

RESEARCH ARTICLE

Delay in breast cancer diagnosis and its clinical consequences during the coronavirus disease pandemic

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Abstract

Objective: At the end of 1 year of the coronavirus disease (COVID-19) pandemic, we aimed to reveal the changes in breast cancer cases in the context of cause and effect based on the data of surgically treated patients in our institution.

Patients and Methods: Patients with breast cancer were divided into two groups. Group 1 consisted of patients who were operated in the year before the COVID-19 pandemic, and Group 2 consisted of patients who were operated within the first year of the pandemic. Tumor size, axillary lymph node positivity, distant organ metastasis status, neoadjuvant chemotherapy, and type of surgery performed were compared between the two groups.

Results: The tumor size, axillary lymph node positivity, and neoadjuvant chemotherapy were higher in Group 2 than in Group 1 ($p = .005$, $p = .012$, $p = .042$, respectively). In addition, the number of breast-conserving surgery + sentinel lymph node biopsy were lower, while the number of mastectomy and modified radical mastectomy were higher in Group 2 than in Group 1 ($p = .034$).

Conclusion: Patients presented with larger breast tumors and increased axillary involvement during the pandemic. Moreover, distant organ metastases may increase in the future.

KEYWORDS

breast cancer, COVID-19, effect of pandemic

1 | INTRODUCTION

Shortly after the first coronavirus disease (COVID-19) case was detected in Wuhan, China, on December 1, 2019, the World Health Organization declared the COVID-19 outbreak as an international public health emergency on January 30, 2020. In Turkey, the first case of COVID-19 was diagnosed on March 11, 2020. Similar to the process experienced worldwide, radical precautions were implemented in health services within the scope of fight against the pandemic in our country. All infrastructure and labor in the health system were focused to fight the pandemic. Most of the beds in the in-patient clinics and intensive care units in the hospitals were allocated to COVID-19 cases. Regardless of their expertise, most doctors were re-assigned to cope with COVID-19. However, the number

of outpatient clinic admissions was limited. All surgeries, except for emergency or cancer surgeries, were postponed. Citizens were advised through the media and social media not to apply to health institutions unless it was compulsory. The perception that hospitals are high-risk areas in terms of COVID-19 transmission risk has been initiated in society. People aged >65 and <20 years of age were banned from leaving the house. Intercity travel was banned, and curfews were imposed from time to time. Although these were reasonable and rational practices, which we are planned to deal with the pandemic, non-COVID-19 public health problems developed during this period. In particular, scientists dealing with cancer quickly realized that something was wrong, and the emergence and rapid growth of COVID-19 and cancer literature in the scientific world was the result of these observations and experiences. A new COVID-19

literature emerged with articles seeking an answer to the question, "How can we treat cancer patients safely in terms of patients and healthcare providers?".¹⁻³ When the first panic period was over, it was understood that the pandemic would be prolonged and a second phase would start. In the second stage, the answer to the question, "What is wrong with the diagnosis and treatment of cancer because of pandemic?" was investigated. Patient attitude questionnaires and studies investigating the reason for the decrease in the number of patients are the best examples of this period.⁴⁻⁷ "What could happen next?" was the question of the third term. Projection studies on the possible consequences of delays in the diagnosis of breast cancer because of the closure of screening programs and other reasons are typical examples of the third period.^{8,9} The fourth period is likely to be the actual clinical results, explained by the longer follow-up periods and patient numbers. In this study, we aimed to reveal the changes in breast cancer cases at the end of 1 year during the pandemic in the context of cause and effect based on the data of surgically treated patients in our institution. We hope to be able to open the door to the fourth term in this study.

2 | PATIENTS AND METHODS

This study was conducted at the Tokat Gaziosmanpasa University (TOGU) Faculty of Medicine General Surgery Clinic. Our institution is located in Tokat, with a population of 600,000 people. A patient pool with a population of 600,000 was screened in this study. Approval was obtained from the Ministry of Health Scientific Research Platform for the study (date: 21/03/19; number: T09-45-19). The number of patients admitted to the outpatient clinic for breast diseases reported to the Ministry of Health for benign or malignant lesions, number of screening mammography at the cancer screening and training center, and number of newly diagnosed breast cancer cases were investigated separately for pre-pandemic and pandemic periods. Duplicate records of the same patient were deleted, and a single application was recorded for each patient to avoid false results. We investigated the changes in the number of outpatient clinic admissions, screening mammography, and number of newly diagnosed breast cancer cases between the two periods. Newly diagnosed breast cancer patients were divided into two groups based on the date (March 11, 2020) when the first COVID-19 case was observed in Turkey. Group 1 consisted of patients who were operated in the year before the COVID-19 pandemic, and Group 2 consisted of patients who were operated within a year after the pandemic started. This study was conducted as a retrospective cohort study and the study approval was obtained from the TOGU Ethics Committee. Patient records, surgery notes, and pathology reports of the patients included in this study were retrieved from our hospital's database. Three patients with incomplete information were excluded from the study. To evaluate the clinical effects of the pandemic, tumor size, axillary lymph node positivity, distant organ metastasis status, neoadjuvant chemotherapy (NAC) status, and the type of surgery performed were recorded for both groups before and during

the pandemic. Tumor sizes were classified as follows: T1: tumor size <2 cm; T2: tumor size >2 cm and <5 cm; T3: tumor size >5 cm; and T4: tumors of any size that spread directly to the chest wall or skin, breast edema, ulceration, and inflammatory breast cancer. Tumor size and axillary lymph node positivity were obtained from pathology reports. The operations were grouped as breast-conserving surgery (BCS) + sentinel lymph node biopsy (SLNB), BCS + axillary lymph node dissection, mastectomy + SLNB, simple mastectomy, and modified radical mastectomy (MRM).

3 | STATISTICAL ANALYSIS

The data were recorded using the Statistical Package for the Social Sciences 15 program. The Student's *t* test was used to compare the mean age between the groups. The Pearson's χ^2 test was used to evaluate whether there was a significant difference between Group 1 and Group 2 in terms of tumor size, positivity of axillary lymph nodes, distant organ metastasis, and the types of surgery performed. Statistical significance was set at $p < .05$.

4 | RESULTS

One hundred and forty-eight patients (two men and 146 women) with a median age of 51.2 years (range: 22-91 years) who were diagnosed with breast cancer in our clinic between March 11, 2019 and March 11, 2021 were included in this study. In Group 1, there were 70 patients (one man, 69 women) with a median age of 51.8 years (range: 22-91 years) and in Group 2 there were 78 patients (one man, 77 woman), with a median age of 52.4 years (range: 24-89 years). During the pandemic period, our hospital was excluded from the pandemic, and the outpatient clinics and surgical activities continued in their normal routine. During the pandemic, all patients were tested for COVID-19 by polymerase chain reaction (PCR) during the preoperative preparation process. The operation of three patients with positive PCR results was performed after COVID-19 treatment. There were no differences between the two groups in terms of age and sex. The size of the tumor was significantly larger in the operated patients in Group 1 than in Group 2 ($p = .005$) (Figure 1). In Group 1, 25 of 70 patients had positive axillary lymph nodes, while in Group 2, 44 of 78 patients had positive axillary lymph nodes. Axillary lymph node positivity was significantly higher in Group 2 than in Group 1 ($p = .012$) (Figure 2). One patient each in both the groups exhibited distant organ metastasis. There was no significant difference between the groups in terms of distant organ metastasis ($p = .9$) (Figure 3). NAC was administered to 26 and 42 patients in Group 1 and Group 2, respectively; it was significantly higher in Group 2 than in Group 1 ($p = .042$). When the types of surgeries performed were examined, BCS + SLNB was significantly lower in Group 2 than in Group 1, while simple mastectomy and MRM were significantly higher in Group 2 than in

FIGURE 1 Graph of change in tumor sizes between periods

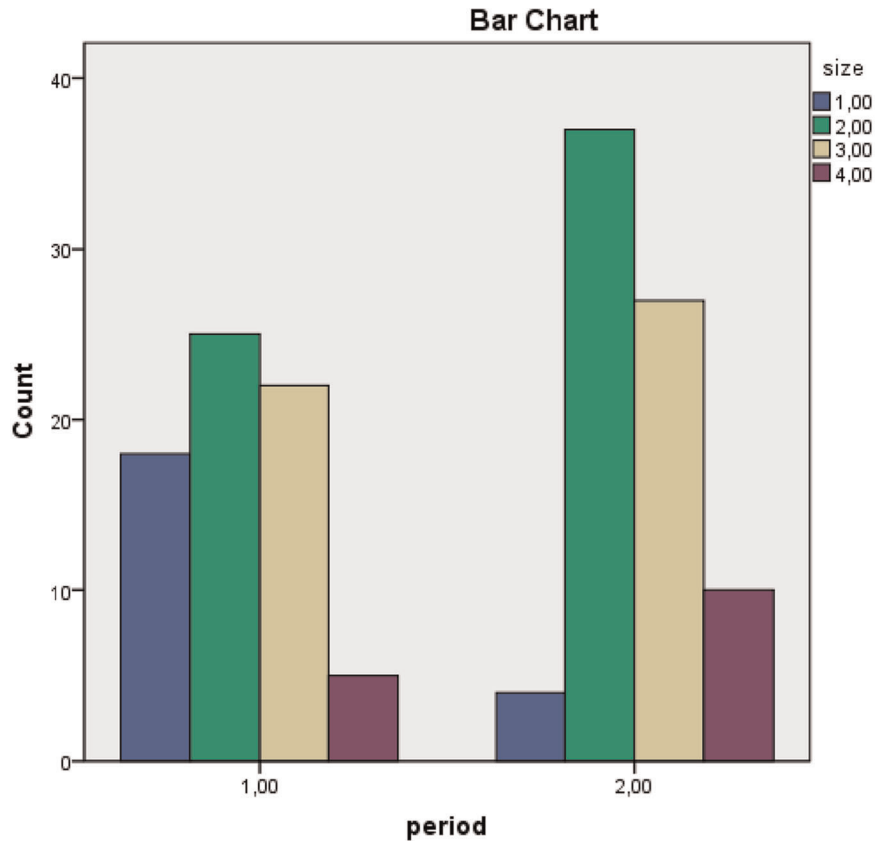
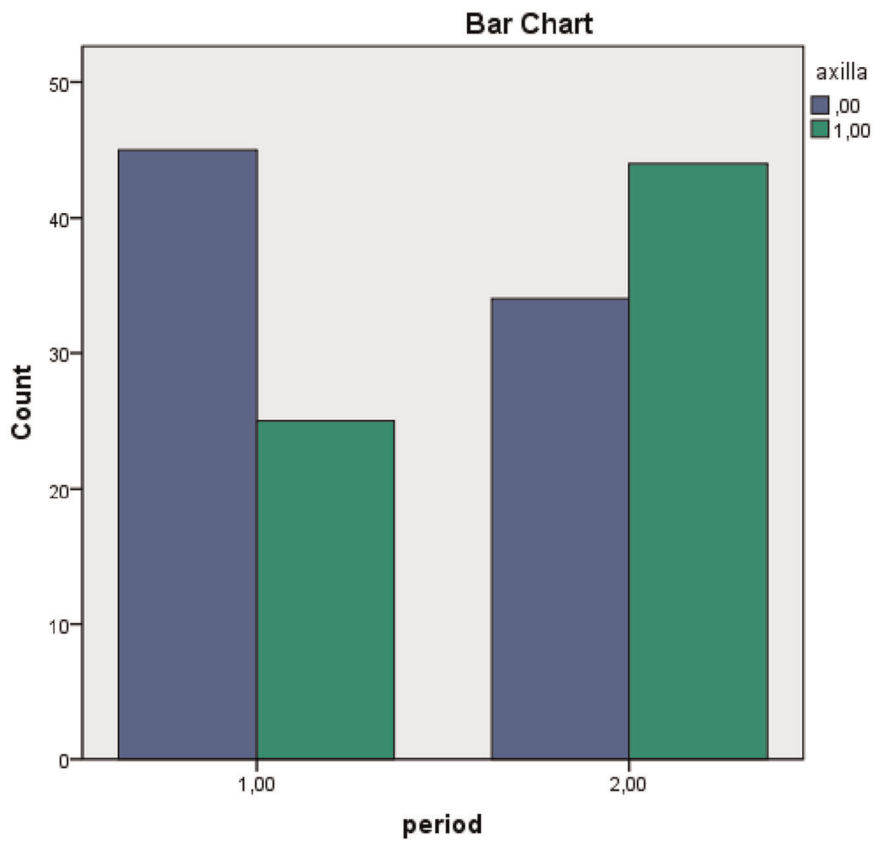


FIGURE 2 Axillary lymph node positivity change graph between periods



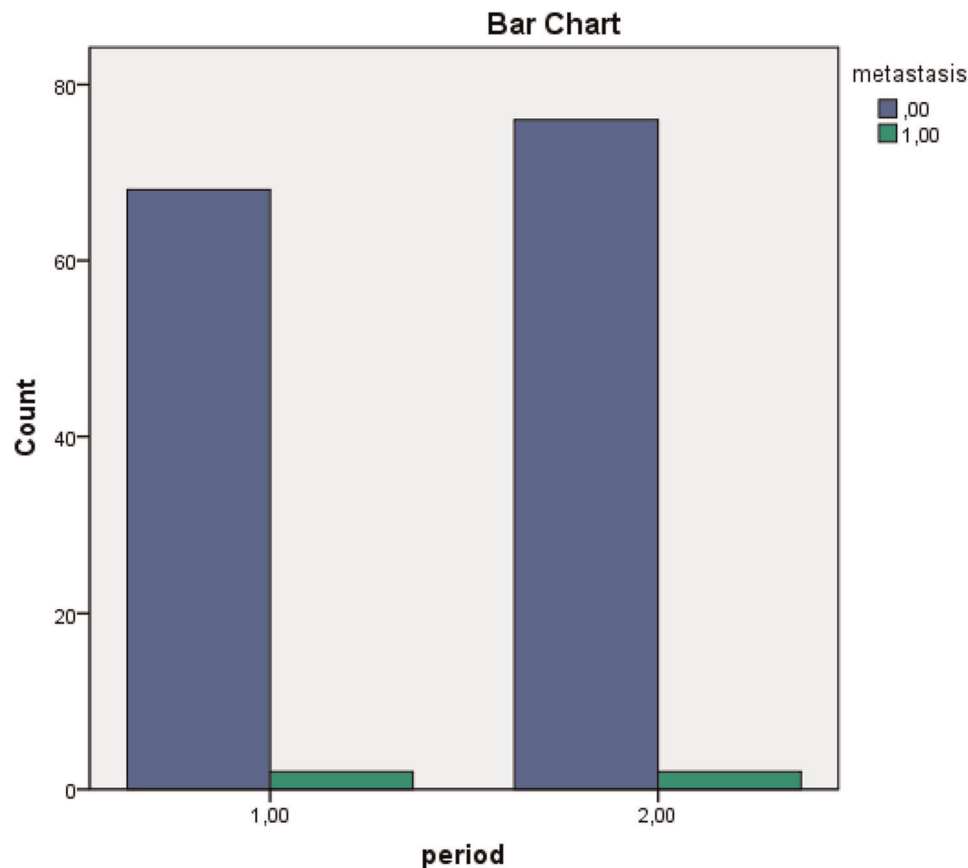


FIGURE 3 Metastasis change graph between periods

Group 1 ($p = .034$) (Figure 4). The general characteristics and statistical results of the patients are shown in Table 1.

5 | EPIDEMIOLOGY RESULTS

In the 1-year period before the pandemic, the number of patients who applied to health institutions because of benign or malignant breast diseases in our city was 8807, and this number decreased to 6483 in the first year during the pandemic. We found a 26.3% decrease in the number of patients who visited breast outpatient clinics during the pandemic period. In the prepandemic period, 2205 patients underwent screening mammography at the cancer screening and education center, while this number decreased to 444 during the pandemic period. A 79.8% decrease in the rate of screening mammography during the pandemic period was noted. While the number of newly diagnosed and operated breast cancer cases was 180 before the pandemic, it was observed that this number decreased to 94 during the pandemic. There was a 47.7% decrease in the number of patients diagnosed and operated during the pandemic. The number of patients who applied to the outpatient clinic, screening mammography, and newly diagnosed breast cancer are shown in Table 2. During the pandemic period, our clinic continued its normal function, since all other ministry hospitals throughout the city were structured

into pandemic hospitals, the number of breast cancer surgeries in our clinic increased slightly. The number of patients who underwent surgery for newly diagnosed breast cancer increased from 70 to 78. However, this increase is not sufficient to compensate for the decrease in the city in general as the number of patients that underwent operation in the pandemic has decreased by 86 compared to the previous year.

6 | DISCUSSION

Breast cancer accounts for 24% of all cancers and for 15% of all cancer-related deaths.¹⁰ It is a serious public health problem in terms of its prevalence and mortality. As in case of all cancers, early diagnosis of breast cancer is the most important factor in increasing treatment success and decreasing mortality. Early diagnosis can be ensured through cancer screening programs. Screening mammography is the most powerful tool available, which performed in women aged 50–69 years reduces mortality due to breast cancer by 16.5%.¹¹ During the COVID-19 pandemic, both cancer screening rates and admissions to breast outpatient clinics have decreased.¹² In a study conducted in Taiwan, Tsai et al.⁵ reported that admissions to breast outpatient clinics in hospitals decreased by 37% during the lockdown period,

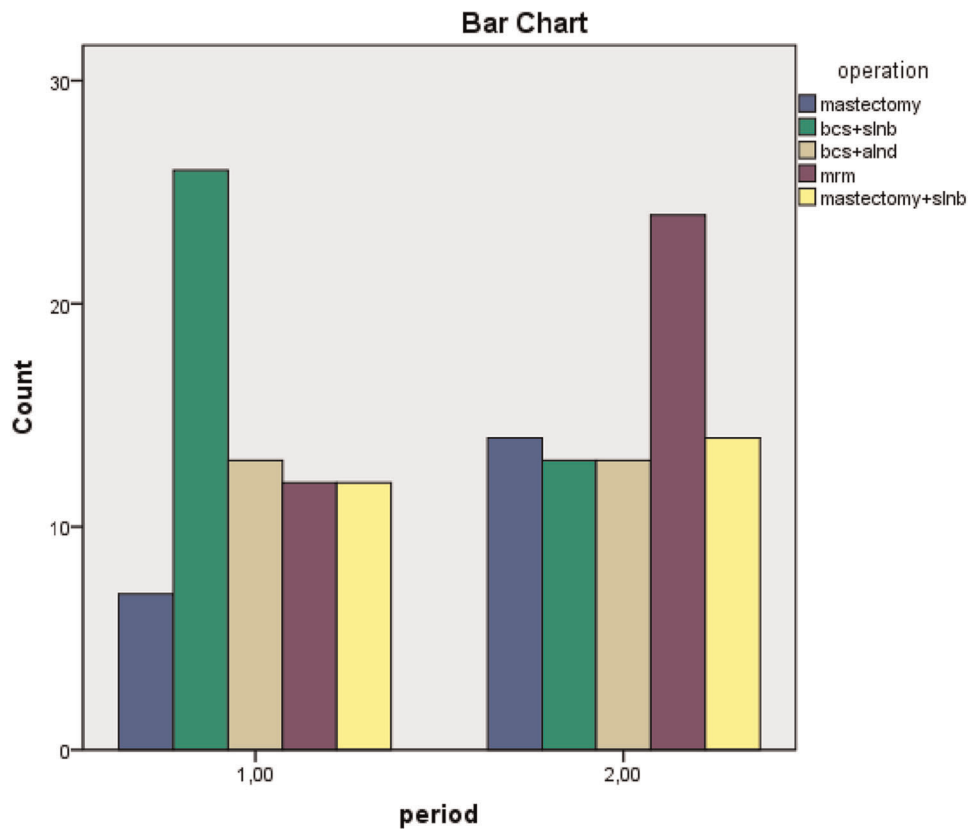


FIGURE 4 The graph of the change in the types of surgery between perio

and breast cancer screening decreased by 22%. In our study, we found that the number of admission to breast outpatient clinics decreased by 26.3% and the number of screening mammography decreased by 79.8% throughout our city in 1 year during the pandemic. Cancer diagnosis is also decreasing because of the decrease in number of patients in the outpatient clinics and cancer screening rates.¹³ In the UK, compared to the first 6 months of 2019, the diagnosis of breast cancer decreased by 16% in the first 6 months of 2020, especially during the period when screening centers were closed.¹⁴ In our study, the reduction rate in the diagnosis of breast cancer in 1 year was 47.7%. Considering that 3 months of data reported from England are included in the pandemic, our rates are in proximity to each other. Furthermore, there were disruptions in the diagnosis of breast cancer in the COVID-19 pandemic. In a study conducted on cancelation of outpatient appointments, 97% of patients canceled their appointments owing to the fear of virus.⁹ COVID-19 anxiety is effective in making decisions regarding treatment options in patients with breast cancer.⁴ “Stay at home” campaigns have also been effective in preventing patients from attending outpatient and cancer screening programs.¹⁵ The UK Office for National Statistics reported that during the pandemic, there was a significant increase in mortality rates due to diagnostic difficulties, a decrease in referral rates, and limitations of elective surgical procedures.⁶ In this emerging picture, it seems that the priority of cancer treatment is postponed and ignored.¹³

The possibility of patients presenting with larger masses or even with increased metastases, due to the disruptions experienced during the pandemic, has been emphasized in various studies.^{16–19} The estimated doubling time for breast cancer ranges between 45 and 260 days.²⁰ In a study conducted in Italy, it was calculated that 43.7% (approximately 6000 cases) of T1 tumors would convert to T2 in a 6-month delay in breast cancer screening, and 600 T2 tumors would convert to T3.⁸ In our series, the T1 tumor rate was 18.7% in the prepandemic period and decreased to 5.1% during the pandemic period. Roughly, this meant 72.7% of patients who could have been diagnosed at T1 stage in the prepandemic phase progressed to T2 stage in the pandemic period. The T2 tumor rate increased from 35.7% to 47.4% and the T4 tumor rate increased from 5.7% to 12.8%. Axillary lymph node positivity was 56.4% (Group 2), which was 20.7% higher than the prepandemic rate (Group 1). In our study, we observed no difference in terms of metastasis. We believe that this result is because of our short follow-up period, and we assume that when we increase the follow-up period and repeat this study, there will be a significant difference in distant organ metastases. In a study conducted in the UK regarding the COVID-19 pandemic, a 3-month delay in diagnosis was reported that could increase the 10-year mortality rate in breast cancer cases by 30%.⁹ We estimate that studies with more definite results on disease-free survival and overall survival will be conducted over the next 5–10 years.

Changes, such as increasing NAC and preoperative hormonal treatments, have been proposed for breast cancer treatment algorithms during the pandemic.¹⁹ In our clinic, breast cancer surgeries were continued in normal routine as before the pandemic. Our study found that the number of NACs increased during the pandemic period. This is a result of increased tumor size and axillary involvement due to delay in diagnosis. When the types of surgeries were

compared, it was observed that there was a decrease in the number of BCS + SLNB and an increase in the number of simple mastectomy and MRM in parallel with the increased tumor size and axillary positivity during the pandemic. The changes in the operation rates will cause increased complications, morbidity, prolonged hospitalization periods, and increased costs in patients. In this study, we aimed to reveal the clinical implications of delays in the diagnosis of breast cancer during the COVID-19 pandemic. We believe that we have achieved this with a real patient group and relatively sufficient follow-up period, although the number is not large.

TABLE 1 General characteristics of the patients

	Prepandemic period	Pandemic period	p value
Age	51.8 (22-91)	52.4 (24-89)	n
Sex			
Male	1 (1.4%)	1 (1.3%)	n
Female	69 (98.6%)	78 (98.7%)	
Tumor size			
T1	18 (25.7%)	4 (5.1%)	.005
T2	25 (35.7%)	37 (47.4%)	
T3	22 (31.4%)	27 (34.6%)	
T4	4 (5.7%)	10 (12.8%)	
Axillary involvement			
Negative	45 (64.3%)	34 (43.6%)	.012
Positive	25 (35.7%)	44 (56.4%)	
Metastas			
Negative	68 (97.1%)	76 (97.4%)	N
Positive	2 (2.9%)	2 (2.6%)	
Neoadjuvant chemotherapy			
Yes	26 (37%)	42 (53.8%)	.042
No	44 (63%)	36 (46.2%)	
Type of operation	26 (37.1%)	13 (16.6%)	.034
BCS + SLNB	12 (17.1%)	14 (17.9%)	
M + SLNB	13 (18.6%)	13 (16.6%)	
BCS + ALNB	7 (10%)	14 (17.9%)	
M MRM	12 (17.1%)	24 (30.7%)	

Abbreviations: ALNB, axillar lymphnode biyopsy; BCS, breast conserving surgery; M, mastectomy; MRM, modified radical mastectomy; SLNB, sentinel lymphnode biopsy.

TABLE 2 Epidemiological characteristics of the patients

	Prepandemic period	Pandemic period	Percentage of change
Number of breast polyclinic patients	8807	6483	-26.3
Screening mammography count	2205	444	-79.8
New breast cancer number	180	94	-47.7

7 | CONCLUSION

Special conditions arising during the pandemic have led to delays in breast cancer diagnosis. Inevitably, the patients presented with larger breast tumors and increased axillary involvement. In case of prolongation of the process, it is possible that distant organ metastases will increase in the future. We predict that deaths due to breast cancer will increase at this point. To prevent delays in diagnosis during the pandemic, outpatient clinical activities should be continued by taking necessary contamination measures. The importance of screening programs in terms of early diagnosis should definitely be explained to the patients, and necessary awareness activities should be conducted meticulously to encourage patients to comply with the screening appointments. Continuation of the screening programs must be ensured.

CONFLICT OF INTERESTS

The authors declare that there are no competing interests

AUTHOR CONTRIBUTIONS

Bulent Koca and Murat Yildirim planned the study, collected the data, drafted the article, did the revision of the article, Bulent Koca and Murat Yildirim drafted the article and revision of the article. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the finding soft his study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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