

Research Article

The Effects of the Covid-19 Pandemic on the Diagnosis and Treatment of Breast Cancer

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Abstract

Objectives: This study aimed to compare the diagnosis stage, tumor characteristics, treatments, COVID-19 positivity and vaccination rates in pre-pandemic and post-lockdown periods in newly diagnosed breast cancer patients.

Methods: A total of 200 patients from the pre-pandemic (from July 1, 2018 to July 1, 2019) and post-lockdown (from July 1, 2020 to July 1, 2021) groups were included in this retrospective single center study. The clinical and pathological characteristics, treatment modalities, vaccination rates against covid-19 and covid-19 positivity of the patients were analyzed and compared between the pre-pandemic group and the post-lockdown group.

Results: There was no statistically significant difference between the demographic and pathological characteristics of the two groups, such as age at diagnosis, tumor diameter, T and N staging, stage at diagnosis, ER status, PR status, HER2 status, ki67 expression index. The rates of treatment modalities such as NACT, primary breast surgery, adjuvant CT, palliative CT, and palliative RT were similar between the two groups and there was no significant difference. However, there was a significant difference between the groups in terms of axillary surgical procedure, adjuvant RT and endocrine treatments ($p=0.001$, $p=0.029$ and $p=0.047$, respectively). There was a significant increase in the rate of SLNB in the post-lockdown group. COVID-19 vaccination rates and COVID-19 positivity rates were similar to Turkey's rates in both breast cancer patient groups.

Conclusion: The fact that there was no significant difference between the pre-pandemic and post-lockdown groups in the characteristics and treatments of breast cancer patients may be related to the continuation of oncology patient care and cancer detection methods even in the lockdown period. However, the rate of SLNB increased significantly in the post-lockdown group.

Keywords: Breast cancer, covid-19, pre-pandemic, post-lockdown

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Coronavirus disease-19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread dramatically worldwide after first recognized on December 30, 2019, in Wuhan, China, and labeled as a global pandemic by the World Health Organization (WHO) on March 11, 2020.^[1] Within this 2-year period, COVID-19

affected approximately 500 million cases and caused approximately 6 million deaths worldwide.^[2]

In Turkey, the first case of COVID-19 was diagnosed on March 11, 2020. With the first case seen in Turkey, contact measures were taken to delay the spread of the pandemic. Public events were postponed and plane flights to most

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countries were cancelled. For epidemic prevention, lockdown was implemented for people with chronic diseases aged >65 or <20 years. These measures have been relaxed or increased over the time according to the number of cases. In the field of health, certain hospitals were designated as pandemic hospitals in addition to services and intensive care units spared for COVID-19 patients.^[3] The COVID-19 vaccination campaign in Turkey started on January, 14, 2021. In our country, COVID-19 pandemic was associated with 15 million cases and approximately 100,000 deaths in two years.

Cancer patients are considered to be at higher risk for severe COVID-19 and a worse prognosis than general population, due to cancer itself as well as the immunosuppressive effects of anti-cancer treatments.^[4] The COVID-19 pandemic has led to changes in the management of patients with breast cancer in clinical practice. Surgery, radiotherapy, chemotherapy and other treatments in breast cancer management were categorized as A, B or C, in order of priority, in accordance with guideline recommendations that aims to minimize patient interactions with health centers, ensure patient safety, and conserve resources while providing effective care.^[5, 6] Accordingly, elective surgeries were postponed, while hormone therapies, neoadjuvant treatments, and hypo-fractionated radiotherapies were continued in suitable patients.

The COVID-19 lockdown phases, particularly in the period of first wave of COVID-19 pandemic resulted in disruptions in provision of the health care to the non-COVID-19 patients in our country. Cancer screenings were suspended in the first months. Accordingly, all these factors are suggested to affect the clinicopathological features and treatment modalities of breast cancer patients during the pandemic, while the previous studies mainly focused on operated breast cancers.^[7, 8]

In this study, we aimed to analyze the effects of the COVID-19 pandemic on the diagnosis and treatment of breast cancer patients in all stages. The results of this study will highlight the importance of multidisciplinary breast cancer care.

Methods

Study Design

This retrospective study was conducted in the oncology clinic of Gaziantep University Faculty of Medicine. Gaziantep University is located in the Southeast region of Turkey and serves for more than 2 million people living in Gaziantep province, and also is a referral hospital for neighboring provinces such as Sanliurfa, Adiyaman and Kilis. Informed

consent was obtained from study participants before the study began. This study was approved by the Gaziantep University Faculty of Medicine Ethics Committee (No: 2021/418).

A total of 200 patient with newly diagnosed breast cancer were divided into two groups including pre-pandemic group ($n=100$, those diagnosed between July 1, 2018 and July 1, 2019) and post-lockdown group ($n=100$, those diagnosed between July 1, 2020 and July 1, 2021, following the prompt strict national lockdown lasted for first 4-months of pandemic). In the power analysis we conducted before the study, 100 patients from each group were considered sufficient to reveal any difference. Interestingly, there were already an equal number of patients in both time periods. Patients with initial diagnosis of breast cancer within the specified time periods, those aged >18 years and those with hospital records available were included in the study. Patients with a second tumor were excluded from the study.

Variables and Outcome Definition

Patients' age at diagnosis, tumor size, disease stage, histological subtype, hormone receptor profile, and treatments were retrieved from the hospital medical files or electronic records.

The tumor diameter (the largest diameter) was measured from the surgical material in operated patients who did not receive neoadjuvant chemotherapy, while the radiological diameter was recorded in inoperable patients and who had received neoadjuvant chemotherapy. According to the 8th edition TNM staging system of The American Joint Committee on Cancer (AJCC), tumor (T), lymph node (N) and metastasis (M) classifications were made for breast cancer.^[9] The histopathological types included ductal carcinoma in situ (DCIS) and invasive carcinomas (ductal carcinoma and invasive lobular carcinoma according to tumor morphology). Estrogen receptor (ER), Progesterone receptor (PR) and Ki67 proliferation index were expressed as percentage of positive cells in the specimens studied by immunohistochemistry. Overexpression of the Her2 gene (HER2) was first identified by immunohistochemistry and as needed by fluorescent in situ hybridization (FISH) and reported as HER2 positive or negative.^[10] According to the hormone receptor (HR), HER2 status and ki67 index, breast cancers were classified in four intrinsic subtypes: luminal A, luminal B, HR-HER2+ and triple negative. For the distinction between luminal A and B, those with a ki67 index ≥ 14 or HR+HER2+ were considered as luminal B.

Overall survival (OS) was defined as the time from the date of diagnosis to the last control or death. Neoadjuvant treat-

ments, surgical treatments, adjuvant or palliative chemotherapy (CT), adjuvant or palliative radiotherapies (RT), and hormone therapy treatments received by patients in both the pre-pandemic group and the post-lockdown group were examined. Surgical treatments were evaluated as modified radical mastectomy (MRM) and breast conserving surgery (BCS) for the breast, and sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) for the axilla. The surgical procedure was planned at the beginning of the treatment in patients who are scheduled for neoadjuvant therapy. For this purpose, image-guided gold wire was placed on the breast or axilla when necessary. Neoadjuvant hormone therapy was used in a few patients and was not included in the analysis. Adjuvant hormone therapy was examined for comparison.

For both pre-pandemic and post-lockdown groups, the COVID-19 history and vaccination status and type of administered vaccines (Sinovac or BioNTech) were recorded. Patients with at least 3 doses of COVID-19 vaccine were considered vaccinated. Patients with positive COVID-19 real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) test in patient records were considered COVID-19 positive. However, those who did not have the test or those who had a negative COVID-19 PCR test and had a viral infection clinic were not included.

Statistical Analysis

The data were recorded using the Statistical Package for the Social Sciences (SPSS) 22 program (SPSS Inc., Chicago, USA). Power analysis was performed before the study, and each group required at least 62 patients. Compliance of numerical variables with normal distribution was tested with the Shapiro Wilk test. Student's t test was used to compare normally distributed variables in two groups, and Mann Whitney U test was used to compare non-normally distributed variables in two groups. Relationships between categorical variables were tested with the Chi-square test. Survival times were estimated by the Kaplan Meier method with use of Log Rank test and Mantel Cox test for intergroup comparisons. Cox Regression analysis was performed to determine the factors affecting survival, age at diagnosis, hormone profile, HER2 status, and treatments received. $p < 0.05$ was considered significant.

Results

The number of patients included in this study was 200. No significant difference was noted between pre-pandemic and post-lockdown groups in terms of patient age (51.3 ± 13.8 vs. 51.6 ± 11.9 years, $p = 0.878$) and the median largest tumor diameter ($3(2.5-4.4)$ cm vs. $3(2.2-4.15)$ cm, $p = 0.380$). There was no significant tumor (T) stage differ-

ence between the two groups, but T2 tumor was seen in 72% of the pre-pandemic group and 59% of the post-lockdown group ($p = 0.25$). There was no significant difference in lymph node (N) stage between the two groups, but the rate of N0 patients was 38% vs. 32% and the rate of N1 patients was 33% vs. 37% in the pre-pandemic and post-lockdown groups, respectively ($p = 0.76$). The rates of patients presenting in the metastatic stage were similar, 19% in the pre-pandemic group and 20% in the post-lockdown group ($p = 0.85$). There was no significant difference between the diagnosis stage distribution of the patients in both groups ($p = 0.72$) (Table 1).

No significant difference was noted between the pre-pandemic and post-lockdown groups in terms of ER positivity (79% vs. 81%, $p = 0.727$), PR positivity (78% vs. 82%, $p = 0.480$), HER2 positivity (27% vs. 31%, $p = 0.533$) and Ki 67 proliferation index (median 30% (IQR 10-50) vs. 30% (IQR 20-47.5), $p = 0.848$). Among the intrinsic subtypes for pre-pandemic vs. post-lockdown groups, luminal-A was noted in 36% vs. 27%, while luminal-B was noted in 48% vs. 57% ($p = 0.543$). DCIS was more common in the post-lockdown group (post-lockdown 6% vs pre-pandemic 2%, $p = 0.315$). There was no difference between the histological subtypes of invasive ductal carcinoma and lobular carcinoma in both groups ($p = 0.315$) (Table 2).

Neoadjuvant chemotherapy was given to 23% of patients in the pre-pandemic group and 22% of the patients in the post-lockdown group ($p = 0.866$). Breast conserving surgery rates were similar in both groups. MRM was applied to 70% of the patients in the pre-pandemic group and 68% of the patients in the post-lockdown group ($p = 0.239$). However, there was a significant difference between procedures applied to the axilla. While the axillary lymph node dissection was performed in 66% vs. 45% of patients in the pre-pandemic and post-lockdown groups, respectively, the sentinel lymph node sampling rates in the groups were 10% and 32%, respectively ($p = 0.001$) (Fig. 1).

Adjuvant chemotherapy rates were similar between study groups ($p = 1.000$). The rates of patients who received adjuvant radiotherapy in both groups were similar, 48% and 46%, respectively. In the post-lockdown group, 5% of the patients were planned to receive adjuvant radiotherapy ($p = 0.029$). A similar proportion of metastatic patients in the pre-pandemic group and the post-lockdown group received palliative systemic chemotherapy (19% vs. 18%, $p = 0.856$). Palliative radiotherapy was applied to 8% of pre-pandemic patients and 4% of post-lockdown patients with brain or bone metastases ($p = 0.234$). Endocrine therapy was administered to patients with positive ER or PR (85% in the pre-pandemic group, 78% in the post-lockdown group). In

Table 1. Baseline characteristics of the patients

	Pre-pandemic (n=100)	Post-lockdown (n=100)	p
Age (year), Mean±SD	51.34±13.84	51.62±11.93	0.878
Tumor diameter (cm), Median (25%-75%)	3 (2.5-4.4)	3 (2.2-4.15)	0.380
T staging, n(%)			0.251
T0	1 (1)	5 (5)	
T1	10 (10)	13 (13)	
T2	72 (72)	59 (59)	
T3	12 (12)	15 (15)	
T4	5 (5)	8 (8)	
N staging, n(%)			0.769
N0	38 (38)	32 (32)	
N1	33 (33)	37 (37)	
N2	18 (18)	17 (17)	
N3	11 (11)	14 (14)	
M staging, n(%)			0.858
M0	81 (81)	80 (80)	
M1	19 (19)	20 (20)	
Stage at diagnosis, n(%)			0.722
DCIS	3 (3)	6 (6)	
Stage-1	6 (6)	3 (3)	
Stage-2	47 (47)	46 (46)	
Stage-3	25 (25)	25 (25)	
Stage-4	19 (19)	20 (20)	

Table 2. Tumor characteristics

	Pre-pandemic (n=100)	Post-lockdown (n=100)	P
ER status, n(%)			0.727
Negative	21 (21)	19 (19)	
Positive	79 (79)	81 (81)	
PR status, n(%)			0.480
Negative	22 (22)	18 (18)	
Positive	78 (78)	82 (82)	
HER2 status, n(%)			0.533
Negative	73 (73)	69 (69)	
Positive	27 (27)	31 (31)	
Ki-67 index, Median (25%-75%)	30.0 (10.0-50.0)	30.0 (20.0-47.5)	0.848
Intrinsic subtypes, n(%)			0.543
luminal-A	36 (36)	27 (27.3)	
Luminal-B	48 (48)	57 (57.6)	
HER+HR-	10 (10)	10 (10.1)	
TNBC	6 (6)	5 (5.1)	
Histological subtypes, n(%)			0.315
DCIS	2 (2)	6 (6)	
Invasive ductal	92 (92)	87 (87)	
Invasive lobular carcinoma	6 (6)	7 (7)	

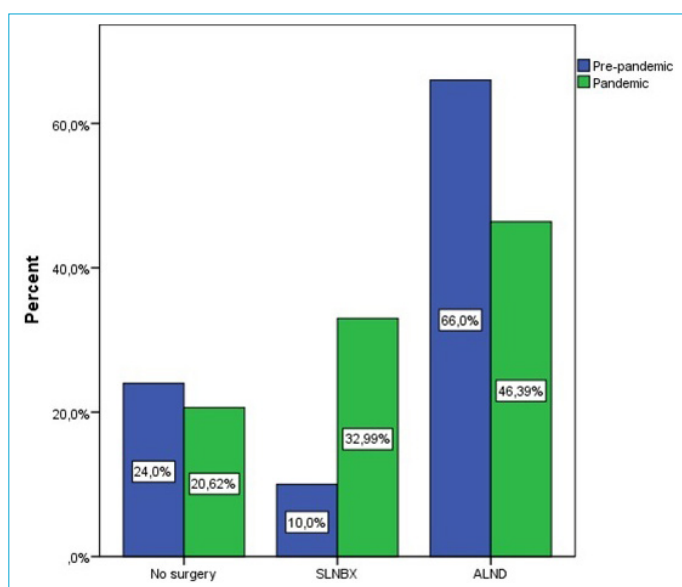


Figure 1. Proportions of patients without axillary surgery, SLNB, and ALND in the pre-pandemic and post-lockdown groups.

the post-lockdown group, 4% of the patients were planned to receive hormonal therapy ($p=0.047$) (Table 3).

The proportion of patients who received at least three doses of COVID-19 vaccine was 69% in the pre-pandemic group and 65% in the post-lockdown group at the time of study ($p=0.547$). The rate of COVID-19 positive patients was 11% and 14%, respectively ($p=0.521$).

Given the short follow up period, the estimated overall survival times were analyzed. Estimated OS times, 36.8 months 95%CI (34.8-38.8) in the pre-pandemic group, 16.2 months 95%CI (15.6-16.8) in the post-lockdown group and 36 months 95%CI(35.3-36.8) in all study patients ($p=0.756$) (Fig. 2A). The OS rate was $91.9\pm 2.7\%$ in the first 12 months, $87.8\pm 3.3\%$ in the 24 months for the pre-pandemic group, and $94.1\pm 2.7\%$ in the first 12 months for the post-lockdown group. The estimated follow-up time for the pre-pandemic group was 36 months, while it was 16 months for the post-lockdown group. During these follow-up periods, 15

Table 3. Treatment modalities applied to the patients

	Pre-pandemic (n=100)	Post-lockdown (n=100)	P
Neoadjuvant therapy, n (%)			
No	77 (77)	78 (78)	0,866
Yes	23 (23)	22 (22)	
Breast surgical procedure, n (%)			
no surgery	19 (19)	18 (18)	0,239
MRM	70 (70)	68 (68)	
BCS	11 (11)	11 (11)	
Surgical plan (+)	0 (0)	3 (3)	
Axilla surgical procedure, n (%)			
no surgery	24 (24)	20 (20)	0,001*
SLNB	10 (10)	32 (32)	
ALND	66 (66)	45 (45)	
There is a surgical plan	0 (0)	3 (3)	
Adjuvant chemotherapy, n (%)			
No	50 (50)	50 (50)	1,000
Yes	50 (50)	50 (50)	
Palliative chemotherapy, n (%)			
No	81 (81)	82 (82)	0,856
Yes	19 (19)	18 (18)	
Adjuvant RT, n (%)			
No	52 (52)	49 (49)	0,029*
Yes	48 (48)	46 (46)	
There is a treatment plan.	0 (0)	5 (5)	
Palliative RT, n (%)			
No	92 (92)	96 (96)	0,234
Yes	8 (8)	4 (4)	
Hormone therapy, n (%)			
No	15 (15)	18 (18)	0,047*
Yes	85 (85)	78 (78)	
There is a treatment plan	0 (0)	4 (4)	

SLNB: Sentinel lymph node biopsy, ALND: Axillary lymph node dissection, MRM: modified radical mastectomy, BCS: Breast-conserving surgery.

Table 4. Cox-regression analysis for factors that may contribute to overall survival.

	p	HR	95.0% CI for HR	
			Lower	Upper
Group	0,22	0.733	.214	2.518
Age	0.080	1.031	.996	1.067
Adjuvant RT	0.008	5.838	1.589	21.443
NACT status	0.734	0.792	.206	3.037
ER status	0.047	4.438	1.017	19.367
PR status	0.827	0.855	.208	3.506
HER2 status	0.182	0.454	.142	1.447

NACT: Neoadjuvant chemotherapy. ER: Estrogen Receptor. PR: Progesterone Receptor.

patients in the pre-pandemic group and 5 patients in the post-lockdown group died ($p=0.018$). Causes of death were due to breast cancer progression in 14 patients and comorbidities in one patient in the pre-pandemic group. The causes of death in the post-lockdown group were breast cancer progression in two patients, COVID-19 positivity in one patient, and comorbidities in two patients.

Cox-regression analysis was performed for factors that may contribute to OS, pre-pandemic or post-lockdown group, age at diagnosis, neoadjuvant therapy, adjuvant RT, ER positivity, PR positivity, and presence of HER2 overexpression. Receiving adjuvant RT (HR:5.8%, 95%CI (1.5-22.4)) and ER positivity (HR:4.4%, 95%CI (1.0-19.3)) were determined to be factors significantly associated with OS (Table 4). Estimated survival at log-rank test 28 months 95%CI (23.6 to 32.6%) in those without axillary surgery, 36.3 months

95%CI (34 to 38.6) in those with SLNB and 39.3 months 95%CI (37.9 to 40.7) in those with ALND (Fig. 2B). These data on survival outcome seem to differ significantly, since the patients who did not undergo surgery to the axilla are usually metastatic patients.

Discussion

There were no significant differences between the pre-pandemic and post-lockdown groups referring to the previous and first year of the pandemic, except for a few parameters. Certain factors are considered likely to explain the observation of similar findings between our study groups. First, the short follow up period of 4-months seems to be one possible factor in identification of similar findings between study groups. Second, during the 4-month lockdown period in our country, outpatient services continued in some hospitals such as our Gaziantep Oncology Hospital. Third, the majority of breast cancers in our country present with symptoms or after noticing a mass in breast self-examination, and mammography screening rates are low (15-20%) in our country.^[11] Fourth, the estimated doubling time in breast cancer is 65-260 days and longer in hormone-positive subtypes.^[12]

In our study, there was no statistical difference between the two groups in terms of median age, median tumor diameter, T staging, and distribution of TNM stage. Since the first period of the epidemic was also closed, the number of patients who applied was low, as expected. In a study conducted by Isiklar et al in the first period of the epidemic in our country, it was seen that there was a decrease in the number of new patients in a breast cancer center.^[13] In the

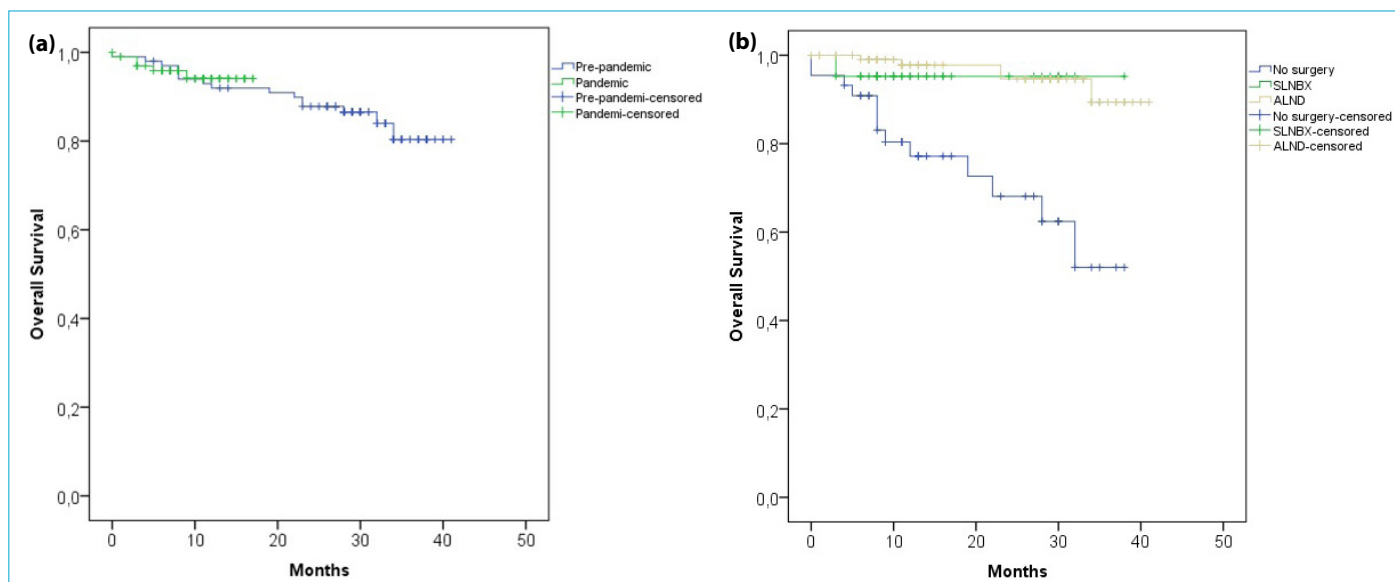


Figure 2. (a) Kaplan-Meier plot of overall survival for pre-epidemic and pandemic patients, (b) Analysis of overall survival for patients who could not be operated, had SLNB, or had ALND.

study conducted in the Netherlands by Eijkelboom et al., it was observed that the number of patients admitted in the early period of the epidemic decreased significantly, apart from the stage 4 patients.^[14] Because our study analyzed patients after lockdown, there were a similar number of patient admissions compared to the previous year. Also in our study, the number of N0 patients in the pre-pandemic group (38% vs. 32%) and the number of N1 patients in the post-lockdown group (37% vs. 33%) were numerically higher. Vanni et al. analyzed 432 patients with operated breast cancer between March and May 2020, and reported a mean tumor diameter of 12 mm and a significant increase in N2 disease in patients during the pandemic period.^[15] While the mean tumor diameter was 12 mm in the study of Vanni et al., it was 30 mm in both groups in our study. The reason for this difference seems to be the inclusion of inoperable patients in our study with consideration of radiologically measured diameter as tumor diameter in these patients. In our cohort, the rates of de novo metastatic patients were found to be higher in both pre-pandemic (19%) and post-lockdown (20%) groups compared to the literature. We think that this is related to the socio-economic status of patients, their beliefs and the rates of having mammography screening.^[16] In addition, our center is close to northern Syria, so these patients can also apply to our center, and the rate of advanced stages is higher in these patients.

In our study, there was no difference in intrinsic subtypes between the two groups. Romics et al. reported that T3-T4 tumor rates and HER2+ HR- patient rates were increased in breast cancer patients who were operated during the lockdown period.^[8] During the lockdown period, it was thought that patients with high proliferation index, especially HER2+ or TNBC cancer, were alert because of the rapidly growing mass and were admitted to hospitals. In addition, an increase in the slow growing luminal A and B subtypes was expected after the lockdown period.^[15] The results of our study were in line with this expectation, given that the rate of luminal B patients in the post-lockdown group was 57%, while it was 47% in the pre-pandemic group. Other subtypes were similar in our study groups. In addition, in our study, the ER, PR, HER2 and ki67-proliferation indexes, which distinguish between intrinsic subtypes in breast cancer, were similarly distributed between both groups.

In our study, the rates of patients underwent NACT and breast surgical procedures, BCS and MRM, were similar ($p=0.866$, $p=0.239$, respectively). However, surgical procedures applied to the axilla were significantly different including SLNB or ALND rates ($p=0.001$). The rates of patients who underwent SLNB in the post-lockdown group and ALND in the pre-pandemic period were significantly higher. Wilke et al. reported that NACT usage rates increased

during the lockdown period.^[17] In the study by Vanni et al, there was no difference between SLNB application in the lockdown group and pre-lockdown, while the rate of patients who underwent ALND in the lockdown group was higher.^[15] In our study, there were reasons for the identification of a higher rate of SLNB application during the pandemic period. The first was to provide shorter hospital stays and fewer hospital visits with SLNB during the pandemic period. Second, the surgeons who performed breast oncology surgery in our center during the post-lockdown and pre-pandemic period were different.

At the onset of the pandemic, many national and international guidelines recommended neoadjuvant chemotherapy and neoadjuvant hormonal therapy to reduce transmission of the COVID-19. In our study, we also investigated the potential changes in our treatment practice during the post-lockdown period, by analyzing the NACT treatments, adjuvant CT, adjuvant RT, palliative RT and hormone therapy treatment rates in pre-epidemic and post-lockdown groups. There was statistical significance between the two groups in terms of adjuvant RT and endocrine therapy ($p=0.029$ and $p=0.047$, respectively), which may be explained by the presence of patients in the pandemic group who were planned but not yet received the adjuvant RT and endocrine therapy. In addition, two patients in our pandemic cohort received neoadjuvant endocrine therapy because of their age and comorbidities. Similarly, Vanni et al. reported that patients in the pandemic period had increased tumor diameters, increased N stage, and increased need for adjuvant RT.^[18] Tonneson et al. reported that neoadjuvant chemotherapy rate was similar but neoadjuvant endocrine therapy increased during the pandemic period compared to the pre-pandemic period. In the same study, the detection of breast cancer was based on imaging in 66% and physical signs/symptoms in 34%, while the rate of detection of breast cancer by imaging was 20% in our country.^[11, 19]

The rate of COVID-19 vaccination is expected to be high in the pre-pandemic group of patients who do not receive active treatment, and the probability of transmission of COVID-19 infection in the post-lockdown group that receives active treatment. In accordance with this expectation, numerically, vaccination rates were 69% in the pre-pandemic group, 65% in the post-lockdown group, and the rate of COVID-19 positivity was 11% and 14%, respectively ($p=0.547$ and $p=0.521$). One patient from the post-lockdown group died due to COVID-19 infection. Guidelines recommend that cancer patients be vaccinated for COVID-19 as a priority. Although it is known that COVID-19 seropositivity is lower in patients receiving active cancer treatment, vaccination is recommended.^[20] In previous studies, the rate

of COVID-19 vaccination in breast cancer patients was not evaluated. In our study, it was seen that 65% of the patients were vaccinated. Our rate of patients with COVID-19 positivity may have been higher because patients who were negative for COVID-19 PCR or did not have a PCR test were not included in the COVID-19 positive group. The rate of COVID-19 vaccination in our cohort of breast cancer patients is consistent with the overall data from the city of Gaziantep, whereas the rate of COVID-19 positivity is lower, which may be related to the fact that cancer patients pay more attention to infection precautions.

The median OS was not reached in the study. Therefore, the estimated OS was calculated. While the 12-month OS rate in the pre-pandemic group was $91.9 \pm 2.7\%$, the 12-month OS rate in the post-lockdown group was $94.1 \pm 2.7\%$ ($p=0.756$). The reason for the low survival rate in the pre-pandemic group was that 15 patients in the pre-pandemic group and 5 patients in the post-lockdown group died during the follow-up period. The causes of death were breast cancer progression in 16 patients, comorbidities in 3 patients, and COVID-19 infection in one patient. Nine of the patients who died from disease progression were at stage-4. Thus, mortality due to COVID-19 infection was noted only in 1 out of 200 breast cancer patients in the present cohort. During the data analysis period, 85 patients in the pre-pandemic group and 95 patients in the post-lockdown group were followed up ($p=0.018$). The reason for the difference between the two groups is that the estimated follow-up period was 36 months in the pre-pandemic group, while it was 16 months in the post-lockdown group. In the cox-regression analysis, adjuvant RT HR:5.8% 95%CI (1.5-22.4) and ER positivity HR:4.4 595CI (1.0-19.3), which are among the factors affecting OS, were found to be significant factors. Here, adjuvant RT was found to be significant because metastatic patients constituted 20% of the patients and adjuvant RT was applied to non-metastatic patients.

This comprehensive study has some limitations. The first is a retrospective and single-center design of the study. Therefore, the results of the study cannot be generalized for all populations, the results may vary according to different races, different ethnicities and socioeconomic conditions. Second, especially the post-lockdown group, the follow-up period was short. Third, we examined the COVID-19 vaccination status of the patients, but we could not assess the seropositivity level. However, we included breast cancer patients of all disease stages in our study and examined these patients with many parameters such as demographic characteristics, pathological characteristics, treatment modalities, COVID-19 positivity and vaccination status.

In conclusion, in the pre-pandemic group and the post-

lockdown group, it was observed that the stage at diagnosis, the biological characteristics of the tumor and the treatment modalities applied were similar. There was no significant change in our treatment and follow-up management of breast cancer. However, in the post-lockdown group, the rate of SLNB was significantly increased in axilla surgery. The rates for COVID-19 positivity and COVID-19 vaccination were also similar to the mean rates in Turkey. Further larger scale multicenter studies with a longer-term follow-up are necessary to reveal the exact impact of the COVID-19 in the oncology setting.

Disclosures

Ethics Committee Approval: This retrospective study was conducted in the oncology clinic of Gaziantep University Faculty of Medicine.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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