



## Original Research

# Identification of Risk Factors for Mastalgia and Its Relationship with Benign or Malignant Breast Diseases

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### Abstract

**Objectives:** Mastalgia is a medical condition that primarily affects women of all age groups. Affected individuals experience excruciating pain, tightness, or a burning sensation in the breast tissue. The aim of this study is to observe the clinicopathologic features of women with mastalgia and compare these features with asymptomatic cases.

**Methods:** A total of 524 female patients who applied to the general surgery outpatient clinic were prospectively evaluated. The patients were divided into two groups. Group 1 (G1) included patients with mastalgia, while Group 2 (G2) included asymptomatic patients. The two groups were compared in terms of clinical, radiological, and pathological features.

**Results:** This study was conducted on 524 women, among whom the prevalence of mastalgia was found to be 61.45%. There were 322 patients in G1 and 202 patients in G2. The mean age was significantly higher in G2 compared to G1 ( $46.33 \pm 10.33$  vs.  $43.58 \pm 10.33$ , respectively;  $p=0.001$ ). Premenopausal women rates for G1 and G2 were 73.91% and 59.4%, respectively ( $p=0.001$ ). The regular exercise rate in G1 was 18.01%, while it was 25.74% in G2 ( $p=0.034$ ). The past history of breast cancer rate was significantly higher in G2 than in G1 ( $p=0.015$ ). The consumption of analgesics was significantly lower in G2 compared to G1 ( $p=0.05$ ). Non-steroidal anti-inflammatory drugs were the most commonly used analgesic drug class in both groups, with significant intergroup differences (G1: 27.63%, G2: 19.8%,  $p=0.043$ ). Screening mammography with or without ultrasound examination was performed significantly more often in G2 compared to G1 (66.33% vs. 55.27% and 82.17% vs. 72.98%,  $p=0.012$  and  $p=0.016$ , respectively). No significant difference was found concerning the frequency of benign or malignant pathologies between the groups.

**Conclusion:** Breast pain is common and should be considered physiological without other breast symptoms and after excluding non-breast causes. It is safe to provide symptom control advice and reassurance to patients who have breast pain but do not have signs or symptoms indicating a possible serious underlying condition requiring further medical intervention.

**Keywords:** Analgesic, breast pain, exercise, mammography, mastalgia, ultrasound

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Mastalgia, a medical term for breast pain, is a prevalent concern among premenopausal and perimenopausal women. Globally, nearly two-thirds of women experience breast pain during their reproductive years and seek medi-

cal attention.<sup>[1]</sup> Typically, breast pain resolves spontaneously without the need for treatment, although some types of breast pain may signal an underlying issue within the breast.<sup>[2]</sup>

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Understanding the nature of breast pain is crucial. Mastalgia can be broadly categorized into three groups: cyclic, non-cyclic, and extramammary.<sup>[3, 4]</sup> Cyclic mastalgia is associated with hormonal fluctuations during the menstrual cycle. It is not related to abnormal hormone levels but rather an increased sensitivity of breast tissue to these hormonal changes. This pain intensifies in the weeks leading up to menstruation, subsides with the onset of the period, and gradually fades away. It typically affects both breasts diffusely but can also be unilateral and extend to the axilla or arms. Noncyclic mastalgia, on the other hand, is unrelated to the menstrual cycle. It may persist continuously or intermittently and is often unilateral, localized to a specific quadrant of the breast. Anatomical changes, previous breast trauma or surgery, infections, or other factors typically underlie noncyclic mastalgia. Extramammary breast pain may originate from intercostal neuralgia, coronary, pulmonary, esophageal, stomach, or gallbladder pathologies, chest wall diseases (such as pectoralis muscle injuries or costochondritis), shingles, spinal and paraspinal muscle disorders, or trauma. While it may feel like the pain originates within the breast, it is, in fact, referred pain originating from outside the breast area.

The exact etiology of mastalgia remains undefined. Some medications, including hormonal medications, certain antidepressants, and antihistamines, have been associated with breast pain. Additionally, anxiety, stress, depression, caffeinated beverages, high-fat diets, and smoking have been suggested as contributing factors by some authors.<sup>[2, 5, 6]</sup>

Effective management of mastalgia necessitates a multidisciplinary approach. This approach includes making an accurate diagnosis through clinical history, physical examination, and imaging methods, addressing patient stress and anxiety, modifying dietary patterns and lifestyle, concurrently ruling out any underlying pathology, and managing recurrent episodes. The physical examination should encompass palpation of both breasts, axillae, chest wall, and the skin of the breast, abdomen, back, shoulders, and upper arms. Breast screening can help alleviate anxiety, and if imaging reveals abnormalities in the localized area of pain, a breast biopsy may be warranted. Despite receiving reassurance from negative imaging results, around 15% of patients may still require treatment due to the negative impact of mastalgia on their quality of life or the increasing intensity and frequency of painful episodes following their initial visit.<sup>[7]</sup> Initially, investigating the exact etiology of mastalgia and focusing on pain relief through conservative treatment is essential. Typically, mastalgia resolves on its own within 3 months to 3 years.<sup>[8]</sup> Pharmacological treatments have shown promising results in most cases

with persistent complaints. In severe and refractory cases, consideration may be given to endocrine treatments, although these should be used cautiously due to potential side effects.<sup>[5]</sup>

The prognosis and clinical significance of mastalgia remain subject to debate. Women presenting with mastalgia often worry about the possibility of breast cancer. However, breast pain is rarely a symptom of breast cancer, occurring in only 0 to 3% of patients subsequently diagnosed with the disease.<sup>[9-11]</sup> Consequently, the differentiation between women with mastalgia and asymptomatic cases based on clinical, radiological, and pathological differences has gained importance in determining follow-up procedures and further testing for mastalgia patients. This study aims to determine the prevalence of mastalgia, identify its underlying risk factors, and explore its relationship with benign and malignant breast diseases.

## Methods

This study included 322 subjects with complaints of breast pain and 202 control subjects who visited our outpatient clinic between September 2022 and November 2022. The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval for this prospective study was obtained from the local Ethics Committee (Date: 01.09.2022, Number: 10-22), and informed consent was obtained from all individual participants included in the study.

Patient data, including medical history, physical examination findings, demographic information, radiological reports, and pathological data, were systematically recorded. A comprehensive survey was conducted for all enrolled patients, covering marital status, employment status, emotional stress levels, caffeine or nicotine consumption, exercise habits, number of infants breastfed, age at first conception, menstrual irregularities, menopausal status, history of prior bilateral salpingo-oophorectomy with or without total abdominal hysterectomy, breast size, recent direct breast trauma, history of hormonal contraception use, family history of breast or ovarian cancer, past history of breast cancer, surgical interventions or biopsies, pain in other parts of the body, and analgesic consumption.

Exclusion criteria were applied to individuals who were unable or insufficient to complete the questionnaires, those who were pregnant or lactating, and those exhibiting red flag signs or symptoms, which included palpable lumps, skin irritation or dimpling, redness, scaliness, or thickening of the nipple or breast skin, nipple shrinkage, mammary structural disorders, nipple discharge, and breast swelling.

The type of pain, its location, and its relationship with the menstrual cycle were assessed for all patients, followed by a comprehensive physical examination. Macromastia was defined as a distance between the sternal notch and the nipple exceeding 33 cm.<sup>[12]</sup> Weight and height measurements were taken, and body mass index (BMI) was calculated as the ratio of weight to height squared ( $\text{kg}/\text{m}^2$ ). Family history of breast or ovarian cancer was recorded for only first-degree relatives.

Women under 40 years of age generally underwent breast ultrasound (US) evaluation. Although the sensitivity of screening mammography (MMG) depends on breast tissue density, it was typically performed in women aged 40 years and older or in patients under 40 years of age with suspicious US findings.<sup>[13, 14]</sup> Radiologists experienced in mammography and breast US with varying levels of expertise conducted all mammograms and ultrasounds.

### Statistical Analysis

The study data were analyzed using SPSS version 25.0 (SPSS, Inc., Chicago, IL). The normal distribution of variables was assessed using the Kolmogorov-Smirnov test. Descriptive statistics, such as mean, standard deviation, median, frequency, and minimum-maximum values, were used to summarize the data. Categorical variables were compared using the Pearson's Chi-Square test, while nonparametric variables that did not exhibit a normal distribution were compared using the Mann-Whitney U test. Logistic regression analysis was employed to evaluate factors such as radiation, radiation in conjunction with menstruation, and laterality of breast pain. Statistical significance was defined as a p-value less than 0.05.

### Results

Demographic and clinical characteristics of the patients analyzed according to the groups are presented in Table 1. In Group 1 (G1), the mean age was  $43.58 \pm 10.33$  (20–73) years, while in Group 2 (G2), it was  $46.33 \pm 10.33$  (19–70) years ( $p=0.001$ ). G1 exhibited significantly lower levels of physical activity compared to G2 (18.01% vs. 25.74%,  $p=0.034$ ). Out of a total of 524 patients, 358 (68.32%) were premenopausal, and 166 (31.67%) were postmenopausal (G1: 238 (73.91%) and 84 (26.08%); G2: 120 (59.4%) and 82 (40.59%),  $p=0.001$ ). Additionally, the past history of breast cancer rate was 0.62% in G1 and 3.46% in G2, with the rate being significantly higher in G2 ( $p=0.015$ ).

The incidence of patients not using analgesics was 62.42% in G1 and 70.79% in G2, with significant intergroup differences ( $p=0.05$ ). The use of non-steroidal anti-inflammatory drugs (NSAIDs) was observed in 27.63% of G1 and 19.8%

of G2 ( $p=0.043$ ). No significant intergroup differences were detected in terms of the use of acetylsalicylic acid (ASA), metamizole, and paracetamol.

Table 2 summarizes the radiological examinations, interventional procedures or biopsies performed, and the distribution of patients newly diagnosed with breast cancer by groups. Mammography (MMG) was used in 401 (76.52%) patients (G1: 235 (72.98%), G2: 166 (82.17%),  $p=0.016$ ). Breast ultrasound (US) was performed on 441 (84.16%) patients (G1: 269 (83.54%), G2: 172 (85.14%),  $p=0.624$ ). A total of 312 (59.54%) patients underwent both US and MMG (G1: 178 (55.27%), G2: 134 (66.33%),  $p=0.012$ ). Most subjects were categorized as BIRADS 0. No significant differences were found in terms of breast density and mammographic BI-RADS category ( $p=0.078$  and  $p=0.24$ , respectively). The majority of women who underwent US had healthy breasts ( $n=235$ , 53.28%).

Surgery was recommended for benign or malignant indications in 12 patients in G1 and 13 patients in G2, without any significant intergroup difference ( $p=0.157$ ). In G1, 1 patient underwent surgery due to a malignant finding, and 3 patients were referred for neoadjuvant chemotherapy. In G2, 3 patients underwent surgery as a result of a malignant finding, and none of the patients were referred for neoadjuvant chemotherapy. Four (1.24%) women in G1 and 3 (1.48%) women in G2 were diagnosed with breast cancer. No significant difference was found concerning the number of patients newly diagnosed with breast cancer ( $p=0.814$ ). All four patients newly diagnosed with breast cancer in G1 presented with localized breast pain at the site of the malignant tumor (Figs. 1, 2).

Breast pain was categorized as diffuse in 106 (32.91%) patients and localized in 216 (67.08%) patients. Ninety-seven (30.12%) patients presented with bilateral mastalgia, 94 (29.19%) with right-sided breast pain, and 131 (40.68%) with left-sided breast pain. Unilateral mastalgia was reported by 225 (69.87%) patients, while 96 (36.36%) patients complained of cyclical mastalgia, and 168 (63.63%) patients had noncyclical mastalgia.

Statistical analysis revealed that bilateral mastalgia was more likely to be associated with diffuse breast pain (26.8% vs. 73.2%), whereas unilateral mastalgia was more likely to be associated with localized breast pain (84.4% vs. 15.56%) ( $p<0.001$ ). Additionally, patients with cyclic mastalgia had a higher rate of diffuse breast pain compared to patients with non-cyclic mastalgia (41.67% vs. 28.57%) ( $p=0.03$ ) (Table 3). Multivariate analysis by binary logistic regression found that bilateral mastalgia is an independent risk factor for diffuse breast pain ( $p<0.001$ ), increasing the likelihood of diffuse breast pain approximately 16.159-fold.

**Table 1.** Demographics and clinical data of the patients applied the outpatient clinic

	Total	Group 1	Group 2	p
Patients, n (%)	524	322 (61.45)	202 (38.54)	
Age				
Mean±SD	44.64±10.42	43.58±10.33	46.33±10.33	0.001
Median (Min-Max)	44 (19-73)	43 (20-73)	46 (19-70)	
Height (cm)				
Mean±SD	161.46±5.76	161.6±5.73	161.23±5.81	0.382
Median (Min-Max)	160 (145-180)	160 (145-180)	160 (146-179)	
Weight (kg)				
Mean±SD	71±12.75	70.8±12.71	71.3±12.8	0.438
Median (Min-Max)	70 (43-138)	70 (44-138)	70 (43-125)	
BMI				
Mean±SD	27.24±4.88	27.12±4.81	27.43±4.99	0.249
Median (Min-Max)	26.75 (14.9-45.7)	26.4 (14.9-45.7)	27.3 (16.6-45)	
Marital status				
Married	449 (85.68)	279 (86.64)	170 (84.15)	0.429
All unmarried	75 (14.31)	43 (13.35)	32 (15.84)	
Employment status, n (%)				
Housewife	431 (82.25)	267 (82.91)	164 (81.18)	0.614
Employed	93 (17.74)	55 (17.08)	38 (18.81)	
Stress, n (%)				
Yes	196 (37.4)	127 (39.44)	69 (34.15)	0.224
No	328 (62.59)	195 (60.55)	133 (65.84)	
Cups of coffee per day, n (%)				
0	392 (74.8)	246 (76.39)	146 (72.27)	0.284
1	67 (12.78)	34 (10.55)	33 (16.33)	
2	45 (8.58)	29 (9)	16 (7.92)	
≥3	20 (3.81)	13 (4.03)	7 (3.46)	
Smoking (cigarettes/day), n (%)				
0	425 (81.1)	257 (79.81)	168 (83.16)	0.796
<5	19 (3.62)	12 (3.72)	7 (3.46)	
5-10	55 (10.49)	36 (11.18)	19 (9.4)	
>10	25 (4.77)	17 (5.27)	8 (3.96)	
Regular exercise				
Yes	110 (20.99)	58 (18.01)	52 (25.74)	0.034
No	414 (79)	264 (81.98)	150 (74.25)	
Lactation (breast-fed infants), n (%)				
0	86 (16.41)	52 (16.14)	34 (16.83)	0.979
1	44 (8.39)	27 (8.38)	17 (8.41)	
2	154 (29.38)	92 (28.57)	62 (30.69)	
3	143 (27.29)	90 (27.95)	53 (26.23)	
≥4	97 (18.51)	61 (18.94)	36 (17.82)	
Age at first conception				
Mean±SD	22.84±5.03	22.8±5.01	22.91±5.06	0.877
Median (Min-Max)	22 (12-43)	22 (12-43)	22 (14-40)	
Menstrual irregularity				
Yes	129 (36.03)	83 (34.87)	46 (38.33)	0.520
No	229 (63.96)	155 (65.12)	74 (61.66)	
Menopause, n (%)				
Premenopausal	358 (68.32)	238 (73.91)	120 (59.4)	0.001
Postmenopausal	166 (31.67)	84 (26.08)	82 (40.59)	

**Table 1. CONT.**

	Total	Group 1	Group 2	p
BSO±TAH, n (%)				
Yes	31 (5.91)	17 (5.27)	14 (6.93)	0.436
No	493 (94.08)	305 (94.72)	188 (93.06)	
Breast size, n (%)				
Normal	445 (84.92)	275 (85.4)	170 (84.15)	0.698
Macromastia	79 (15.07)	47 (14.59)	32 (15.84)	
Recent breast trauma, n (%)				
Yes	14 (2.67)	8 (2.48)	6 (2.97)	0.737
No	510 (97.32)	314 (97.51)	196 (97.02)	
History of hormonal contraception use, n (%)				
Oral contraceptives	81 (15.45)	51 (15.83)	30 (14.85)	0.761
Intrauterine contraceptive methods	70 (13.35)	45 (13.97)	25 (12.37)	0.601
None	392 (74.8)	235 (72.98)	157 (77.72)	0.224
Family history of breast cancer				
Yes	160 (30.53)	93 (28.88)	67 (33.16)	0.300
No	364 (69.46)	229 (71.11)	135 (66.83)	
Family history of ovarian cancer				
Yes	23 (4.38)	11 (3.41)	12 (5.94)	0.170
No	501 (95.61)	311 (96.58)	190 (94.05)	
Past history of breast cancer				
Yes	9 (1.71)	2 (0.62)	7 (3.46)	0.015
No	515 (98.28)	320 (99.37)	195 (96.53)	
Past history of breast surgery				
Yes	32 (6.1)	19 (5.9)	13 (6.43)	0.803
No	492 (93.89)	303 (94.09)	189 (93.56)	
Past history of breast biopsy				
Yes	54 (10.3)	32 (9.93)	22 (10.89)	0.727
No	470 (89.69)	290 (90.06)	180 (89.1)	
Pain in other sites of the body				
Yes	346 (66.03)	215 (66.77)	131 (64.85)	0.652
No	178 (33.96)	107 (33.22)	71 (35.14)	
Analgesic consumption				
None	344 (65.64)	201 (62.42)	143 (70.79)	0.050
ASA	4 (0.76)	1 (0.31)	3 (1.48)	0.133
Metamizole	6 (1.14)	5 (1.55)	1 (0.49)	0.268
NSAIDs	129 (24.61)	89 (27.63)	40 (19.8)	0.043
Paracetamol	89 (16.98)	57 (17.7)	32 (15.84)	0.581

BMI: body mass index, BSO±TAH: bilateral salpingo-oophorectomy with or without total abdominal hysterectomy, ASA: acetylsalicylic acid, NSAIDs: non-steroidal anti-inflammatory drugs.

Unilateral breast pain rate was significantly higher in patients with noncyclic mastalgia compared to those with cyclic mastalgia (75.6% vs. 59.38%). In contrast, bilateral breast pain rate was significantly higher in patients with cyclic mastalgia compared to those with noncyclic mastalgia (40.63% vs. 24.4%) ( $p=0.006$ ) (Table 4). Multivariate analysis by binary logistic regression found that localized breast pain is an independent risk factor for unilateral mastalgia ( $p<0.001$ ), increasing the incidence of unilateral mastalgia

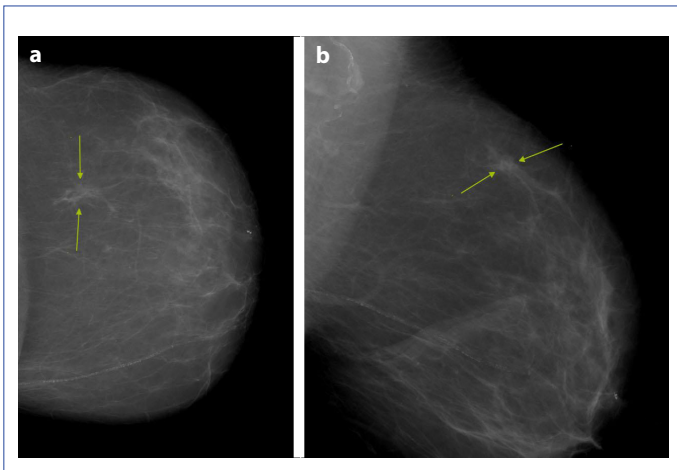
approximately 16.159-fold.

Patients with localized breast pain tended to have a higher rate of noncyclic mastalgia than patients with diffuse breast pain (68.18% vs. 54.55%,  $p=0.03$ ). The rate of noncyclic breast pain in patients with unilateral mastalgia was significantly higher compared to those with bilateral mastalgia (69.02% vs. 51.25%,  $p=0.006$ ) (Table 5). However, radiation and laterality of breast pain were not independent predictors of radiation of breast pain with menstruation ac-

**Table 2.** Comparison of radiological examinations, interventional procedures and the distribution of patients newly diagnosed with breast cancer according to groups.

	Total	Group 1	Group 2	p
MMG taken				0.016
Yes	401 (76.52)	235 (72.98)	166 (82.17)	
No	123 (23.47)	87 (27.01)	36 (17.82)	
US taken				0.624
Yes	441 (84.16)	269 (83.54)	172 (85.14)	
No	83 (15.83)	53 (16.45)	30 (14.85)	
MMG and US taken				0.012
Yes	312 (59.54)	178 (55.27)	134 (66.33)	
No	212 (40.45)	144 (44.72)	68 (33.66)	
Mammographic breast density				0.078
A	39 (9.72)	22 (9.36)	17 (10.24)	
B	49 (12.21)	26 (11.06)	23 (13.85)	
C	264 (65.83)	150 (63.82)	114 (68.67)	
D	49 (12.21)	37 (15.74)	12 (7.22)	
Mammographic BI-RADS category				0.240
0	285 (71.07)	174 (74.04)	111 (66.86)	
1	51 (12.71)	25 (10.63)	26 (15.66)	
2	40 (9.97)	21 (8.93)	19 (11.44)	
3	15 (3.74)	11 (4.68)	4 (2.4)	
4	9 (2.24)	4 (1.7)	5 (3.01)	
5	1 (0.24)	0 (0)	1 (0.6)	
US findings				
Normal	235 (53.28)	143 (53.15)	92 (53.48)	0.946
Symple cyst(s)	232 (52.6)	140 (52.04)	92 (53.48)	0.767
Fibroadenoma(s)	70 (15.87)	48 (17.84)	22 (12.79)	0.157
Fibrocystic disease	71 (16.09)	50 (18.58)	21 (12.2)	0.075
Ductal ectasia	99 (22.44)	65 (24.16)	34 (19.76)	0.281
Intraductal papilloma	6 (1.36)	4 (1.48)	2 (1.16)	0.774
Lymphadenopathy	68 (15.41)	41 (15.24)	27 (15.69)	0.897
Solid lesions	78 (17.68)	45 (16.72)	33 (19.18)	0.509
Lipoma	22 (4.98)	14 (5.2)	8 (4.65)	0.795
IMLN	36 (8.16)	23 (8.55)	13 (7.55)	0.711
Complex cyst(s)	86 (19.5)	50 (18.58)	36 (20.93)	0.545
Fatty tissue necrosis	30 (6.8)	21 (7.8)	9 (5.23)	0.295
MRI taken				0.847
Yes	106 (20.22)	66 (20.49)	40 (19.8)	
No	418 (79.77)	256 (79.50)	162 (80.19)	
Biopsy recommended				0.710
Yes	97 (18.51)	58 (18.01)	39 (19.3)	
No	427 (81.48)	264 (81.98)	163 (80.69)	
Surgery recommended				0.157
Yes	25 (4.77)	12 (3.72)	13 (6.43)	
No	499 (95.22)	310 (96.27)	189 (93.56)	
Newly diagnosed breast cancer				0.814
Yes	7 (1.33)	4 (1.24)	3 (1.48)	
No	517 (98.66)	318 (98.75)	199 (98.51)	

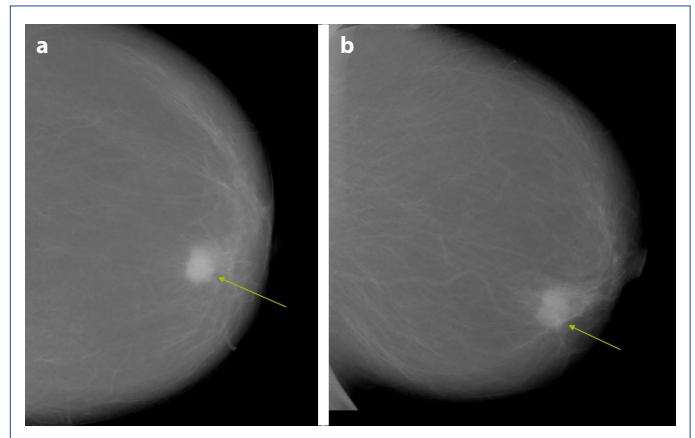
MMG: mammography, US: ultrasound, IMLN: intramammary lymph node, MRI: Magnetic resonance imaging.



**Figure 1.** Image of a 67-year-old woman presenting with localized breast pain in the upper outer left breast who was diagnosed with invasive ductal carcinoma at the site of pain. Cranio-caudal (CC) (a) and medio-lateral oblique (MLO) (b) views of left breast shows an asymmetric opacity at the 1 o'clock position.

According to multivariate binary logistic regression analysis ( $p=0.485$  and  $p=0.069$ ).

There was no statistically significant difference observed between the patients in the diffuse and localized subgroups of G1 in terms of benign breast lesions seen on a US scan (Table 6).



**Figure 2.** Image of a 62-year-old woman presenting with localized breast pain in the lower inner left breast extending the periareolar area who was diagnosed with invasive ductal carcinoma at the site of pain. Cranio-caudal (CC) (a) and medio-lateral oblique (MLO) (b) views of left breast shows an irregular hypoechoic mass with microlobulated margins at the 7 o'clock position.

### Discussion

Mastalgia, characterized by breast pain, is a common complaint among women, especially during the premenopausal and perimenopausal periods, typically occurring between the ages of 30 and 50.<sup>[15]</sup> As supported by the

**Table 3.** The radiation of breast pain and its relationship with laterality and radiation with menstruation

	Radiation				p
	Localized		Diffuse		
	n	%	n	%	
Laterality					
Bilateral	26	(26.80)	71	(73.20)	<0.001
Unilateral	190	(84.44)	35	(15.56)	
Radiation with menstruation					
Cyclic	56	(58.33)	40	(41.67)	0.030
Noncyclic	120	(71.43)	48	(28.57)	

**Table 4.** The laterality of breast pain and its relationship with radiation and radiation with menstruation

	Laterality				p
	Bilateral		Unilateral		
	n	%	n	%	
Radiation					
Localized	26	(12.04)	190	(87.96)	<0.001
Diffuse	71	(66.98)	35	(33.02)	
Radiation with menstruation					
Cyclic	39	(40.63)	57	(59.38)	0.006
Noncyclic	41	(24.40)	127	(75.60)	

**Table 5.** The radiation with menstruation of breast pain and its relationship with radiation and laterality

	Radiation with menstruation				p
	Cyclic		Noncyclic		
	n	%	n	%	
Radiation					
Localized	56	(31.82)	120	(68.18)	0.030
Diffuse	40	(45.45)	48	(54.55)	
Laterality					
Bilateral	39	(48.75)	41	(51.25)	0.006
Unilateral	57	(30.98)	127	(69.02)	

**Table 6.** Ultrasound findings of the patients according to diffuse and localized breast pain subgroups

Radiation (diffuse/localized)	Diffuse, n(%)	Localized, n(%)	p
US findings			
Normal	48 (56.47)	95 (51.35)	0.460
Simple cyst(s)	43 (50.58)	97 (52.43)	0.745
Fibroadenoma(s)	15 (17.64)	33 (17.83)	0.954
Fibrocystic disease	12 (14.11)	38 (20.54)	0.200
Ductal ectasia	22 (25.88)	43 (23.24)	0.654
Intraductal papilloma	1 (1.17)	3 (1.62)	0.775
Lymphadenopathy	11 (12.94)	30 (16.21)	0.476
Solid lesions	15 (17.64)	30 (16.21)	0.784
Lipoma	4 (4.7)	10 (5.4)	0.802
IMLN	5 (5.88)	18 (9.72)	0.288
Complex cyst(s)	20 (23.52)	30 (16.21)	0.157
Fatty tissue necrosis	8 (9.41)	13 (7.02)	0.505

US: ultrasound, IMLN: intramammary lymph node.

literature, the prevalence of mastalgia among women can reach up to 70-80%.<sup>[10]</sup> In our study, women with mastalgia accounted for 61.45% of the study population, with an average age of 43.58 years. Additionally, the prevalence of premenopausal participants in the mastalgia group was significantly higher than in the control group (73.91% vs. 59.4%,  $p=0.001$ ).

Numerous studies have attempted to elucidate the causes of mastalgia, and various factors, including hormonal fluctuations, high-fat diet, smoking, caffeine consumption, and stress, have been suggested. Despite the association of several factors with the risk of developing breast pain, the precise etiology of mastalgia remains unclear.<sup>[2, 5, 6]</sup> In our study, we evaluated patients who presented to our outpatient clinic with complaints of mastalgia and those who sought medical attention for other reasons, considering their demographic and clinical characteristics, radiological findings, interventional procedures, and mastalgia type.

Regular physical activity is known to be protective against

various chronic diseases, such as heart disease, hypertension, and type 2 diabetes. Although the effectiveness of exercise in the treatment of mastalgia is still uncertain, it has been demonstrated that mastalgia patients tend to have sedentary lifestyles, and regular exercise can lead to an increase in endorphin levels, potentially alleviating pain. Moreover, exercise may contribute to pain reduction by promoting weight loss and subsequently reducing estrogen levels. The significantly higher rate of regular exercise in the control group compared to the mastalgia group in our study suggests that regular exercise may be effective in the treatment of mastalgia and its prevention (25.74% vs. 18.01%,  $p=0.034$ ). This finding aligns with the results of a randomized controlled trial conducted by Genc et al.,<sup>[16]</sup> which reported that exercise therapy was effective for mastalgia patients. They observed significant improvements in the sensory component of the breast pain questionnaire and visual analogue scale values in the exercise group ( $p=0.012$  and  $p=0.016$ , respectively).



In our study, we examined the history of breast cancer among the participants in both groups. We found that 0.62% of G1 had a history of breast cancer, while 3.46% of G2 had a history of breast cancer, and this difference was statistically significant ( $p=0.015$ ). However, there was no significant difference between the groups in terms of the incidence of newly diagnosed breast cancer cases ( $p=0.814$ ). These findings are consistent with previous literature.<sup>[11, 17]</sup> For example, Noroozian et al.<sup>[18]</sup> reported that pain was the reason for referral in 617 women, and the prevalence of breast cancer among symptomatic women was 1.8%, which is notably higher than the 1.24% cancer prevalence found in our symptomatic group. However, it is important to note that most patients in Noroozian's study were diagnosed after their initial presentation.

Dense breast tissue is more common in young women but can be observed in individuals of all age groups and breast types. In our study, no significant difference was observed between the two groups in terms of mammographic breast density and BI-RADS category. Nevertheless, a higher proportion of patients in G1 had a BI-RADS category of 0 compared to G2 (74.04% vs. 66.86%). Due to the dense nature of breast tissue in young women, mammography's sensitivity is limited, and patients are often referred for breast ultrasound (US) to obtain a more thorough evaluation or undergo both mammography and US simultaneously. In a study conducted by Lehman et al.,<sup>[19]</sup> which evaluated the accuracy and value of breast US in 1208 consecutive US examinations in 954 patients, US was found to be the primary imaging modality for women under 40 years of age, with a sensitivity and negative predictive value of 95.7% and 99.9%, respectively. We observed that the use of mammography or a combination of mammography and US was higher in the control group compared to the mastalgia group ( $p=0.016$  and  $p=0.012$ , respectively). This difference may be attributed to the higher mean age of the control group.

The management of mastalgia involves essential elements such as reassuring patients that cancer is not the cause, providing physical support, and administering analgesics. Typically, breast pain resolves spontaneously within 3 months to 3 years with conservative approaches.<sup>[8]</sup> Non-steroidal anti-inflammatory drugs (NSAIDs), including acetaminophen or ibuprofen, either orally or topically (e.g., diclofenac gel/patch), are commonly used for symptomatic treatment.<sup>[4, 20]</sup> In our study, the use of analgesics was more prevalent in the mastalgia group, particularly the use of NSAIDs. Hafiz et al.<sup>[21]</sup> also found that adding topical NSAIDs to first-line therapy, which includes reassurance and a well-fitting, supportive bra, provided relief for 70-92% of women.

When evaluating breast pain, it is important to consider

whether it is unilateral or bilateral, diffuse throughout the breast, or localized to a specific area, and whether it corresponds with the menstrual cycle or not. These characteristics can provide valuable clues to the underlying cause. Cyclic breast pain typically presents as bilateral and diffuse, whereas noncyclic mastalgia is often unilateral and localized to a specific part of the breast.<sup>[5]</sup> In our study, individuals with cyclic mastalgia exhibited a higher incidence of bilateral and diffuse pain compared to those with noncyclic mastalgia (40.63% vs. 24.4% and 41.67% vs. 28.57%,  $p=0.006$  and  $p=0.03$ , respectively). These findings are consistent with existing literature.

Several studies have reported no significant association between breast cancer and localized breast pain.<sup>[22, 23]</sup> Localized mastalgia is more likely to yield positive imaging findings, which are generally benign.<sup>[4]</sup> Our study also indicated that localized mastalgia was more likely to be associated with a breast lesion, while diffuse mastalgia often resulted in normal breast imaging findings, although this difference was not statistically significant ( $p=0.46$ ).

## Conclusion

In conclusion, determining the precise cause of breast pain is often challenging. This study identified that factors such as young age, a sedentary lifestyle, and being in the premenopausal period were associated with mastalgia. Raising awareness among women regarding the risk factors for mastalgia and encouraging lifestyle modifications can contribute to better management of mastalgia. It is crucial to emphasize that breast pain is rarely indicative of breast cancer in the majority of cases. Consequently, the diagnostic evaluation of breast pain may result in unnecessary investigations and biopsies, leading to the overutilization of healthcare resources.

## Disclosures

**Ethics Committee Approval:** Approval was obtained from Firat University Medical Faculty local ethics committee for this study with the decision number 10-22 dated September 1, 2022.

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