

## ORIGINAL ARTICLE

# The reliability of breast cancer surgery in a regional pandemic hospital during the COVID-19 pandemic: Delay or Do?

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## Summary

**Purpose:** The purpose of this study was to examine the effect of COVID-19 infection on the morbidity and mortality rates of breast cancer patients performed in the East Mediterranean region of Turkey during the COVID-19 pandemic and to share the results of those investigations.

**Methods:** This retrospective study included all breast cancer patients that underwent surgery during the COVID-19 pandemic in the General Surgery Clinic of Adana City Training and Research Hospital, a regional pandemic hospital, between March 11, 2020 and December 25, 2020. The patients were evaluated preoperatively and postoperatively (the first 30 days) in terms of COVID-19 infection. Moreover, these patients were also evaluated in terms of admission to the hospital, length of hospital stay, and mortality due to COVID-19 infection during the follow-up period of the study.

**Results:** Included in the study were 139 patients that underwent surgery for breast cancer during the pandemic period, with no observed mortality or morbidity associated with COVID-19 in any patient postoperatively within the first 30 days. In addition, within  $121.22 \pm 70.05$  days, the mean and standard deviation of the study's follow-up period, 19 patients (15.7%) were admitted to the hospital with a suspected COVID-19 infection (after the first 30 days postoperatively) and 6 of them (4.3%) returned a positive PCR test. All of the COVID-19 positive patients (6 patients, 4.3%) were hospitalised and 3 of them (2.2%) died due to the COVID-19 infection.

**Conclusions:** Breast cancer surgery can be performed safely during the COVID-19 pandemic period after taking the necessary precautions.

**Key words:** breast cancer, COVID-19, mortality, surgery

## Introduction

The World Health Organisation (WHO) declared the COVID-19 outbreak a pandemic on March 11, 2020 [1]. On the same day, Turkey announced its first case of COVID-19 and instituted some restrictions across the country due to the infection. After that date, upon a decision taken by the scientific committee of the Ministry of Health, elective operations were halted and only emergency and oncological operations were permitted in Turkey. Although the mortality rate reported by WHO for COVID-19 infection varies, it is reported at about 3%, with mortality and morbidity rates increasing

in elderly, hypertensive and immunosuppressed patients, those with a history of surgery, and those with cancer [2-4].

Breast cancer, the most common cancer in women, affects about 1 in 8 women throughout their lives [5]. The treatment of breast cancer usually includes surgery, chemotherapy and radiotherapy. Therefore, patients with breast cancer are in contact with the hospital environment and staff for an extended period of time after diagnosis. Since COVID-19 has the potential of nosocomial transmission, the prevalence of COVID-19 is expected

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to be high in patients with breast cancer who are receiving active treatment. Moreover, since breast cancer treatment involves immunosuppression (especially via surgery and systemic chemotherapy, for example), morbidity and mortality are expected to be high in cases of COVID-19 infection. However, in the literature this is more controversial than it appears on the surface. Some studies have reported that the mortality rate is higher in cancer patients infected with COVID-19 and receiving systemic chemotherapy, while there are other studies asserting that a COVID-19 infection has no effect on the clinical results of this patient group [6-9]. In the initial COVID-19 pandemic period it was assumed that a COVID-19 infection would have a high probability of transmission in patients receiving treatment for breast cancer and consequently lead to higher morbidity and mortality. Therefore, routine recommendations for the treatment and follow-up of breast cancer were changed in many professional guidelines during this initial period, and various recommendations were made to reduce COVID-19 transmissibility. For example, it was recommended that systemic chemotherapy or hormonotherapy be preferred to surgery in newly diagnosed early-stage breast cancer patients and that surgical operations be postponed in these cases where there were no poor prognostic factors [10,11].

Unfortunately, there is a limited number of studies on breast cancer surgical treatment during the COVID-19 pandemic. It is still debated when and by which procedures surgical treatment should be offered. On the other hand, in the hospitals where cancer surgery is frequent, breast cancer surgery had to be performed in line with the local precautions and recommendations [12,13]. As an example of these precautions, some centres requested a COVID-19 PCR test from all patients before surgery, and in suspicious cases others requested supplemental tests such as a thorax CT in addition to the PCR test. Moreover, after surgery, most centres discharged their patients earlier than was their usual practice prior to the pandemic [14].

The purpose of this study was to examine the effects of COVID-19 on the breast cancer surgery performed under pandemic conditions in the reference hospital in the East Mediterranean region of southern Turkey and to share the results of those investigations.

## Methods

### *Ethics and patient selection*

This study was carried out with the permission of the Adana City Training and Research Hospital Ethics Committee decision dated 30.12.2020. (Session No: 73

and Decision No: 1193). This retrospective study included all breast cancer patients who underwent surgery in the General Surgery and Surgical Oncology Clinic, Adana City Training and Research Hospital (a pandemic hospital), University of Health Sciences between March 11, 2020 and December 25, 2020. Patient information was collected and analysed using the hospital data system. The patients were evaluated in terms of age, gender, American Society of Anaesthesiologists (ASA) score, comorbidity, clinical stage and histopathological result at the time of diagnosis. The evaluation was accomplished irrespective of whether the patients had received neoadjuvant chemotherapy, preoperative COVID-19 PCR test result, and a CO-RADS score in the thorax computed tomography. Moreover, the following patient data was also examined using the hospital information system: type of surgical operation, duration of hospital stay, early postoperative complications (according to the Clavien-Dindo classification), complications associated with COVID-19 infection, as well as re-admission to hospital, length of hospital stay, and death due to COVID-19 infection in the first 30 days after discharge from the hospital. Excluded from the study were patients whose surgery involved ductal carcinoma *in situ*, as well as the patients with T4 tumours who underwent reconstructive procedures (latissimus dorsi flap, split-thickness skin graft) to close the defect after mastectomy.

### *Perioperative approach and follow-up*

During the study period, the patients who were newly diagnosed with breast cancer were treated in the same way as before the COVID-19 pandemic; that is, no treatment procedure specific to the COVID-19 infection was applied. The patients were clinically staged at the time of diagnosis, and the appropriate treatment (surgery, neoadjuvant chemotherapy) was initiated. The patients who received neoadjuvant chemotherapy underwent surgery at least 3 weeks after the last systemic chemotherapy.

The patients were tested for COVID-19 using a PCR test with a nasopharyngeal swab at least 48 h before the operation. The patients with symptoms were evaluated through a Thorax CT scan. Surgery was then performed only on patients who had no symptoms and a negative PCR test result. The Clinic of Infectious Diseases was consulted for the patients with positive PCR tests, then the treatment for a COVID-19 infection was initiated and the patients were discharged in line with the isolation measures. Three weeks later, these patients were re-evaluated, and those who returned a negative PCR test and who had completely recovered were operated on. The surgeries were performed under general anaesthesia. An interval of at least 45 min was left between surgeries for cleaning and disinfecting the operating theatre and only then the subsequent surgery began.

After the surgery, in cases where no serious complications appeared, the patients were discharged as soon as their clinical conditions allowed in order to reduce the risk of COVID-19 contact. Patients who underwent a breast-conserving surgery were discharged with drains on postoperative day 1, and those who underwent a modified radical mastectomy were discharged on postoperative day 2 or 3. After discharge, the patients were

invited to the hospital once a week to have their wound sites and drains examined. The patients who did not develop any complications were referred to the medical oncology and/or radiation oncology clinics for additional postoperative treatment.

#### Hospital facilities and regulations

The hospital where these operations were performed is one of the recently constructed city hospitals in Turkey that has a highly developed infrastructure and technological opportunities. This regional hospital offers healthcare services to a city with a central population of 2.5 million. This population reaches 4.5 million when the referrals from surrounding provinces are included. During the COVID-19 pandemic, the hospital served as a pandemic hospital. In addition to treating patients with COVID-19, the hospital offered emergency and oncological operations simultaneously. The hospital consists of 5 separate blocks within the same building, and all the operating rooms have a negative pressure system. During the pandemic, separate operating rooms were reserved for those infected or suspected to be infected with COVID-19.

Moreover, similar to before the pandemic, emergency operations during the pandemic period were performed in a separate operating room. The majority of the service rooms in the hospital are designed for a single patient, and the rest are double rooms. During the pandemic, only a single patient was admitted to each room in order to prevent a possible viral transmission. In cases where patients tested positive for COVID-19, they were followed up in a separate service reserved for COVID-19 patients or in the intensive care unit. Regarding hospital staff, any with COVID-19 infections were immediately sent on a leave under isolation conditions, and were allowed back to work only after a 10-day quarantine and when they no longer had symptoms.

#### Statistics

The statistical analyses were carried out using SPSS 25 (SPSS Inc). Numerical data were presented in mean±standard deviation (SD) and categorical data in numbers and percentages (%).

## Results

The data of 144 patients were analysed between March 11, 2020 and December 25, 2020. In order to homogenize the patient group, several patients were excluded from the study: 2 patients operated on for ductal carcinoma *in situ*, 1 male patient operated on for breast cancer, and 2 patients with a T4 tumour who underwent salvage mastectomy and reconstruction. This left 139 female patients as the population for this study with their mean age being 54.06±11.31 years. Among these patients, 43 (30.9%) had hypertension, 22 (15.8%) had diabetes, 23 (16.5%) had coronary artery disease, and 9 (6.5%) had chronic pulmonary disease as a comorbidity. According to ASA classification, 5 patients (3.6%) were classified as ASA I, 87 patients

**Table 1.** Patient characteristics

Characteristics	n (%)
Age, years, mean ±SD	54,06±11,31
ASA score	
I	5 (3,6)
II	87 (62,6)
III	44 (31,7)
IV	3( 2,2)
Co-morbidities	
HT	43(30,9)
DM	22 (15,8)
CAD	23 (16,5)
Pulmonary	9 (6,5)
Others	2 (1,4)
Tumour size	
T1	31 (22,3)
T2	98 (70,5)
T3	8 (5,8)
T4	2 (1,4)
Axillary nodal status	
NO	63 (45,3)
N1	69 (49,6)
N2	6 (4,3)
N3	1 (0,7)
Stage	
IB	21 (15,1)
IIA	51 (36,7)
IIB	54 (38,8)
IIIA	10 (7,2)
IIIB	2 (1,4)
IIIC	1 (0,7)
Neoadjuvant chemotherapy	
Yes	77 (55,4)
No	62 (44,6)
Preoperative PCR	
Positive	1 (0,7)
Negative	138(99,3)
Operation	
Modified radical mastectomy	74 (53,2)
Lumpectomy + SLNB	35 (25,2)
Lumpectomy + ALND	5 (3,6)
Total mastectomy+ SLNB	20 (14,4)
SLNB	3 (2,2)
Bilateral modified radical mastectomy	2 (1,4)
Clavien-Dindo Classification	
None	131 (94,2)
Grade1	4 (2,9)
Grade2	3 (2,2)
Grade3	1 (0,7)
Histopathology	
Invasive ductal carcinoma	125 (89,9)
Invasive lobular carcinoma	8 (5,8)
Others	6 (4,3)
Length of hospital stay, day ± SD	5.23±2,42
Follow up time , day ± SD	121.22±70,05

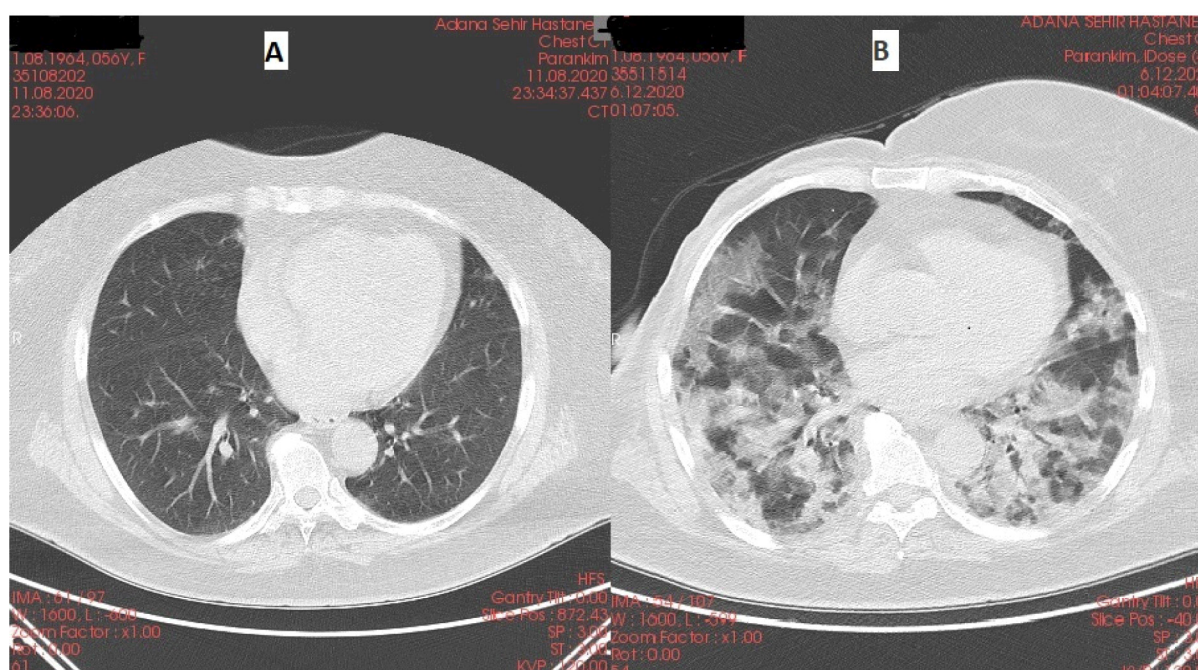
(62.6%) as ASA II, 44 patients (31.7%) as ASA III, and 3 patients (2.2%) as ASA IV. As a result of the clinical staging at the time of initial diagnosis, 21 patients (15.1%) were found to be at stage IB, 51 patients (36.7%) at stage IIA, 54 patients (38.8%) at stage IIB, 10 patients (7.2%) at stage IIIA, 2 patients (1.4%) at stage IIIB, and 1 patient (0.7%) at stage IIIC. In line with this clinical staging, neoadjuvant chemotherapy was applied to 77 patients

**Table 2.** Follow-up outcomes of patients in terms of Covid-19 infection (except for the first 30 postoperative days)

Characteristics	n (%)
Readmission	
Yes	19 (13,7)
No	120 (86,3)
Hospitalisation	
Yes	6 (4,3)
No	133 (95,7)
PCR	
Absent	120 (86,3)
Positive	6 (4,3)
Negative	13 (9,4)
Thorax computed tomography	
Absent	120 (86,3)
CORADS1	14 (10,1)
CORADS5	5 (3,6)
Exitus	
Yes	3 (2,2)
No	136 (97,8)

(55.4%) and they underwent surgery. Additionally, 74 patients (53.2%) underwent modified radical mastectomy (MRM), 35 patients (25.2%) lumpectomy and sentinel lymph node biopsy (SLNB), 20 patients (14.4%) had total mastectomy and SLNB, 5 patients (3.2%) underwent lumpectomy and axillary lymph node dissection, 3 patients (2.2%) had SLNB alone, and 2 patients (1.4%) had bilateral MRM. Subsequently, 8 patients (5.8%) developed postoperative complications. According to the Clavien-Dindo Classification, a Grade 1 complication was observed in 4 patients (2.9%), Grade 2 in 3 patients (2.2%), and Grade 3 in 1 patient (0.7%). In the histopathological evaluation of the patients, 125 patients (89.9%) were found to have invasive ductal carcinoma and 8 patients (5.8%) were found to have invasive lobular carcinoma (Table 1). The mean length of hospital stay among the patients was  $5.23 \pm 2.42$  days.

One patient (0.7%) tested positive in the preoperative PCR test. This patient was operated on after receiving medical treatment for COVID-19, having a negative PCR test result (after 2 weeks), and showing no symptoms at all (3 weeks in total). The patient developed no complications in the postoperative period. No patients were found to have abnormal findings associated with a COVID-19 infection in the preoperative thorax CT (CO-RADS 1). No patients were found to have a COVID-19 infection or complications associated with it in the first 30 postoperative days. In addition, no patients were admitted to the hospital or hospitalized due to COVID-19 in the first 30 postoperative days.



**Figure 1.** Thorax tomography images of an exitus patient: **A:** preoperative image and **B:** after infected with Covid-19.

**Table 3.** Characteristics of patients with a positive PCR test for Covid-19

Patient	Age	Stage	NACT	Comorbidities	Operation	Postoperative complication	Histopathology	Treatment of patients when PCR is positive	Exitus
1	66	IB	None	HT+DM	BCS	None	IDC	Hormonotherapy	Yes
2	50	IB	None	None	BCS	None	IDC	Adjuvant CT	Yes
3	63	IIA	None	None	BCS	None	IDC	Adjuvant CT	No
4	56	IIB	Yes	HT	MRM	None	IDC	Hormonotherapy	Yes
5	51	IIA	None	HT+DM	BCS	None	IDC	Adjuvant CT	No
6	49	IIA	None	None	MRM	None	IDC	Adjuvant CT	No

HT: hypertension, MRM: modified radical mastectomy, DM: diabetes mellitus, IDC: invasive ductal carcinoma, BCS: breast conserving surgery, CT: chemotherapy

The mean follow-up period was  $121.22 \pm 70.05$  days in this study, and 19 patients (13.7%) were admitted to the hospital due to a suspected COVID-19 infection after the first 30 postoperative days. Six of these patients (4.3%) tested positive in the PCR test performed using a nasopharyngeal swab and 5 patients (3.6%) showed findings consistent with CO-RADS 5 in the Thorax CT (Figure 1). Six patients (4.3%) were hospitalized and 3 of them (2.2%) died due to their COVID-19 infection (Table 2). Four of the patients (66.6%) with a positive PCR test had hypertension as a comorbidity. All the patients were at an early stage and 4 of them (66.6%) tested positive in the PCR test while receiving postoperative adjuvant systemic chemotherapy. Two patients completed the surgery, systemic chemotherapy and radiotherapy and were receiving hormonotherapy (Table 3).

## Discussion

At the beginning of the COVID-19 pandemic, surgery was reported to be associated with high mortality in cancer patients infected with COVID-19, especially in the studies carried out in the People's Republic of China. Zhang et al carried out a study on 35 patients and reported a mortality of about 22.5% in the surgical patients infected with COVID-19 [15]. This high mortality rate elicited the idea of postponing surgical treatment in cancer patients in a way that would minimally affect survival rates. Therefore, it was recommended to postpone breast cancer surgery instead to starting adjuvant treatments such as hormonotherapy and systemic chemotherapy, especially among those at an early stage of breast cancer with a better prognosis and a positive hormone receptor.

On the contrary, in the clinic where this research was performed, the same surgical procedures were followed for breast cancer patients as before the COVID-19 pandemic, aside from taking

some minor precautions both preoperatively and postoperatively. All patients were evaluated before the surgery based on the results of PCR tests performed using nasopharyngeal swabs and a thorax CT in case the patient had symptoms or suspected contact. As a result of this evaluation, in cases where the patient was suspected to have COVID-19, the operation was postponed with a subsequent evaluation after a minimum of 3 weeks, and the patient was then retested and after a negative result for COVID-19 the operation was scheduled. All patients were discharged as soon as possible after the operation and the frequency of their follow-up appointments in hospital were kept to a minimum. Even in emergency operations during the pandemic, morbidity and mortality due to COVID-19 infection were not at significant levels despite the preoperative COVID-19 evaluation of patients being relatively limited. Likewise, since there was no significant rise in the level of complications in patients who had breast cancer surgery, no changes to the treatment procedures were deemed necessary.

In this study, in a period of 9 months during the COVID-19 pandemic, no mortality and morbidity were observed due to COVID-19 infection in patients who underwent breast cancer surgery in the first 30 postoperative days. Similar to the current results, in their study examining the reliability of breast cancer surgery on 179 patients during the pandemic period, Romics et al reported no mortality and morbidity associated with COVID-19 infection in the perioperative period [13]. The current authors are of the view that measures taken during the pandemic in the hospital where this study took place are responsible for the results observed. In addition, it is also surmised that the physical structure of the hospital made it possible to take these measures. During this period, we were able to offer surgery to breast cancer patients without significantly changing the procedures of the breast cancer treatment.

The mean follow-up period was  $121.22 \pm 70.05$  days in this study, and 19 patients (13.7%) were admitted to hospital with suspected COVID-19 infection after the first 30 postoperative days. Six of these patients (4.3%) tested positive in the PCR test performed using a nasopharyngeal swab. In 3 of these patients (2.2%), the COVID-19 infection proved fatal. As of December 25, 2020, the last day of this study, the Turkish Ministry of Health reported a total of 2,118,255 positive PCR tests in a population of about 82 million in Turkey. The ratio of the number of these cases to the total population is about 2.4%. The ratio in our patient group was higher than the national ratio for Turkey because breast cancer treatment is multidisciplinary, has a lengthy treatment period with many of the treatments leading to immunosuppression, as well as results in repeated visits to the hospital. Similar to this study, previous studies also reported that the incidence of COVID-19 infection was high in cancer patients [16,17].

When the characteristics of the 6 patients with positive PCR tests in this study were examined, it was found that 4 of them (66.6%) had hypertension as a comorbidity, with 2 of these 4 patients subsequently dying. Previous studies reported that hypertension increased the mortality and morbidity in people with COVID-19 [2]. Moreover, when the 6 patients had the timings of their COVID-19 infections examined, it was found that 4 of them (66.6%) were infected while receiving neoadjuvant systemic chemotherapy after the surgery. This may be due to the immunosuppressive nature of systemic chemotherapy. Therefore, it is an important finding that no mortality and morbidity were observed due to COVID-19 in the first 30 postoperative days, while 4 patients returned positive PCR tests while receiving adjuvant chemotherapy, with 2 of these patients dying. The authors recommend that in the COVID-19 pandemic period, taking more preventive measures for patients with risk factors and informing them in this regard may reduce the transmission and, consequently, morbidity and mortality due to COVID-19.

Looking at this issue from a broader perspective, there are three main problems that could arise. First, due to the delay in breast cancer treatment and delayed admission of patients for diagnosis, an increase in the rate of locally advanced breast cancer (stage II and III) may be seen over an extended period and may worsen patients' clinical outcomes. Postponing all oncological and surgi-

cal treatments until the end of the epidemic is undoubtedly unrealistic for breast cancer patients. It is obviously not known when the epidemic will end, particularly considering the negative effects of new mutations on global vaccination efforts. Moreover, the comparison between the well-known long-term consequences of breast cancer and the outcomes of COVID-19 patients is still in its very early stages.

Second, undiagnosed COVID-19 patients, whether symptomatic or not, could come in contact with breast cancer patients within the healthcare system. There was no method to protect breast cancer patients completely from COVID-19 at the time of writing. However, it is presumed by the authors that COVID-19 vaccinations may have a positive effect for cancer patients who have surgery or who start oncological treatment. However, to substantiate this, more data on the topic will be needed.

The third important point is that the mental health of cancer patients is already affected by the primary disease but may also be negatively affected by delayed treatments due to the COVID-19 threat and its consequences. It should be kept in mind that this situation may have adverse effects on adherence to treatment. Due to the reasons above, healthcare providers should take all measures to ensure successful and uninterrupted treatment of breast cancer patients during the COVID-19 pandemic.

This was a retrospective study and its sample size was small, however this study is valuable in that it provides insights into the reliability of surgical treatment in breast cancer, one of the most common cancers, and the measures to be taken in a pandemic hospital during the COVID-19 pandemic.

## Conclusion

In conclusion, the anxiety and caution associated with COVID-19 is an understandable and normal response to a new epidemic. However, our results suggest that breast cancer surgery can be performed safely during the COVID-19 pandemic period after taking the necessary precautions. Conducting prospective studies on the subject with larger samples sizes would contribute further to the literature.

## Conflict of interests

The authors declare no conflict of interests.

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