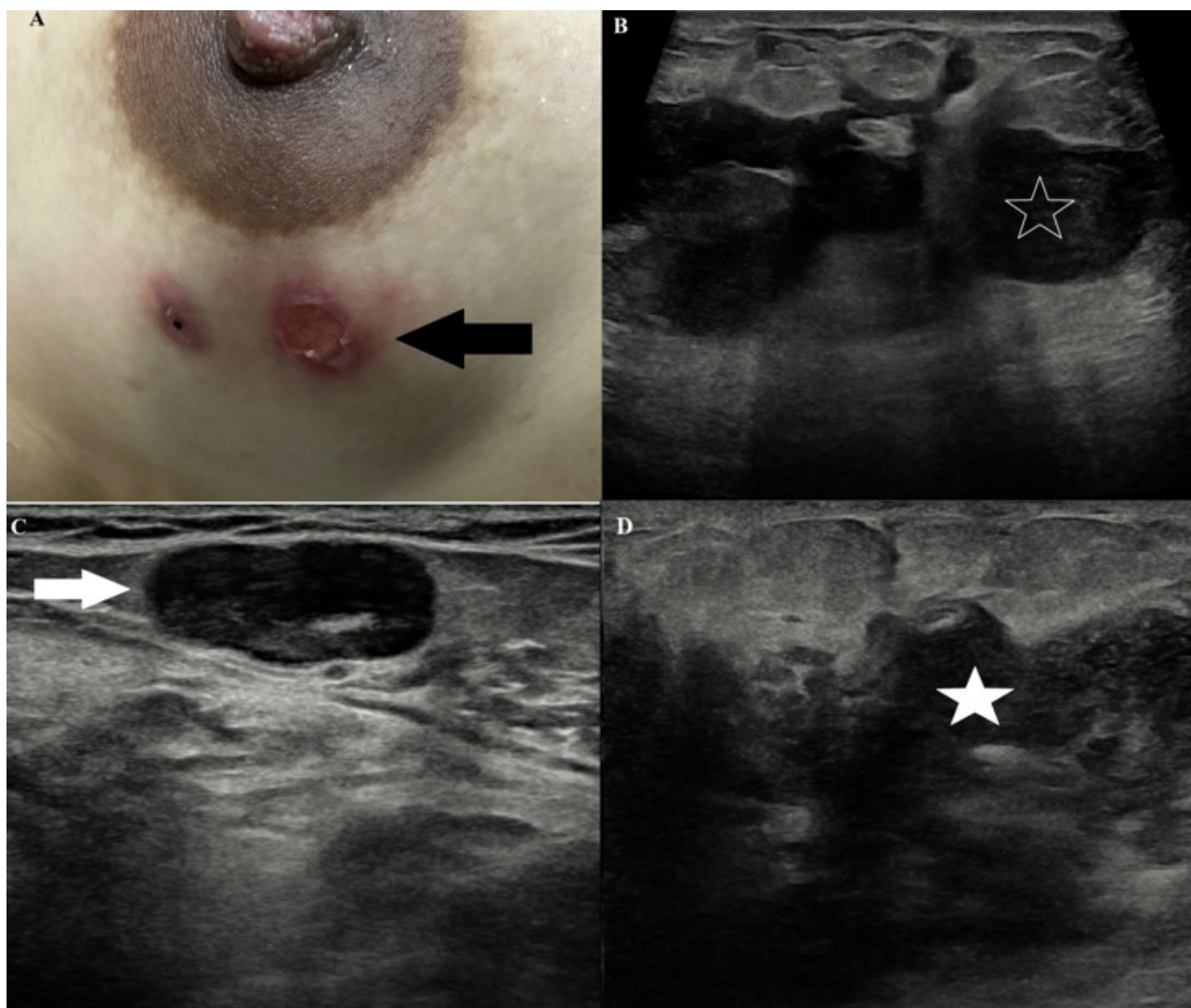
Although there is no accepted definition for IGM remission in the literature, remission was defined as the complete disappearance of clinical complaints and inflammatory symptoms. In patients whose treatment was completed, the recurrence of clinical complaints and radiological imaging findings after at least 3 months of follow-up was considered as recurrence.<sup>4</sup> Patients who did not have sufficient follow-up information after treatment were questioned in terms of complete remission and recurrence in telephone interviews.

### Statistical Analysis

Data analyzes of our study were determined using SPSS 20.0 software (Statistical Package for the Social Sciences, Chicago, IL). Variables regarding qualitative data are expressed as number (n) and percentage (%), and variables regarding quantitative data are expressed as mean  $\pm$  standard deviation (SD). In the evaluation of the study data, Student's t test was used for intergroup comparisons of normally distributed variables and Mann-Whitney U test was used for intergroup comparisons of parameters that did not show normal distribution. Chi-square test or Fisher's exact test was applied for the comparison of categorical variables depending on the sample size. Univariate and Multivariate Binary Logistic Regression analyses were used to determine the effective risk factors on IGM recurrence. ROC (Receiver Operating Characteristic) curve analysis was used to determine whether TyG index and breastfeeding duration were prognostic indicators in forecasting recurrence and to determine the optimal cut-off values. The significance level for statistical results was accepted as  $p < 0.05$ .

## RESULTS

This study included 92 female patients with histopathological diagnosis of IGM and complete follow-up data. The mean age at the time of diagnosis was  $32.1 \pm 5.9$  years and the mean follow-up period was  $27.6 \pm 4.6$  months. It was determined that 92.3% (n=85) of the patients had a history of at least one birth and 94.5% (n=87) were in the premenopausal period. The majority of the patients (86.5%, n=80) had a history of breastfeeding



**Figure 1.** Ulcerative lesion on the skin in the lower quadrants of the left breast in a 36-year-old female patient with histopathological diagnosis of IGM (A, black arrow). USG examination of the same patient revealed heterogeneous lesions with irregular borders in the breast parenchyma (B, open star) and a lymph node with cortical thickening in the right axillary region (C, white arrow). The patient, who had complete remission after treatment, had a recurrence in the same breast 8 months later, and a simultaneous USG examination revealed that heterogeneous lesions reappeared in the breast parenchyma (D, closed star).

and the average duration of breastfeeding was  $15.9 \pm 8.6$  months. The mean body mass index was  $30.3 \pm 5.5$  kg/m<sup>2</sup>. In the study group, 26.1% (n=24) had a history of oral contraceptive use and 9.2% (n=9) had a history of smoking. The right breast was affected in 57.6% (n=53) of the patients and the left breast was affected in 42.4% (n=39). Histopathological diagnosis was made by fine needle biopsy in 4 patients (4.3%), tru-cut biopsy in 68 patients (73.9%) and excisional breast biopsy in 20 patients (21.8%) (Table 1).

Patients were divided into two groups according to recurrence status. There were 68 (73.9%) patients in the group without recurrence and 24 (26.1%) patients in the group with recurrence. No statistically significant difference was found between the two groups in terms of age, follow-up period, menopausal status, breastfeeding, oral contraceptive and smoking history, parity and pathological diagnosis ( $p > 0.05$  for all, Table 1). However, breastfeeding duration was found to be statistically higher in the recurrence group ( $p < 0.001$ , Table 1, Figure 2A). When laboratory parameters were compared, serum albumin, total protein, globulin and AGR values were found to be statistically

higher in the recurrence group ( $p < 0.05$  for all, Table 1). TyG index was significantly higher in the recurrence group ( $p < 0.001$ , Figure 2B). However, no statistically significant difference was detected between laboratory parameters such as serum sedimentation (ESR), C-reactive protein (CRP), fasting glucose and triglyceride, and hematological values (Hb, neutrophil, lymphocyte, platelet and leukocyte levels) between the two groups (all for  $p > 0.05$ , Table 1).

Pain (n=83), palpable mass (n=68), erythema (n=43), induration (n=14) and dermal sinus (n=14) were among the most common clinical findings in the patients included in the study. USG reports revealed poorly circumscribed, irregular, heterogeneous lesions in 33.6% (n=31), multiloculated abscess collections in 28.2% (n=26), well-circumscribed hypoechoic mass in 16.3% (n=15), hypoechoic mass and heterogeneous lesions in 13.1% (n=12), and abscess collections and heterogeneous lesions in 15.2% (n=14). The results of the study indicated that there was no statistically significant difference between the clinical and ultrasonographic findings in both groups. Axillary lymphadenopathy was found in 34.7% (n=32) of all patients in

Table 1. Baseline characteristics and comparison of variables among IGM recurrence groups

Parameters	IGM Recurrence			p values
	No recurrence (n=68)	Recurrence (n=24)	Total (n=92)	
Age (years)	31.5±6.2	33.7±4.6	32.1±5.9	0.125 <sup>a</sup>
BMI (kg/m <sup>2</sup> )	29.9±5.7	31.4±4.8	30.3±5.5	0.259 <sup>a</sup>
Follow-up (month)	27.2±4.5	29.1±4.7	27.6±4.6	0.091 <sup>a</sup>
Breastfeeding n (%)				0.725 <sup>b</sup>
No	10 (14.7%)	2 (8.4%)	12 (13.1%)	
Yes	58 (85.3%)	22 (91.6%)	80 (86.9%)	
Breastfeeding duration (month)	14±7.6	21.5±8.9	15.9±8.6	<0.001 <sup>a</sup>
Oral contraceptive use n (%)				0.888 <sup>b</sup>
No	50 (73.5%)	18 (75%)	68 (73.9%)	
Yes	18 (26.5%)	6 (25%)	24 (26.1%)	
Smoking n (%)				0.692 <sup>b</sup>
No	62 (91.2%)	21 (87.5)	83 (90.2%)	
Yes	6 (8.8%)	3 (12.5%)	9 (9.2%)	
Parity n (%)				0.876 <sup>c</sup>
Nulliparous	5 (7.3%)	2 (8.3%)	7 (7.6%)	
Parous	63 (92.7%)	22 (91.7%)	85 (92.4%)	
Menopausal status, n (%)				0.466 <sup>b</sup>
Premenopausal	65 (95.6%)	22 (91.6%)	87 (94.5%)	
Postmenopausal	3 (4.4%)	2 (8.4%)	5 (5.5%)	
Lesion side				0.691 <sup>c</sup>
Right breast	40 (58.8%)	13 (54.2%)	53 (57.6%)	
Left breast	28 (41.2%)	11 (45.8%)	39 (42.4%)	
Pathological diagnosis, n (%)				0.990 <sup>b</sup>
FNAC	3 (4.4%)	1 (4.1%)	4 (4.3%)	
Core needle biopsy	50 (73.5%)	18 (75%)	68 (73.9%)	
Surgical excision	15 (22.1%)	5 (20.9%)	20 (21.8%)	
HB (gr/dl)	12.4±1.2	12.2±1.11	12.3±1.2	0.577 <sup>d</sup>
WBC (10 <sup>9</sup> /L)	9.4±2.5	10.2±2.4	9.6±2.5	0.193 <sup>d</sup>
CRP (mg/dl)	4.6±2.8	3.9±2.8	4.4±2.8	0.362 <sup>d</sup>
Sedimentation (mm/h)	23.8±12.7	25.8±11.9	24.3±12.5	0.503 <sup>d</sup>
Neutrophil (10 <sup>9</sup> /L)	5.1±1.1	5.4±1.1	5.2±1	0.213 <sup>d</sup>
Lymphocyte (10 <sup>9</sup> /L)	2.7±0.8	2.9±0.9	2.7±0.8	0.423 <sup>d</sup>
PLT (10 <sup>9</sup> /L)	281±53	291±47	284±52	0.442 <sup>d</sup>
ALB (g/L)	4.55±0.8	3.99±0.9	4.4±0.86	0.006 <sup>d</sup>
Protein (g/L)	7.06±1.27	7.69±1.1	7.22±1.25	0.036 <sup>d</sup>
Globulin (g/L)	3.1±0.6	3.3±0.4	3.2±0.6	0.009 <sup>d</sup>
NLR	2.07±0.85	2.08±0.81	2.08±0.84	0.960 <sup>d</sup>
PLR	112.7±40.4	108.8±33.8	111.7±38.6	0.682 <sup>d</sup>
AGR	1.6±0.56	1.19±0.28	1.49±0.53	0.001 <sup>d</sup>
Glucose (mg/dL)	97.4±13.7	102.8±12.1	98.8±13.5	0.087 <sup>d</sup>
Triglyceride (mg/dL)	116.9±17.8	124.9±18.7	118.9±18.2	0.062 <sup>d</sup>
TyG index	8.57±0.23	8.81±0.17	8.64±0.23	<0.001 <sup>d</sup>

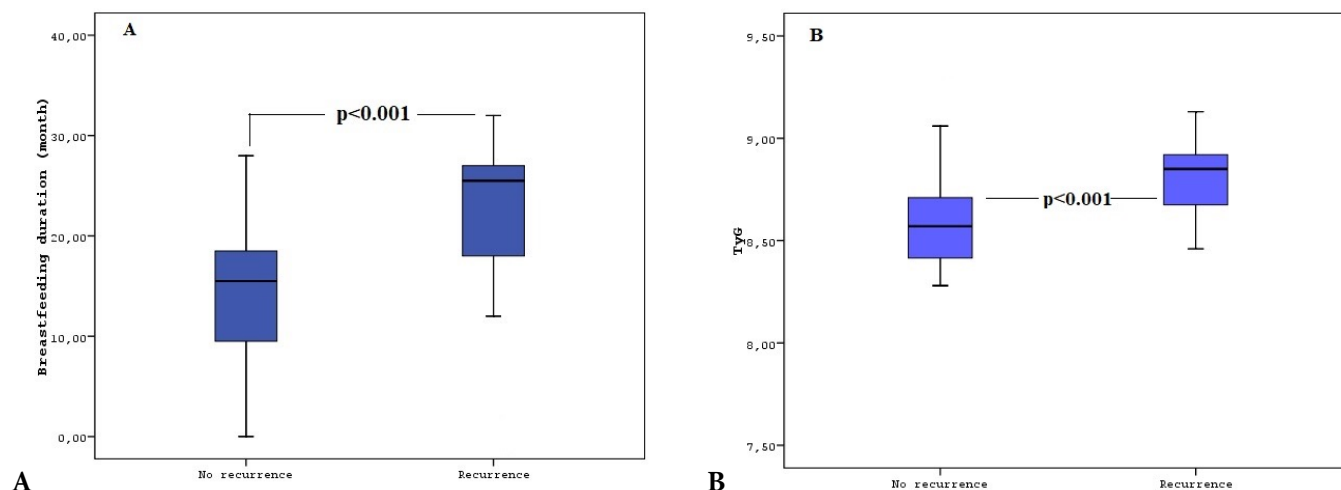
Notes: <sup>a</sup>Student's t-test with mean±standard deviation (SD). <sup>b</sup>Fisher's Exact test with n (%). <sup>c</sup>Chi-Square with n (%). <sup>d</sup>Mann Whitney U-test with median±interquartile range (IQR). Statistically significant results (p < 0.05).

Abbreviations: IGM, Idiopathic granulomatous mastitis; BMI, Body mass index; HB, Hemoglobin; WBC, White blood cell count; CRP, C-reactive protein; PLT, platelets; SM, Segmental mastectomy; FNAC, Fine needle aspiration cytology; TyG index, Triglyceride-glucose index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio

USG reports. Axillary lymphadenopathy was present in 26.5% (n=18) of patients with complete remission, while this rate was 58.3% (n=14) in recurrence patients. The chi-square test results indicated that the frequency of axillary lymphadenopathy was statistically significantly higher in patients who experienced recurrence (p=0.005, Table 2).

The AUC values of TyG index and breastfeeding duration in the receiver operating characteristics (ROC) curve analysis test were 0.805 (0.708-0.903) and 0.771 (0.644-0.899) with 95% confidence interval, respectively, and were therefore considered statistically significant (p<0.001 for all, Figure 3). Accordingly, when the TyG index cut-off was ≥8.68, its sensitivity and specificity were 75% and 70.6%, respectively, and when the





**Figure 2.** Boxplot of the distribution of (A) breastfeeding duration, (B) TyG index values among IGM recurrence groups. The horizontal lines inside each box represent the mean values and the lower and upper rows of each box represent the minimum and maximum values, respectively.

Parameters	IGM Recurrence		Total (n=92)	p values
	No recurrence (n=68)	Recurrence (n=24)		
<b>Clinical findings</b>				
Mass	49 (72.1%)	19 (79.1%)	68 (73.9%)	0.495 <sup>a</sup>
Pain	63 (92.6%)	20 (83.3%)	83 (90.2%)	0.187 <sup>a</sup>
Erythema	32 (47.1%)	11 (45.8%)	43 (46.7%)	0.918 <sup>b</sup>
Induration	11 (16.2%)	3 (12.5%)	14 (15.2%)	0.666 <sup>a</sup>
Sinus or ulcer	12 (17.6%)	2 (8.3%)	14 (15.2%)	0.275 <sup>b</sup>
<b>Ultrasound findings</b>				
Ill-defined, irregular, heterogeneous lesions	24 (35.2%)	7 (29.1%)	31 (33.6%)	0.585 <sup>b</sup>
Multiloculated abscess collections	17 (25%)	9 (37.5%)	26 (28.2%)	0.242 <sup>a</sup>
Well-circumscribed hypochoic mass	10 (14.7%)	5 (20.8%)	15 (16.3%)	0.485 <sup>a</sup>
Hypochoic mass and heterogeneous lesions	8 (11.7%)	4 (16.6%)	12 (13.1%)	0.540 <sup>a</sup>
Abscess collections and heterogeneous lesions	12 (17.6%)	2 (8.3%)	14 (15.2%)	0.275 <sup>a</sup>
<b>Axillary lymphadenopathy</b>				
Negative	50 (73.5%)	10 (41.6%)	60 (65.2%)	0.005 <sup>b</sup>
Positive	18 (26.5%)	14 (58.3%)	32 (34.7%)	

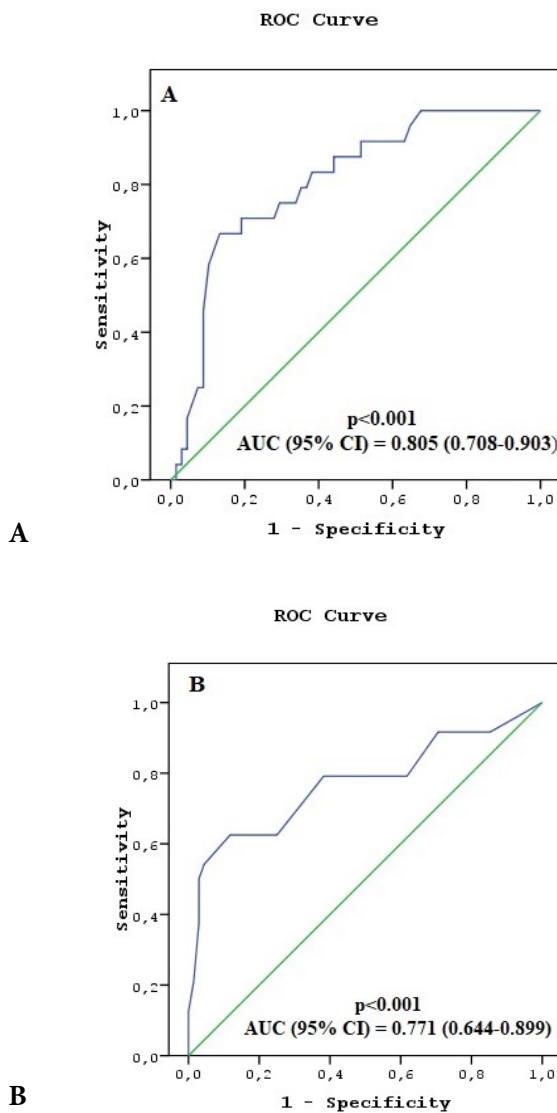
Notes: <sup>a</sup>Fisher's Exact test with n (%). <sup>b</sup>Chi-Square with n (%). Statistically significant results (p < 0.05).  
Abbreviations: IGM, Idiopathic granulomatous mastitis

breastfeeding duration cut-off was  $\geq 24.5$  months, its sensitivity and specificity were 79.2% and 61.8%, respectively, in predicting IGM recurrence.

Regression analysis was used to determine the effective parameters for IGM recurrence. In univariate regression analysis, axillary LAP (yes or no), long breastfeeding duration ( $\geq 24.5$  months), low AGR values ( $\leq 1.183$ ) and high TyG index ( $\geq 8.68$ ) were identified as risk factors for IGM recurrence. In multivariate regression analysis, the cut-off value of breastfeeding duration greater than 24.5 months ( $p=0.042$ , OR: 4.12; 95% confidence interval (CI), 1.05-16.11) and the cut-off value of TyG index above 8.68 ( $p=0.005$ , OR: 5.75; 95% confidence interval (CI), 1.69-19.54) were found to be independent risk factors for IGM recurrence (Table 3).

## DISCUSSION

IGM is a breast disease that can be confused clinically and radiologically with malignant and benign breast lesions and requires histopathological confirmation for definitive diagnosis.<sup>1,22</sup> Although IGM is considered a benign lesion of the breast, it still poses serious problems due to the development of permanent complications and recurrences.<sup>4,22</sup> Although many treatments and combinations have been used to treat IGM, including antibiotics, steroids, methotrexate and surgery, recurrence rates of up to 50% have been reported.<sup>3,6</sup> Therefore, knowing the risk of IGM recurrence and factors that can predict recurrence will influence patient-specific treatment and follow-up and increase the chance of success. In our study, we analysed the clinical, radiological and laboratory risk factors associated with IGM recurrence and found that the TyG index may be an effective biomarker in predicting recurrence and breastfeeding duration was an independent risk factor for recurrence.



**Figure 3.** The receiver operating characteristic (ROC) curve and the area under the ROC (AUC) of (A) TyG index and (B) breastfeeding duration in IGM recurrence prediction.

**Table 3.** Univariate and multivariate binary logistic regression analysis results to determine risk factors effective in IGM recurrence

	Univariate		Multivariate	
	p values	OR (CI 95%)	p values	OR (CI 95%)
Axillary LAP Yes, against no	0.006	3.88 (1.46-10.03)	ns	
Breastfeeding duration (month) ≥24.5 against <24.5	0.002	6.33 (1.95-20.05)	0.042	4.12 (1.05-16.11)
AGR ≤1.183 against ≥1.183	0.001	0,18 (0.66-0.51)	ns	
TyG index ≥8.68 against <8,68	0.001	6.27 (2.18-18.01)	0.005	5.75 (1.69-19.54)

Note: Statistically significant results ( $p < 0.05$ ).  
Abbreviations: ns, not significant; OR, Odds ratio; CI, Confidence interval; TyG, Triglyceride-glucose index; AGR, Albumin-to-globulin ratio; LAP, Lymphadenopathy

Insulin resistance is defined as a reduced response to normal concentrations of insulin in the bloodstream. Metabolic disturbances caused by IR can induce oxidative stress, exacerbate inflammatory responses and impair endothelial function.<sup>23,24</sup> The TyG index, which is a good indicator of IR, has been associated with many diseases including cardiovascular, cerebrovascular and renal disease, subclinical atherosclerosis, non-alcoholic fatty liver disease and malignancy.<sup>8,9,12-19</sup> In addition, there are studies showing that the TyG index is associated with poor prognosis in infectious diseases such as COVID-19, chronic hepatitis B and C.<sup>10,11</sup> Although there are a few studies investigating the relationship between the TyG index and breast cancer, we did not find any studies investigating the relationship between IGM and the TyG index. To our knowledge, this is the first study to investigate the role of the TyG index in predicting recurrence in IGM patients. In our study, the TyG index was significantly higher in the recurrence group and the cut-off value in the ROC analysis was 8.68. A TyG index above this value emerged as an independent risk factor for recurrence in multivariate logistic regression analysis. Therefore, our findings suggest that the TyG index may be an effective and reliable biomarker for predicting recurrence in patients with IGM.

At this stage, it does not seem possible to point to a clear mechanism to explain the relationship between the TyG index and the recurrence of IGM. However, it is likely that the relationship between IR and chronic inflammation may be mediated by a number of different mechanisms. IR is known to cause an increase in pro-inflammatory cytokines, including tumour necrosis factor (TNF) and interleukin (IL).<sup>25</sup> In addition, IR can cause inflammation and tissue damage by activating cytokine producers in inflammatory cells that contribute to oxidative stress.<sup>26</sup> As a result, the altered immune response associated with IR may predispose patients with IGM to complications such as recurrence.

In our study, we did not detect a significant relationship between laboratory parameters such as WBC, CRP, ESR, lymphocyte and neutrophil between both groups. However, previous studies have found a significant association between the inflammatory biomarkers NLR and PLR and IGM recurrence.<sup>27,28</sup> However, our study did not find an association between these biomarkers and IGM recurrence. Ciftci et al.<sup>4</sup> found that low AGR was an independent risk factor for IGM recurrence in a study. In this study, the association of AGR with IGM recurrence was significant in univariate regression analysis but not in multivariate regression analysis. This may be because the concentrations of albumin and globulin are affected by a number of factors, such as the individual's diet and body fluid volume status.

In our study, the mean age at diagnosis of IGM patients was  $32.1 \pm 5.9$  years, with a follow-up of  $27.6 \pm 4.6$  months and a recurrence rate of 26%, which is consistent with previous literature studies.<sup>3,5,22,27-31</sup> However, similar to many studies in the literature, the majority of our patients were premenopausal (94.5%), had given birth at least once (92.4%) and most had a history of breastfeeding (86.9%).<sup>3,5,30,31</sup> In our study, we found that 73.9% of patients had a history of oral contraceptive use and 9.2% of them had a history of smoking. In the literature,

there is a significant association between history of pregnancy,<sup>3</sup> breastfeeding,<sup>3,5</sup> average number of births,<sup>5</sup> smoking,<sup>3,5</sup> BMI<sup>5,32</sup> and history of oral contraceptive use<sup>33,34</sup> and IGM recurrence. While there are studies reporting an association, there are also studies reporting the opposite.<sup>22,31,35-37</sup> In our study, no association was found between these findings and IGM recurrence.

Many studies suggest that breastfeeding is one of the most important risk factors for developing IGM.<sup>5,38-40</sup> During breastfeeding, the breast lobules secrete a protein-rich fluid and the milk ducts expand. After prolonged breastfeeding, the acini and ducts remain constantly active and dilated, facilitating rupture of these structures and causing local inflammation as a result of the spread of luminal secretions into the connective tissue. As a result, lymphocytes and macrophages migrating to this area initiate the granulomatous inflammatory response.<sup>40</sup> Yilmaz et al.<sup>5</sup> found that breastfeeding for more than 18 months may be a risk factor for IGM recurrence. In our study, prolonged breastfeeding was significantly higher in the recurrence group, and the cut-off in the ROC analysis was 24.5 months. In multivariable logistic regression analysis, breastfeeding duration above this level was an independent risk factor for recurrence. Therefore, our results indicate that IGM patients with a history of long-term breastfeeding should be informed and monitored more closely in case of recurrence.

The most common clinical finding in IGM is usually a painful or painless palpable mass in the unilateral breast.<sup>41</sup> The most common presenting complaint in this study was a palpable breast mass (68 patients, 73.9%), which is consistent with the literature. IGM are usually unilateral and bilateral involvement has rarely been reported.<sup>6,42</sup> While bilateral involvement was not observed in our study, 53 (57.6%) patients had right breast involvement and 39 (42.4%) patients had left breast involvement. Tasci et al.<sup>33</sup> reported in a study they performed that clinical data had no statistical effect on recurrence. Similarly, our study showed that patients' clinical findings did not have a significant impact on recurrence.

The definitive diagnosis of IGM is made by tru-cut biopsy, FNAC and surgical excision. In our study, tru-cut biopsy was the most commonly used diagnostic method, with a rate of 73.9%, because it is less invasive and provides a highly accurate diagnosis. FNAC is the least used diagnostic method because cytological diagnostic criteria have not been fully determined, its diagnostic power is low, and it can rarely be confused with carcinoma.<sup>43</sup> In our study, no statistical relationship was found between diagnostic methods and IGM recurrence.

Although there are no disease-specific imaging findings in the diagnosis of IGM, the most commonly used imaging modality is USG due to the young patient population.<sup>44,45</sup> Hypoechoic, heterogeneous, tubular-configured lesions, hypoechoic masses with lobulated contours, multiloculated abscess collections and skin fistulization can be visualized on USG.<sup>46</sup> Abscess formation is an important complication that determines the severity of IGM.<sup>5</sup> A few studies in the literature have reported that the presence of abscess detected by USG is a risk factor for recurrence.<sup>5,47</sup> In contrast, Abbi et al.<sup>34</sup> showed in their study that the absence of an abscess on histopathology was a

risk factor for recurrence. Tasci et al.<sup>33</sup> reported in their study that radiological findings in the breast parenchyma did not have a statistically significant effect on recurrence. In this study, we found that radiological findings detected in the breast parenchyma by USG did not have a significant effect on recurrence.

Axillary lymph node involvement may be seen in IGM patients and may be of concern. It has been reported in the literature that unilateral axillary lymphadenopathy, with cortical thickening and usually involving the hilar region, may develop in up to 70% of patients.<sup>42,46,48,49</sup> In this study, 34.7% of all IGM patients had axillary lymphadenopathy, compared to 58.3% of recurrent patients. We found that axillary lymphadenopathy was statistically significantly higher in patients with recurrence. The association of axillary lymphadenopathy with IGM recurrence was significant in univariate regression analysis. This study shows that axillary lymphadenopathy may be an effective factor in predicting IGM recurrence.

### Limitations

The main limitation of this study is the relatively small number of patients who developed a recurrence. Secondly, the fact that the study was conducted in a single centre prevents us from making generalisations. For these reasons, future multicentre studies with a larger number of patients are needed to support our findings.

## CONCLUSION

In conclusion, our results show that the risk of recurrence is higher in IGM patients with a TyG index greater than 8.68 at the time of initial presentation and a breastfeeding history of more than 24.5 months. Therefore, asking about breastfeeding history at admission and measuring and analysing the TyG index can identify patients at high risk of recurrence.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics Committee Approval was obtained from the Siirt University Non-invasive Ethics Committee (Date: 22.02.2024, Decision No: 101661).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients. .

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

## Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## Acknowledgments

The author would like to thank Dr Enver Ay from the Department of General Surgery for his help in the preparation of this study.

## REFERENCES

- Martinez-Ramos D, Simon-Monterde L, Suelves-Piqueres C, et al. Idiopathic granulomatous mastitis: a systematic review of 3060 patients. *Breast J*. 2019;25(6):1245-1250. doi:10.1111/tbj.13446
- Altintoprak F, Kivilcim T, Ozkan OV. Aetiology of idiopathic granulomatous mastitis. *World J Clin Cases: WJCC*. 2014;2(12):852. doi: 10.12998/wjcc.v2.i12.852
- Uysal E, Soran A, Sezgin E. Granulomatous mastitis study group. Factors related to recurrence of idiopathic granulomatous mastitis: what do we learn from a multicentre study? *ANZ J Surg*. 2018;88(6):635-639. doi: 10.1111/ans.14115
- Ciftci AB, Bük ÖF, Yemez K, Polat S, Yazıcıoğlu İM. Risk factors and the role of the albumin-to-globulin ratio in predicting recurrence among patients with idiopathic granulomatous mastitis. *J Inflamm Res*. 2022;5401-5412. doi: 10.2147/JIR.S377804
- Yılmaz TU, Gürel B, Güler SA, et al. Scoring idiopathic granulomatous mastitis: an effective system for predicting recurrence? *Eur J Breast Health*. 2018;14:112-116. doi: 10.5152/ejbh.2018.3709
- Aghajanzadeh M, Hassanzadeh R, Alizadeh Sefat S, et al. Granulomatous mastitis: presentations, diagnosis, treatment and outcome in 206 patients from the north of Iran *Breast*. 2015;24:456-460. doi: 10.1016/j.breast.2015.04.003
- Baslaim MM, Khayat HA, Al-Amoudi SA. Idiopathic granulomatous mastitis: a heterogeneous disease with variable clinical presentation. *World J Surg* 2007;31:1677-1681. doi:10.1007/s00268-007-9116-1
- Su J, Li Z, Huang M, et al. Triglyceride glucose index for the detection of the severity of coronary artery disease in different glucose metabolic states in patients with coronary heart disease: a RCSCD-TCM study in China. *Cardiovasc Diabetol*. 2022; 21(1): p.96. doi:10.1186/s12933-022-01523-7
- Zhang S, Du T, Zhang J et al. The triglyceride and glucose index (TyG) is an effective biomarker to identify nonalcoholic fatty liver disease. *Lipids Health Dis*. 2017;16,1-8. doi: 10.1186/s12944-017-0409-6
- Sterling RK, King WC, Khalili M, Kleiner DE, Hinerman AS, Sulkowski M. Performance of serum-based scores for identification of mild hepatic steatosis in hbv mono-infected and HBV-HIV Co-infected adults. *Digest Dis Sci*. 2021;1-13. doi:10.1007/s10620-021-06860-3
- Ren H, Yang Y, Wang F, et al. Association of the insulin resistance marker TyG index with the severity and mortality of COVID-19. *Cardiovasc Diabetol*. 2020;19:1-8. doi:10.1186/s12933-020-01035-2
- Wei Y, Guo J. High triglyceride-glucose index is associated with poor prognosis in patients with acute pancreatitis. *Digest Dis Sci*. 2023;68(3):978-987. doi:10.1007/s10620-022-07567-9
- Fang Y, Xiong B, Shang X, Yang F, Yin Y, Sun Z. Triglyceride-glucose index predicts sepsis-associated acute kidney injury and length of stay in sepsis: a MIMIC-IV cohort study. *Heliyon*. 2024; 10(7). doi:10.1016/j.heliyon.2024.e29257
- Lin HY, Zhang XJ, Liu YM, Geng LY, Guan LY, Li, XH. Comparison of the triglyceride glucose index and blood leukocyte indices as predictors of metabolic syndrome in healthy Chinese population. *Sci Rep*. 2021;11(1):p.10036. doi:10.1038/s41598-021-89494-9
- Yan F, Yan S, Wang J, et al. Association between triglyceride glucose index and risk of cerebrovascular disease: systematic review and meta-analysis. *Cardiovasc Diabetol*. 2022;21(1):p.226. doi:10.1186/s12933-022-01664-9
- Cai C, Chen C, Lin X, et al. An analysis of the relationship of triglyceride glucose index with gastric cancer prognosis: a retrospective study. *Cancer Med*. 2024; 13(3):e6837. doi:10.1002/cam4.6837
- Shi H, Zhou L, Yang S, Zhou H. The relationship between triglyceride and glycose (TyG) index and the risk of gynaecologic and breast cancers. *Clin Nutr ESPEN*. 2022;51:345-52. doi:10.1016/j.clnesp.2022.08.004
- Alkurt EG, Ozkan MB, Turhan VB. Predictive value of triglyceride/glucose index (TyG) in predicting breast cancer in patients with breast mass. *Eur Rev Med Pharmacol Sci*. 2022; 26:4671-6. doi: 10.26355/eurrev\_202207\_29191
- Zhang J, Yin B, Xi Y, Bai Y. Triglyceride-glucose index is a risk factor for breast cancer in China: a cross-sectional study. *Lipids Health Dis*. 2024;23(1):29. doi:10.1186/s12944-024-02008-0
- Liu X, Tan Z, Huang Y, et al. Relationship between the triglyceride-glucose index and risk of cardiovascular diseases and mortality in the general population: a systematic review and meta-analysis. *Cardiovasc Diabetol*. 2022;21:124. doi:10.1186/s12933-022-01546-0
- Bedi DG, Krishnamurthy R, Krishnamurthy S et al. Cortical morphologic features of axillary lymph nodes as a predictor of metastasis in breast cancer: in vitro sonographic study. *AJR*. 2008; 191(3):646-652. doi:10.2214/AJR.07.2460
- Azizi A, Prasath V, Canner J, et al. Idiopathic granulomatous mastitis: management and predictors of recurrence in 474 patients. *Breast J*. 2020; 26(7):1358-1362. doi: 10.1111/tbj.13822
- Zhang B, Peng A, Li S, Li F, Wan J, Lu J. Association of triglyceride-glucose index and neutrophil-to-lymphocyte ratio with coronary artery disease. *BMC Cardiovasc Disord*. 2023; 23(1), 534. doi: 10.1186/s12872-023-03564-6
- Hao B, Lyu L, Xu J, et al. The relationship between triglyceride-glucose index and prospective key clinical outcomes in patients hospitalised for coronary artery disease. *Cardiovasc Diabetol*. 2024;23(1):40. doi:10.1186/s12933-024-02132-2
- Yan Y, Zhou L, La R, et al. The association between triglyceride glucose index and arthritis: a population-based study. *Lipids Health Dis*. 2023;22(1):132. doi: 10.1186/s12944-023-01899-9
- Hu M, Zhang Y, Guo X, et al. Hyperandrogenism and insulin resistance induce gravid uterine defects in association with mitochondrial dysfunction and aberrant reactive oxygen species production. *Am J Physiol Endocrinol Metab*. 2019;316:E794-e809. doi: 10.1152/ajpendo.00359.2018
- Cetinkaya OA, Celik SU, Terzioglu SG, Eroglu A. The predictive value of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in patients with recurrent idiopathic granulomatous mastitis. *Eur J Breast Health*. 2020;16(1):61-65. doi:10.5152/ejbh.2019.5187
- Kargin S, Turan E, Esen HH, Çetin Kargin N. Role of pre-treatment neutrophil-lymphocyte ratio in the prediction of recurrences after granulomatous mastitis treatment. *Türk Klinikleri J Med Sci*. 2020;40(1):46-51. doi:10.5336/medsci.2019-66835
- Basim P, Argun D, Argun F. Risk factors for idiopathic granulomatous mastitis recurrence after patient-tailored treatment: do we need an escalating treatment algorithm? *Breast Care*. 2022;17(2):172-179. doi:10.1159/000517399



30. Velidedeoglu M, Umman V, Kilic F, et al. Idiopathic granulomatous mastitis: introducing a diagnostic algorithm based on 5 years of follow-up of 152 cases from Turkey and a review of the literature. *Surg Today*. 2022;52(4):668–680. doi:10.1007/s00595-021-02367-6
31. Huang YM, Lo C, Cheng CF, Lu CH, Hsieh SC, Li KJ. Serum C-reactive protein and interleukin-6 levels as biomarkers for disease severity and clinical outcomes in patients with idiopathic granulomatous mastitis. *J Clin Med*. 2021;10:10. doi:10.3390/jcm10102077
32. Huang Y, Wu H. A retrospective analysis of recurrence risk factors for granulomatous lobular mastitis in 130 patients: more attention should be paid to prolactin level. *Ann Palliat Med* 2021;10(3):2824831-2822831. doi:10.21037/apm-20-1972
33. Tasci HI, Turk E, Erinanc OH, Erkan S, Gundogdu R, Karagulle E. Factors affecting recurrence of idiopathic granulomatous mastitis. *JCPSP*. 2022; 32(2):161-166. doi:10.29271/jcpsp.2022.02.161
34. Abbi B, Sanghavi N, Lanjewar S et al. Clinical, histological features, and predictors of relapse in patients with idiopathic granulomatous mastitis. *Medicine*. 2023;102(44):e35679. doi:10.1097/MD.00000000000035679
35. Çetinkaya ÖA, Çelik SU, Terzioğlu SG, Eroğlu A. The predictive value of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in patients with recurrent idiopathic granulomatous mastitis. *Eur J Breast Health*. 2020;16(1):61. doi:10.5152/ejbh.2019.5187
36. Fattahi AS, Amini G, Sajedi F, Mehrad-Majd H. Factors affecting recurrence of idiopathic granulomatous mastitis: a systematic review. *Breast J*. 2023;2023. doi:10.1155/2023/9947797
37. Aydın HO, Baykal A, Konan A, Kaynaroğlu V. Idiopathic granulomatous mastitis: factors influencing recovery and recurrence. *Eur J*. 2019;5(5):768-775. doi:10.18621/eurj.424016
38. Oltean HN, Soliman AS, Omar OS, et al. Risk factors for chronic mastitis in Morocco and Egypt. *Int J Inf*. 2013;184921. doi:10.1155/2013/184921
39. Erhan Y, Veral A, Kara E, et al. A clinicopathologic study of a rare clinical entity mimicking breast carcinoma: idiopathic granulomatous mastitis. *Breast*. 2000;9:52–56. doi:10.1054/brst.1999.0072
40. Verfaillie G, Breucq C, Sacre R, Bourgain C, Lamote J. Granulomatous lobular mastitis: a rare chronic inflammatory disease of the breast which can mimic breast carcinoma. *Acta Chir Belg*. 2006;106:222–224. doi:10.1080/00015458.2006.11679876
41. Akcan A, Akyildiz H, Deneme MA, Akgun H, Aritas Y: Granulomatous lobular mastitis: a complex diagnostic and therapeutic problem. *World J Surg*. 2006;30:1403-1409. doi:10.1007/s00268-005-0476-0
42. Fazio RT, Shah SS, Sandhu NP, Glazebrook KN. Idiopathic granulomatous mastitis: imaging update and review. *Insights Imaging*. 2016;7(4):531–539. https://doi.org/10.1007/s13244-016-0499-0
43. Bani-Hani KE, Yaghan RJ, Matalka II, Shatnawi NJ. Idiopathic granulomatous mastitis: time to avoid unnecessary mastectomies. *Breast J*. 2004;10:318-322. doi:10.1111/j.1075-122X.2004.21336.x
44. Zhou F, Liu L, Liu L, et al. Comparison of conservative versus surgical treatment protocols in treating idiopathic granulomatous mastitis: a meta-analysis. *Breast Care*. 2020;15(4):415-420. doi:10.1159/000503602
45. Vanovcanova L, Lehotska V, Machalekova K, et al. Idiopathic granulomatous mastitis-a new approach in diagnostics and treatment. *Neoplasma*. 2019;66(4):661-668. doi:10.4149/neo\_2019\_190201N100
46. Gautier N, Lalonde L, Tran-Thanh D, El Khoury M, David J, Labelle M. Chronic granulomatous mastitis: imaging, pathology and management. *Eur J Radiol*. 2013;82(4):e165-e175. doi:10.1016/j.ejrad.2012.11.010
47. Lermi N, Ekin A, Ocak T, Bozkurt ZY, Ötegeçeli MA, Yağız B. What predicts the recurrence in idiopathic granulomatous mastitis?. *Clin Rheumatol*. 2023;42(9):2491-2500. doi:10.1007/s10067-023-06651-3
48. Yildiz S, Aralasmak A, Kadioglu H, et al. Radiologic findings of idiopathic granulomatous mastitis. *Med Ultrason*. 2015;17:39-44. doi:10.11152/mu.2013.2066.171.rfm
49. Teke M, Teke F, Alan B, et al. Differential diagnosis of idiopathic granulomatous mastitis and breast cancer using acoustic radiation force impulse imaging. *J Med Ultrason*. 2001;2017;44:109-115. doi:10.1007/s10396-016-0749-2