

# Ultrasonographic Findings and Breast Cancer Risk in Women with Mastalgia Under 40 Years

## Mastalji Yakınması Olan Kırk Yaş Altındaki Kadınlarda Ultrason Bulguları ve Meme Kanseri Riski

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### ABSTRACT

**Objective:** Breast pain is a very common condition among young women. The aim of this study is to provide supplementary and specific data especially in addition to available literature information about the ultrasonographic findings and breast cancer risk in women younger than 40 years who applied to the breast outpatient clinic with isolated mastalgia, and had no breast cancer risk factor.

**Method:** Ultrasonographic examination results of women between dates 01/01/2011 and 01/01/2015, and contribution of ultrasonography to diagnostic procedure of breast cancer were retrospectively evaluated.

**Results:** A total of 1066 patients were included in the study. There were 555 (52%) women with focal and 511 (48%) women with diffuse mastalgia. US examination revealed only 7 suspicious cases, all of whom were over 30 years of age. Of women with suspicious masses, 6 had focal mastalgia, and invasive cancer was diagnosed in 3 of cases after core biopsy. In only one patient in the diffuse mastalgia group a suspect mass was detected which revealed to be a benign lesion on histopathological examination of core biopsy specimen

**Conclusion:** Careful clinical examination may be adequate especially in women younger than 30 years of age who have no breast cancer risk factor, and only diffuse mastalgia complaint. However, possibility of breast cancer should be considered in women older than 30 years even they have no breast cancer risk factor, and no complaint other than focal mastalgia.

**Keywords:** mastalgia, ultrasonography, breast cancer

### ÖZ

**Amaç:** Meme ağrısı genç kadınlar arasında çok yaygın bir durumdur. Bu çalışmanın amacı, meme hastalıkları polikliniğine izole mastalji ile başvuran ve meme kanseri risk faktörü olmayan 40 yaşından küçük kadınlarda özellikle ultrasonografik bulgular ve meme kanseri riski hakkında mevcut literatür bilgilerinin yanı sıra ek ve spesifik veriler sağlamaktır.

**Yöntem:** 01/01/2011 ve 01/01/2015 tarihleri arasında kadınların ultrasonografik inceleme sonuçları ve meme kanseri tanısında ultrasonografinin katkısı retrospektif olarak değerlendirildi.

**Bulgular:** Çalışmaya toplam 1.066 hasta dâhil edildi. Fokal mastaljisi olan 555 (%52) kadın ve yaygın mastaljisi olan 511 (%48) kadın vardı. Ultrasonografik muayenesinde, her biri 30 yaşın üzerinde olan yalnızca 7 şüpheli olgu ortaya çıktı. Şüpheli kitleleri olan kadınların 6'sında fokal mastalji vardı ve kor biyopsiden sonra 3 olguya invaziv kanser teşhisi konuldu. Yaygın mastalji grubunda yalnızca 1 hastada şüpheli kitle vardı ve kor biyopside benign bir lezyon saptandı.

**Sonuç:** Özellikle meme kanseri risk faktörü olmayan ve yalnızca yaygın mastalji yakınması olan 30 yaşından küçük kadınlarda dikkatli klinik muayene yeterli olabilir. Bununla birlikte, meme kanseri risk faktörü olmayan ve fokal mastalji dışında hiçbir şikayeti olmayan 30 yaşından büyük kadınlarda meme kanseri olasılığı göz önünde bulundurulmalıdır.

**Anahtar kelimeler:** mastalji, ultrasonografi, meme kanseri

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## INTRODUCTION

Breast pain called as mastalgia or mastodynia is a very common condition among women. There may be a feeling of extreme tenderness, sharp burning sensation or tightness in the breast. The pain may be constant or it may only occasionally occur. In previous studies, prevalence of mastalgia was reported as 41-69%<sup>(1,2)</sup>. Although mastalgia is not a risk factor for breast cancer, the vast majority of women are concerned about the likelihood of breast cancer<sup>(3,4)</sup>. Mastalgia is divided into two forms as cyclic and non-cyclic. The etiology of cyclic mastalgia is not fully defined. Cyclic mastalgia is clearly associated with the menstrual cycle. Pain is usually bilateral and felt especially on the upper and outer quadrants of the breast, and may extend to the axillary region. Non-cyclic mastalgia is not related with the menstrual cycle and is characterized by continuous or intermittent pain. In addition, non-cyclic mastalgia is usually unilateral and there is localized pain which may be sharp or burning<sup>(5)</sup>.

Oral contraceptives, hormone containing drugs, psychotropic drugs, and some cardiovascular agents may cause mastalgia<sup>(6)</sup>. Moreover, it has been reported that excessive breast movements, particularly during intense physical activity such as running sports, may result in exercise-related mastalgia<sup>(7)</sup>.

Specialist in breast diseases should evaluate the characteristics, duration, place, and extension of the pain as well as the should ask about the activities about trauma and the activities which intensify the pain. After obtaining a detailed anamnesis, a physical examination should be performed carefully.

Although mastalgia is observed frequently in 2-7% of women with breast cancer, the incidence of breast cancer is quite low in women who apply to breast outpatient clinic with mastalgia (0.5-3.3%)<sup>(2)</sup>. In contrast to diffuse breast pain, focal breast pain benefits more from diagnostic imaging methods<sup>(2,6,8-9)</sup>. Approximately half of women who apply to breast

outpatient clinic with mastalgia are younger than 40 years of age. Women younger than 30 years with breast pain are generally evaluated by physical examination and ultrasonography (US). Women older than 30 years of age may undergo mammography, if required<sup>(2,6,8,11)</sup>. If results of clinical examination and imaging are normal, malignancy risk is quite low<sup>(2-4,6,9,10)</sup>.

In our clinic, US is routinely performed following physical examination in women less than 40 years of age who have mastalgia. There are limited number of studies reporting ultrasonographic findings of patients who have applied with breast pain. The aim of this study was to provide supplementary and specific data especially in addition to available literature information. Therefore, the ultrasonographic findings and breast cancer risk in women younger than 40 years who applied for the first time with only breast pain (diffuse or focal), and had no risk factor for breast cancer were analyzed.

## MATERIALS and METHODS

The study protocol was approved by the Institutional Ethics Committee of University of Health Sciences, İstanbul Okmeydanı Education and Research Hospital. The study was carried out according to the principles of the Helsinki Declaration. All the patients were routinely informed about the procedure and provided their written, informed consent. In this study, contribution of US in diagnosing breast cancer were retrospectively evaluated in 1066 consecutive women younger than 40 years of age who applied to the breast outpatient clinic for the first time with complaints of mastalgia between 01 January 2011 and 01 January 2015,. All women had a careful physical examination, and then their personal and familial histories were questioned. Additionally, all women were evaluated according to the National Comprehensive Cancer Network (NCCN) guidelines for risk assesment in breast cancer<sup>(12)</sup>. Women who had personal or familial risk factors for breast cancer, nipple discharge, present of past history of breast

surgery or core biopsy, hormone replacement treatment, psychosomatic disease, mastitis, drug treatment which might cause mastalgia, and pregnant or lactating women were excluded from the study. According to our data, the duration of the pain was largely variable in women with mastalgia. For this reason it was not considered as a safe parameter and was not included in this study. In addition, because of the number of women engaged in regular sports or excessive physical activity is very low, physical activity was not assessed in this study.

A total of 1066 women were followed up for a mean duration of 24 (12-48) months. During the follow-up period, the patients underwent ultrasonographic evaluation at 6 month- intervals in first year, and then this evaluation was repeated once a year.

In previous studies, mastalgia has been classified as cyclical or acyclical; or focal and diffuse; or resulting from other diseases <sup>(6,13)</sup>. In a woman with diffuse mastalgia, if there are no additional signs or symptoms, the probability of cancer is extremely low. On the other hand, even if there are no additional signs or symptoms, focal mastalgia should be evaluated to rule out the underlying breast disease. We preferred to classify mastalgia in focal and diffuse groups since we have examined all patients with US. We first divided these two groups into two subgroups as patients in age groups of 20-29, and 30-39 years We aimed to determine the accurate indication for advanced imaging according to the age range of women. All US examinations were performed by experienced radiologists in breast imaging. Hitachi Avius (Hivision), model: EZU- MT29-S1, and high resolution (5-13 MHz) linear probe was used for US examinations..

The US findings were grouped as follows; normal breast tissue, fibrocystic changes, fibroadenoma, simple cyst, complicated cyst, ductal ectasia, accessory breast tissue, intramammary lymph node and suspicious mass (Table 1). Findings such as spiculation, taller than wide, angular margins, shadowing,

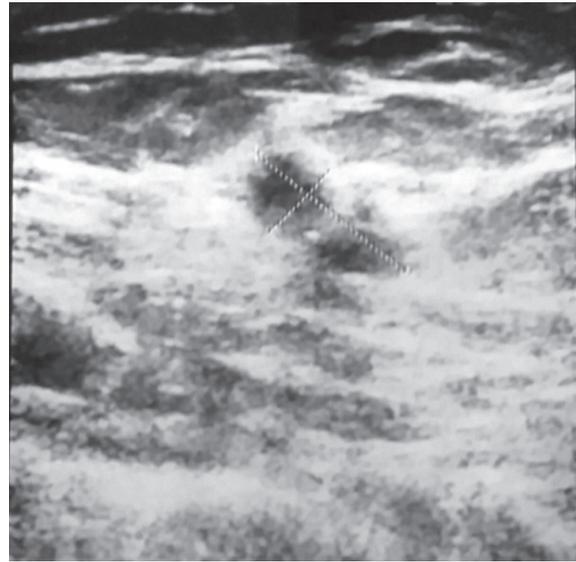


Figure 1. Suspicious malignant hypoechoic lesion with irregular borders, and perpendicular to the breast axle.

branching pattern, hypoechogenicity, calcifications, duct extension, branching pattern, and microlobulation were considered as suspicious <sup>(14)</sup> (Figure 1). Adult women over 30 years of age with suspected mass also underwent breast MRI and were subjected to a mammographic examination. Subsequently, core biopsy was performed under US guidance for suspicious masses, and tissue samples were examined by a pathologist who was experienced in the pathology of breast diseases.

The total number of 72 959 patients applied to our breast outpatient clinic between the dates 01/01/2011 and 01/01/2015, while, 21015. women were aged 20-39 years. Also, 8615 of these patients were younger than 40 years and had breast pain. A total of 1066 patients were included in the study. There were 555 (52%) women with focal and 511 (48%) women with diffuse mastalgia. Of women with focal mastalgia, 351 (63%) of them aged between 30-39 years, and 204 (37%) aof them aged between 20-29 years. Of women with diffuse mastalgia, 311 (61%) were aged between 30-39 years, and 200 (39%) aged between 20-29 years.

The statistical analyses were performed using SPSS

for Windows, Version 15.0 (SPSS Inc., Chicago, IL, USA). The ultrasonographic findings and the pathological distribution of lesions were analyzed using numbers, and percentages.

## RESULTS

The most common cause of breast pain in both groups was fibrocystic changes. In ultrasonographic evaluation, fibrocystic changes was determined in 292 (57.14%) patients with diffuse mastalgia, and in 223 (40.18%) patients with focal mastalgia. Moreover, normal breast tissue was reported in 59 (11.54%) patients with diffuse mastalgia, and in 52 (9.37%) patients with focal mastalgia. Results according to age groups are shown in detail in Table 1 and 2.

There were 7 (0.65%) suspicious cases detected by US examination. Six of them had focal, and one case with diffuse mastalgia. Mammography and breast MRI examination were performed on these patients. No additional pathology was detected in these images. Definite diagnosis was made by core biopsy under US guidance for these 7 patients. The core biopsy result of the woman with diffuse mastalgia complaint was benign. In 3 of 6 women with focal mastalgia, the core biopsy results were malignant. The overall incidence of cancer was 0.28% in women who included in the study. However, breast cancer was not encountered in women who were younger than 40 years with no personal or familial risk factor(s) and had only diffuse mastalgia. Additionally, there was no cancer case in women who were younger than 30 years with focal mastalgia. All of the three cancer cases were over 30 years old and had focal mastalgia complaint. Moreover, 0.85% of women aged 30-39 years had complaints of focal mastalgia. The median diameter of invasive cancer was 1.5 cm (range 1.2-1.8 cm). Breast conserving surgery and sentinel lymph node biopsy were performed in these 3 patients who had T1 early-stage breast cancer. Sentinel lymph nodes of all 3 patients were reported as negative.

In physical examination, palpable mass was detected in 306 (28.7%) women, and 301 women had benign ultrasonographic findings. A mass lesion was determined in 128 (91%), 105 (66%), and 68 (84%) patients in physical examination among patients, whose US evaluations revealed 140 fibroadenomas, 159 simple cysts, and 81 complex cysts, respectively. However, a mass was located in 5 (71.4%) women, while we could not find any palpable mass during physical examination of 2 (28.6%) women whose US findings suggested the presence of a suspect mass. One of these women had complaints of diffuse mastalgia, and the other patient has focal mastalgia complaint and a mass smaller than 1 cm in diameter. However, both of the core biopsies were reported as benign. During the follow-up (mean duration of 24 months), no new invasive cancer case was encountered, and also, no change in US findings observed in benign cases.

## DISCUSSION

Mastalgia is a widespread symptom in women that requires medical assessment<sup>(2)</sup>. It can be combined with breast-related symptoms like mass, nodularity, nipple discharge, and skin changes. Usually unilateral, permanent and severe mastalgia is associated with breast cancer<sup>(2)</sup>. However, there is not enough data in written literature related to the long-term results of mastalgia without other breast-related symptoms or signs. These cases are described as isolated breast pain.

Breast cancer is currently the most frequently diagnosed cancer and is the leading cause of cancer-related death in women. In fact, in 2012, a total of 1.7 million new cases with breast cancer and 521,000 cases of breast cancer-related deaths were reported worldwide<sup>(15)</sup>. Incidence rate and prevalence have increased three times within the last decades in Turkey<sup>(16)</sup>. Nowadays, social media and internet have raised awareness of women about breast cancer. Because of the concern of breast cancer, even a mild complaint related with breast like mastalgia causes

anxiety and depression in women, and seriously affects quality of life. The statistical studies clearly showed that, most women who apply to breast outpatient clinic have mastalgia complaints<sup>(9)</sup>. However, it is still a problem that the records of women with mastalgia complaints are not kept carefully<sup>(2)</sup>. The number of studies examining the relationship between isolated mastalgia complaints and breast cancer risk is very few. In addition, women who were older than 40 years and have a breast cancer risk were included in previous studies. In this study, the relationship of breast pain and breast cancer were investigated in a selective group of young women.

In this study, there was no cancer case in women with diffuse mastalgia who were younger than 40 years of age. Among young women with focal mastalgia, cancer rate was 0.54%, and when it was considered that all of these women were in the age group of 30-39 years, the cancer rate in this group was determined as 0.85%. Our findings were consistent with previous study results about mastalgia and breast cancer incidence (0.5-3.3%) in the medical literature<sup>(2)</sup>. Mass lesions which were suspected of malignancy, were detected in US examination in 3 cases with cancer just at the location of pain. Cancer was detected in none of women who had mastalgia complaint, and any suspicious mass in clinical or sonographic examinations were not detected. In a similar study; 149 patient with mastalgia complaints have been examined by a physician and later evaluated with breast US performed by a four- year experienced radiologist. Besides, no exclusion criteria was applied to the examined cases, in the study<sup>(17)</sup>. However, the exclusion criteria were carefully implemented and eventually 1066 patients were included in this study. Patients were firstly examined by experienced breast surgeons, and than radiologists who had more than 10- year experience analyzed the patients by scanning their US.

Recently, Noroozian et al.<sup>(16)</sup> published a long-term follow-up results of 617 patients with breast cancer risk who had mastalgia complaint. However, in con-

trast to this study, they included patients with familial history of breast cancer, and surgical interventions in their study. The average age of their patients was 49 (median,42, and range, 23-88) years with the median follow-up duration of 51.1 months. That is, the investigators performed their study not only on women younger than 40 years of age who had mastalgia complaint, but on women in all age groups. Nevertheless, it is known that breast cancer risk is increased as the age increases in women. However, the follow-up period was longer than our study. The investigators determined breast cancer in 11 (1.8%) cases and they detected cancer in 3 women in contralateral breast which did not cause pain. While breast cancer was localized at the location of pain in 9 out of 11 women, it was localized at another quadrant in 1 patient, and the other patient had diffuse mastalgia.

Actually, it is generally accepted that imaging methods are of no use in breast pain management. Imaging methods are recommended to decrease anxiety, and this request is increasing over time in women with complaints of mastalgia<sup>(3)</sup>. Besides, normal test results are not definitive, and even they may increase the anxiety level. Therefore, new guidelines are required to minimize differences in physician's attitudes which may differ individually in management of women who have only mastalgia without any suspicious signs for malignancy detected during clinical examination<sup>(19)</sup>. It is obvious that further studies may contribute to these guidelines. Although other signs such as nipple discharge, mass in the breast, changes in breast skin, and asymmetrical thickening/nodularity are described in detail as diagnostic criteria in breast cancer screening in clinical practice guidelines published by the National Comprehensive Cancer Network, mastalgia is not referred<sup>(20)</sup>. As there is no abnormal physical examination finding in women with mastalgia complaint, requesting imaging methods have always been a subject of debate. Moreover, American College of Radiology (ACR) guideline states that US examination is indicated if there is a palpable mass, and

other related signs and symptoms in the breast without mentioning about breast pain <sup>(21)</sup>.

US is the best radiological tool to assess a clinically benign breast lump and has been shown to have significantly better accuracy (97% vs 87%), sensitivity (93% vs 57%) and negative predictive values (99% vs 92%) than mammography in this respect <sup>(11,22)</sup>. US has a higher diagnostic sensitivity because it may identify breast cancer at an early stage on the basis of the detected mass, even in the dense parenchyma of young women. Previous studies have demonstrated that mammography with adjunctive US improved screening sensitivity and diagnosis rates and dropped the frequency of interval cancers in women with dense breasts <sup>(23-25)</sup>. Ohuchi N, et al. <sup>(25)</sup> researched the benefit of adjunctive US to mammography for breast cancer screening in young women or women with dense breasts. Their study makes a great contribution to comprehension of the benefit of adjunctive US in breast cancer screening of women aged 40-49 years and provides generalisable data. They emphasized that US could provide an inexpensive way to improve rates of sensitivity and diagnosis of early cancers in women with dense breasts.

Actually, US is playing a more important role in breast cancer evaluation. It is quite useful in evaluation of clinically suspicious breast lesions and palpable masses which cannot be visualized in mammography in women especially younger than 30 years of age. Initially US was used primarily to differentiate solid breast masses from cystic ones as a cheaper and effective method. Besides, it is currently known that US provides precious information about solid masses, and the characteristics and the content of lesions in the contralateral breasts. US is the preferred imaging method in younger women, since the possibility of breast cancer is quite rare. Besides, there is no risk of radiation exposure; it is a comfortable procedure, and it is possible to perform biopsy at the same time. US has a higher sensitivity than mammography in especially younger women <sup>(26,27)</sup>.

Screening breast US provides important contributions to early diagnosis of breast cancer in women with high risk, and with dense mammary tissues <sup>(28)</sup>. Disadvantages of US examination are that its results depend on the operator; it has a suspicious cost-effectiveness; and it has a relatively high false positivity rate <sup>(29)</sup>. One of the advantages of this study was that operating radiologists were quite experienced in sonographic evaluation of patients.

Although possibility of breast cancer is quite low in patients with complaints of mastalgia, US examination should be performed to diagnose treatable benign lesions such as fibrocystic changes, cyst, and fibroadenoma <sup>(9)</sup>. In studies performed on women with complaints of mastalgia, fibrocystic changes were the most commonly diagnosed pathology, and it was noted that there was a relationship between this disease, and breast pain. In this present study, we diagnosed fibrocystic changes in 57.14% of diffuse mastalgia, and 40.18% of focal mastalgia cases. However, as no pathological US finding was detected in 11.54% of the patients complaining of diffuse mastalgia, and in 9.37% of the cases with focal mastalgia, it was thought that there should be psychological factors affecting the complaints of mastalgia.

In conclusion, the data of this study support that malignancy is a low risk in women younger than 40 years of age who have only complaints of mastalgia. Careful clinical examination may be adequate especially in women younger than 30 years of age who have no personal or familial breast cancer risk factor, and have complaints of only diffuse mastalgia. However, in women who are older than 30 years, although they have no personal or familial breast cancer risk factor, and no complaint other than focal mastalgia the possibility of breast cancer should be considered. Therefore, a careful physical examination followed by US imaging performed by an experienced specialist should be included in the diagnostic decision-making process. Further studies performed on large number of patients for longer periods of follow up will be more useful.

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