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Impact of COVID-19 Pandemic on Breast Cancer Screening and Diagnosis Process

COVID-19 Pandemisinin Meme Kanseri Tarama ve Tanı Sürecine Etkisi

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ÖZET

AMAÇ: COVID-19 pandemisi meme kanseri taramalarında ve tanısal işlemlerinde gecikmeye neden oldu. Bu çalışmanın amacı; pandemi sürecindeki meme kanseri tarama ve tanısal işlemleri ile yeni tanı konan meme kanseri olgularının pandemi öncesindeki dönemle karşılaştırılmasıydı.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmada pandemi öncesinde (Mart 2019-Şubat 2020) ve pandemi sürecinde (Mart 2020- Şubat 2021) yapılan mamografi taramaları, görüntüleme eşliğinde meme biyopsileri ve yeni tanı alan meme kanseri vakaları değerlendirildi. Mamografi ve biyopsilerin sayıları ve zamana göre dağılımı karşılaştırıldı. Meme kanseri vakalarında ise tümörün histopatolojik özellikleri ve evresi karşılaştırıldı.

BULGULAR: Pandemi öncesine kıyasla pandemi sürecinde en belirgini Nisan (-%98) ve Mayıs (-%93) aylarında olmak üzere mamografi sayılarında toplamda %44 azalma olduğu görüldü. Görüntüleme eşliğinde biyopsi sayılarında Nisan (-%100) ve Mayıs (-%69) aylarında önemli miktarda azalma olmakla birlikte Haziran ayında %29 ile başlayan ve devam eden artışla tüm pandemi periyodu değerlendirildiğinde azalma olmadığı görüldü. Meme kanseri grubunda ise pandemi öncesine kıyasla pandemi döneminde tanı anında metastaz ile başvuran hasta sayısında anlamlı artış olduğu görüldü (p=0.001). İki grup arasında tümörün hormon reseptör durumu, HER2 pozitifliği ya da derece açısından anlamlı fark olmadığı görüldü (p>0.05).

SONUÇ: Bu çalışmada COVID-19 pandemisi sırasında meme kanserinde hem tarama hem de tanı süreçlerinin önemli ölçüde etkilendiği gözlemlendi. Pandeminin ilk aylarında hastaneye başvurunun gecikmesinin tanı anında metastatik olan hastalarda artışa neden olduğu görüldü.

Anahtar Kelimeler: COVID-19, meme kanseri, kanser taraması

ABSTRACT

AIM: The COVID-19 pandemic has caused delays in breast cancer screening and diagnostic procedures. The aim of this research was to compare the status of breast cancer screenings and newly diagnosed breast cancer cases during the pandemic compared to the pre-pandemic period.

MATERIAL AND METHOD: This retrospective study included patients with screening mammography, imaging-guided biopsies, and newly diagnosed breast cancer from March 2020– February 2021 (during-COVID-19) were compared with March 2019–February 2020 (pre-COVID-19). We compared numbers and distribution over time of mammography and biopsies between the time periods. In the breast cancer group; the stage at diagnosis and histopathological features of the tumor were also compared.

RESULTS: Compared to pre-pandemic mammography scans, a 44% decrease was observed in total during pandemic, the most significant being in April (-98%) and May (-93%). While there was a significant decrease in the number of biopsies in April (-100%) and May (-69%), it was seen that there was no decrease in the pandemic period when the whole year was looked at with a rebound increase that started with 29% in June. In the breast cancer group, there was a significant increase in the number of patients who were metastatic at the time of diagnosis compared to the pre-pandemic period (p=0.001). No significant difference was observed between the two groups in terms of tumor grade, hormone receptor status, or HER2 positivity (p>0.05).

CONCLUSION: In this study, it was observed that both screening and diagnosis processes in breast cancer were significantly affected during the COVID-19 pandemic. It was observed that the delay in admission to the hospital in the first months of the pandemic resulted in an increase in patients who were metastatic at the time of diagnosis.

Keywords: COVID-19, breast cancer, cancer screening

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INTRODUCTION

COVID-19 disease was first seen in the world in November 2019 and still continues all over the world.[1] The first case was reported in Turkey on March 11, 2020, the day the disease was declared a pandemic.[2] The American College of Radiology (ACR) and Centers for Disease Control (CDC) recommended reprogramming of screening mammograms, non-emergency computed tomography, ultrasound, and other radiology-guided examinations and procedures in radiology departments. [3] Breast units are one of the units most affected by these restrictions.

Breast cancer constitutes 14% of cancer diagnoses, and 30% of cancers diagnosed in women are breast cancer.[4] The incidence of breast cancer in Turkey is 47.7 per 100000 women. [5] Early diagnosis is of great importance in breast cancer prognosis and in reducing mortality.[6] This is possible with breast cancer screening programs. A study of 400,000 patients concluded that participation in screening programs is associated with a reduction of approximately 30% in stage II+ tumors.[7] There has been a change in the process of diagnosis and screening of breast cancer due to the pandemic-related change in approaches to the use of resources and triage of patients in our country as well as in the whole world. Initially, there was a pause in mammography screenings and elective surgeries.[8] As of April 2020, almost a complete decrease was observed in the treatment programs, and as of the beginning of summer, the patients were encouraged to have mammography again and returned to the routine.[9-11] One study reported a 20% decrease in the diagnosis of breast cancer during the lockdown period and an increase of 48% after this period.[12] Simao et al. showed a 40% decrease in the diagnosis of breast cancer during the pandemic period, an increase in the number of metastatic patients who applied for systemic treatment at the time of diagnosis, and an increase in the rate of bilateral breast cancer .[13] Although the delays in diagnosis and treatment during the pandemic are of great concern, the actual effect has not yet been clearly demonstrated.[14,15],

This retrospective study aimed to compare the status of breast cancer screenings and newly diagnosed breast cancer cases in a tertiary healthcare institution during the pandemic compared to the pre-pandemic period.

MATERIAL AND METHOD

With Institutional Ethics Board approval (dated March 29, 2022, numbered 2022/74) we scanned all patients referred to our breast unit for mammography from March 2020 to February 2021 (study group). The study was conducted in accordance with the Declaration of Helsinki. We compared them to patients referred in the same period of the previous year: March 2019 to February 2020 (control group). Firstly, the numbers of mammograms performed on female patients older than 18 years were recorded in these two-time intervals. Only patients under the age of 40 who had a family history of breast cancer, breast examination findings, and/or findings suggestive of malignant pathology on ultrasound or magnetic resonance imaging (MRI) underwent mammography.

Secondly, the number of lesions who underwent imaging-guided interventional procedures for the breast (cutting needle biopsy or wire-guided excision biopsy) was recorded. In diagnostic mammograms, breast ultrasound, or MRI, the result of Breast Imaging and Reporting Data System (BI-RADS) evaluation category 4 (suspected) or 5 (highly suggestive of malignancy) was considered an indication for biopsy. In addition, the age of the patients and the months of mammogram and procedure were also recorded. Pathology results of biopsies were recorded as malignant or benign.

Thirdly, the number of patients newly diagnosed with breast cancer in the same time period was determined. Patients with a recurrent cancer diagnosis from the same breast were excluded from the study. Patients diagnosed with bilateral breast cancer were recorded with the characteristics of the side with a more advanced stage. Patient age, the month of diagnosis, TNM stage of the tumor, pathological subtype, grade, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status were recorded from the clinical records of the patients. Hormone receptor status was considered positive for ER and/or PR when nuclear staining was >10%. The positivity criteria for HER2 were fluorescence in situ hybridization (FISH)+ or +3 on immunohistochemical (IHC) examination. Those with 0 or +1 on IHC and those with FISH - were considered HER2-. Histological types of cancer were classified as invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC) and others (papillary, mucinous..)

Clinical TNM staging was performed according to the 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual.16 In our hospital, axillary ultrasound is routinely performed on all patients. Lymph nodes with abnormal morphological features such as spherical shape, increased diameter, or cortical thickening (>3 mm) were evaluated with fine-needle aspiration biopsy (FNAB). FNAB was not performed on lymph nodes with a typical metastatic appearance with a cortex thickness >6 mm. Lymph node positivity was decided according to imaging findings in patients did not undergo FNAB. If available, sentinel lymph node biopsy (SLNB) and axillary lymph node dissection data were also evaluated. Since some of the patients applied to other centers for surgical treatment or chemotherapy and this information could not be reached, data about treatment were not included in the study. The written informed consent from patients was waived because of the retrospective design.

Statistical Analysis

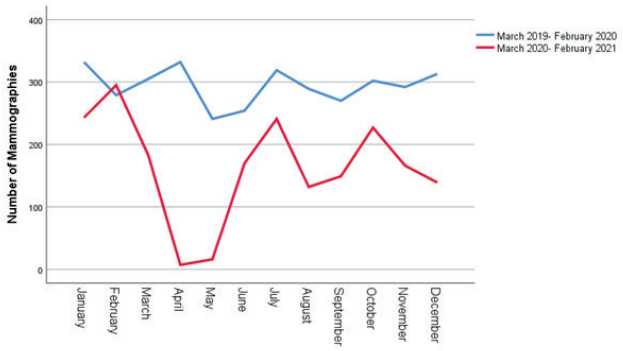
Statistical analyzes were performed using SPSS software version 24 (SPSS Inc, Chicago, IL). Descriptive variables were presented as mean±standard deviation (SD), median, and range. Categorical variables were presented as frequency tables. The Pearson chi-square test was used to analyze the T stage of the tumor. Comparison of axillary lymph node metastasis (N), distant metastasis (M), and biopsy results were performed using Fisher's exact test. P <0.05 was considered statistically significant in all analyzes.

RESULTS

Number of mammograms and distribution over time

It was determined that 3453 patients were applied breast unit for mammography scan in the pre-pandemic period, and this number was 1919 during the pandemic period. According to this data, it is seen that there is a 44% decrease in mammography scans during the pandemic period compared to the pre-pandemic period. The most significant decreases were seen in April with 98% and in May with 93%. When the whole month is evaluated, while the decline in mammography scans is 40% in March, this decrease reaches 82% when the mammography scans performed after the first case in Turkey are evaluated. While the number of mammograms decreased the most in April and May compared to the pre-pandemic period, an increase was observed in February; the last month evaluated in the pandemic period compared to the pre-pandemic period

Figure 1: The numbers of mammography during pre-pandemic and pandemic periods.

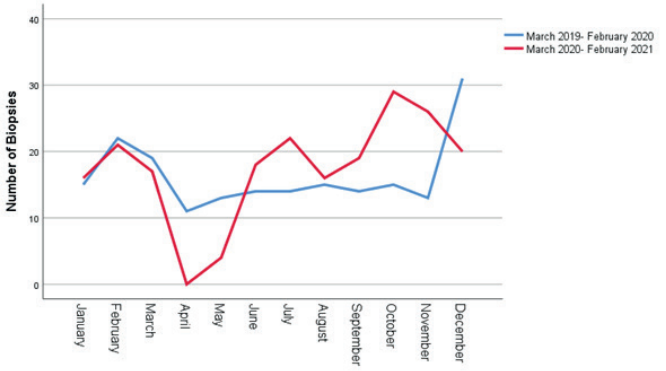


There was no significant difference between the mean age of the patients in both groups (52.48±9.78, 52.45±9.57; p=0.914).

Number of interventional procedures and distribution over time

While imaging-guided interventional procedures were performed on 218 lesions of 196 patients before the pandemic, 229 lesions of 208 patients were treated during the pandemic. The most significant decrease in the number of biopsies in our hospital was in April, and this rate was 100%. There was no significant difference between the mean age of the patients in both groups (51.86±13.90, 50.83±14.54; p=0.465). While 82 (38%) of the lesions that were biopsied before the pandemic were benign and 136 (62%) were malignant, 100 (44%) of the lesions that were biopsied during the pandemic were diagnosed as benign, and 129 (56%) were malignant (p=0.193). While the number of invasive procedures decreased significantly in April (100%) and May (69%) during the pandemic period compared to the pre-pandemic period, it increased again as of June (+29%)

Figure 2: The numbers of imaging-guided biopsies during pre-pandemic and pandemic periods.



Characteristics of newly diagnosed breast cancer cases
The characteristics of patients newly diagnosed with breast cancer before and during the pandemic are summarized in

Table 1: The characteristics of breast cancer cases compared between pre-COVID and during-COVID time periods

	Pre-COVID N	During-COVID N	Total N	P value
Age (at visit)				0.977
Mean	56.40±13.09	56.55±12.91	56.47±12.97	
Median	55	55	55	
Range	30-90	30-89	30-90	
Clinical T category				0.328
Tis	2 (2%)	0	2	
T1	33 (29%)	41 (36.7%)	74 (33.2%)	0.258
T2	64 (57%)	53 (47.3%)	117 (52.5%)	0.183
T3	5 (4%)	5 (4.4%)	10 (4.5%)	1
T4	9 (8%)	13 (11.6%)	22 (9.8)	0.379
Lymph node metastasis				0.060
Positive	55 (48.6%)	42 (37.5%)	97 (43.1%)	
Negative	58 (51.4%)	70 (62.5%)	128 (56.9%)	
Distant metastasis				**0.001***
Missing	11	16	27	
Positive	11 (10.8%)	28 (29.2%)	39 (19.7%)	
Negative	91 (89.2%)	68(70.8%)	159 (80.3%)	
ER status				0.743
Missing	2		2	
Positive	22 (19.8%)	25 (22.3%)	47 (21.1%)	
Negative	89 (80.2%)	87 (77.7%)	176 (78.9%)	
Grade				0.839
Missing	65	48	113	
I	2 (4.2%)	4 (6.3%)	6 (5.4%)	
II	38 (79.2.4%)	48 (75%)	85 (75.9%)	
III	8 (16.6%)	12 (18.8%)	19 (16.7%)	
PR status				1.000
Missing	5		5	
Positive	37 (34.3%)	39 (34.8%)	76 (34.5%)	
Negative	71 (65.7%)	73 (65.2%)	144 (65.5%)	
HER2 status				0.873
Missing	4	1	5	
Positive	85 (78%)	85 (76.6%)	170 (77.3%)	
Negative	24 (22%)	26 (23.4%)	50 (22.7%)	
Histological type				
IDC	93	96	189	0.181
ILC	8	12	20	
Others	10	4	14	

COVID-19: Coronavirus-19 disease, ER: Estrogen receptor, PR: Progesterone receptor HER2: Human epidermal growth factor receptor 2, IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma

The mean and median ages of the patients diagnosed with cancer in these two periods were quite close (p=0.997). The percentage of patients diagnosed at the T4 stage increased slightly during the pandemic (8.1% - 11.6%), but it was not statistically significant.
There was no significant difference between the two groups in terms of lymph node positivity. (p=0.060). While the number of patients whose lymph node positivity was evaluated with FNAB before the pandemic was 27 (24.3%), this number was 22 (19.7%) during the pandemic period (p=0.399). While the rate of lymph node positivity in patients without FNAB was 29 (34.5%) before the pandemic, it was 47 (52.2%) during the pandemic period. (p=0.044).
Patients with distant metastases at the time of diagnosis were statistically significantly higher during the pandemic (p=0.020). Tumor grade, histological types, ER and PR status, and HER2 positivity did not differ significantly between the two groups (p>0.05).

DISCUSSION

In this study, we investigated the effect of the COVID-19 pandemic on breast cancer screening and diagnosis processes. We have shown that breast cancer screenings have decreased by 44% compared to the pre-pandemic period. We also revealed that distant metastases at the time of diagnosis in patients diagnosed with breast cancer are significantly higher during the pandemic period (p=0.001).
Primary and secondary prevention are very important in breast cancer, which is the most common type of cancer among women. Secondary prevention includes recognizing precursor symptoms before the development of a malignant tumor is completed. At this stage, radiological examinations are critical.[17] Although digital mammography is the gold standard imaging method in early diagnosis, digital breast tomosynthesis, breast ultrasound, and breast MRI are significant in evaluating suspicious findings in mammography, tumor staging, and follow-up.[18] With the implementation of these screening programs, there have been significant improvements in prognosis thanks to early diagnosis and advances in treatment methods.19,20 The impact of the COVID 19 pandemic on public health is not yet fully known. At the beginning of the pandemic, there was a delay in screening tests with the CDC's recommendation. However, the number of screening tests that have been disrupted due to this and the extent of its effect on the number of biopsies and the diagnosis of breast cancer are not precise.

Similar to other studies, our study showed that mammography scans decreased with the onset of the pandemic. In a study conducted in New York, where the first case was seen on March 1 (week 10, day 1 of 2020), the most significant decrease in mammography numbers was observed between the 11th and 14th weeks of the year.21 The reduction in the first 16 weeks was found to be 94% compared to the previous year. In another study in the USA, the decrease in mammography numbers was 99%, and the number was lowest at the 15th and 16th weeks of the year.[22] In our study, similar to the others, the decrease rate in the first three weeks after March 11, when the first case was seen, was 82%, 98% in April, and 93% in May. The decrease in the number of biopsies in our study (100% in April) was higher than the other study, which reported a 40% decrease in May.[23] Several factors contributed to this decline. One of these is the suggestion of postponing breast screening by associations such as the ACR, and the American Society of Breast Surgeons was effective in this decrease.[24] As a result, the scheduling of routine scans was delayed until June. In addition, outpatient services of other departments that would refer patients to radiology were reduced. The "stay at home" message given to the public during this period was also very effective in reducing hospital admissions.

With the removal of some restrictions applied due to the pandemic in our country on June 1, 2020, the number of mammograms began to increase. The same upward trend was also reflected in the number of biopsies, with a 29% increase in biopsies performed in June compared to the pre-pandemic period. This result was consistent with other studies that showed a rebound in the number of breast scans and biopsies in May-June.[23,25] Similarly, in a study conducted in Brazil, it was seen that there was an increase in the number of biopsies as of the second half of 2020, and the number in this period was higher than in 2019.[26] In a study conducted in Turkey, there was no significant difference in the rate of malignant and benign pathological diagnosis of lesions biopsied during the pandemic period when compared to the pre-pandemic period. This finding is similar to our study.[27]

In addition to the decrease in the number of breast screenings and biopsies, the reduction in newly diagnosed breast cancer cases is one of the most important results of the postponement of health practices during the pandemic. In our study, a decrease was observed in patients diagnosed with breast cancer in the early stages of the pandemic, similarly to literature.[9,10] In the study conducted in

England and comparing the first six months of 2020 with the same period of 2019, it was determined that there was a 16% decrease in the number of patients who applied for the first treatment of breast cancer. Based on this result, it was concluded that the diagnosis of breast cancer did not decrease as much as initially feared for the first six months of 2020.10 Also, in our study, when the whole year was evaluated, the numbers of newly diagnosed breast cancers were very close to each other.

A significant increase was observed in patients with metastasis at the time of diagnosis, compared to the pre-pandemic period, due to patients' avoidance of coming to the hospital and/or disruption of health services. Similarly, in a study conducted in Portugal and examining the same time intervals, it was observed that there was a significant increase in metastatic patients who applied for systemic treatment during the pandemic period.[13] In the same study, no significant difference was observed in T and N stages, hormone receptors, and HER2 status, similar to our results. Ilgun et al. showed a significant increase in de-novo stage 4 patients during the pandemic period. [28]

In a study conducted in Italy investigating the effects of the first three months of the pandemic, it was found that the waiting time, lymph node positivity, and tumor grade were significantly different in the pandemic process. In the multivariate analysis, long waiting time was a significant predictive factor for lymph node positivity.[29] In our study, it was seen that tumor grade was not significantly associated with the pandemic process. Gursoy et al. did not detect any difference in the histological subtype or tumor grade of the tumor between the groups, but showed that lymph node positivity increased statistically significantly during the pandemic period. They also showed that tumor size and time from diagnosis to surgery were higher during the pandemic period in this study.[30]

Eijkelboom et al. compared patients diagnosed with breast cancer in weeks 2-17 of 2020 with the average of 2018 and 2019. In this study, no significant difference was observed in tumor stage, grade, and size between the two groups. However, metastatic disease was found to be significantly higher in the study group.[9]

Metastatic breast cancers have a poor prognosis, and the median survival is 2-3 years.[31] In a study estimating cancer survival during the pandemic, breast cancer deaths were predicted to increase by 10.4% between 2022 and 2024.32 The significant increase in the number of breast cancer metastatic at the time of diagnosis during the pandemic period in this study will be analyzed in future survival studies.

The retrospective design of the study was one of its limitations. The presence of axillary lymph node involvement was determined according to imaging findings in patients without FNAB or SLNB. Post-diagnosis treatment of all included breast cancer patients was not performed in our hospital. Therefore, the effect of the pandemic process on the waiting time after diagnosis, treatment options, and prognosis could not be evaluated. Factors unrelated to the pandemic that affected the number of patients between the two groups were not considered.

CONCLUSION

This study revealed a decrease in mammography scans during the pandemic period and a significant increase in metastatic patients at the time of diagnosis. This study presents the data of only one tertiary hospital in Turkey, and multicenter studies are needed to investigate the effects of changes in the pandemic period on breast cancer screening and diagnosis throughout Turkey and make survival studies more valuable.

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