








# Anxiety levels of breast cancer patients in Turkey during the COVID-19 pandemic

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**Aim:** To assess the anxiety levels of breast cancer patients during the COVID-19 pandemic. **Materials & methods:** A total of 298 patients completed the State-Trait Anxiety Inventory (STAI-S and STAI-T) and the Visual Analogue Scale for Anxiety (VAS) and VAS for Anxiety in COVID-19 (VAS-CoV). **Results:** 144 patients were in the high anxiety category for STAI-S, and 202 patients were in the high anxiety category for STAI-T. STAI-T score was significantly high in the metastatic group ( $p = 0.017$ ). VAS-CoV score in the hormone therapy group was significantly higher than in the no-treatment group ( $p = 0.023$ ). There was a positive correlation between VAS-CoV and VAS levels ( $r = 0.708$ ,  $p < 0.001$ ), VAS-CoV and STAI-S and STAI-T scores ( $r = 0.402$ ,  $p < 0.001$ ;  $r = 0.185$ ,  $p = 0.001$ , respectively), and a negative correlation between education years and STAI-T scores ( $r = -0.172$ ,  $p = 0.003$ ). **Conclusion:** The COVID-19 pandemic is related to high anxiety levels in breast cancer patients.

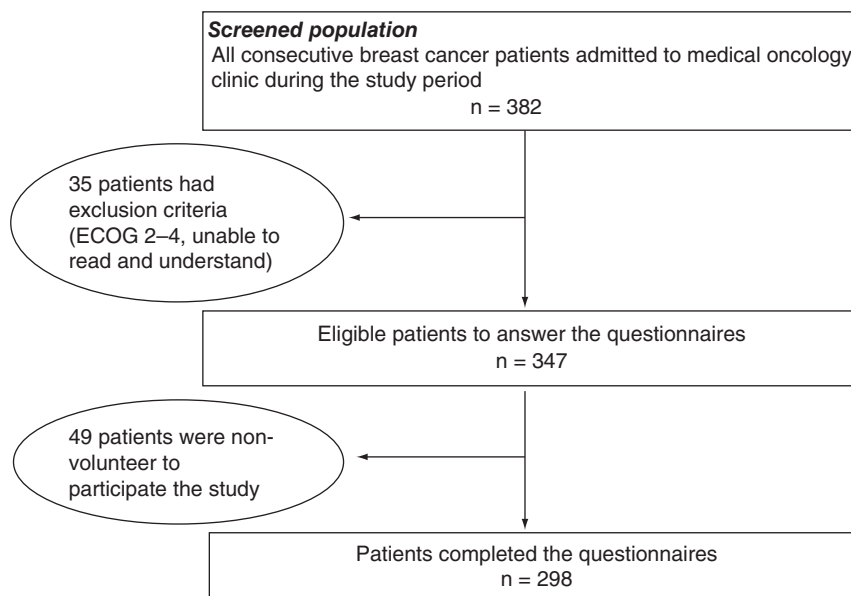
**Lay abstract:** COVID-19 pandemic is related to rapidly rising anxiety levels worldwide. Because of the high mortality of COVID-19 in cancer patients, changing treatment routines and disruptions of the healthcare system, cancer patients are the most affected population in this situation. Anxiety among females and breast cancer patients tend to be high, although anxiety levels in cancer patients during the pandemic period varies according to the cancer type, treatment status and sociodemographic factors. This study assessed the effect of the COVID-19 pandemic on breast cancer patients' anxiety levels according to treatment status and stage of the disease. A total of 298 breast cancer patients completed the universally validated anxiety questionnaires. Results demonstrated high trait anxiety in breast cancer patients, particularly in the metastatic group. The current findings highlighted the importance of intensive assessment and close monitoring of breast cancer patients' psychological situations. It is crucial to provide psychological support to breast cancer patients to contribute to both treatment and follow-up processes during the pandemic.

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**Keywords:** breast cancer • chemotherapy • hormonal therapy • metastasis • women's health

COVID-19, a highly transmissible and often lethal disease caused by the SARS-CoV-2 virus, first appeared in China and has reached pandemic scale worldwide in 2020 [1]. In Turkey, the first case was reported on 11 March 2020. As of October 2020, the total number of reported cases globally was more than 10 million, with more than 600,000 deaths.

The COVID-19 pandemic has changed daily life in many ways. Restriction of social life, concerns about health status and economic issues increased anxiety and other psychological disorders [2]. Various changes have also occurred in the health system's functioning because of the measures taken due to the increasing number of cases. To prevent unnecessary exposure and hospital admissions, appointments were postponed, and treatment modalities were changed. Cancer patients can be immunosuppressive because of both the disease and oncologic treatments, and so they are considered in a high-risk group for COVID-19. Previous studies conducted on COVID-19 showed that cancer patients' mortality rate is higher compared with the healthy population [3–5]. Gosain *et al.* reported in



**Figure 1.** Flow chart of the patient selection process.

the review of cancer and COVID-19 that the mortality rate due to COVID-19 infection is 2.3% in noncancer patients, compared with 28.6% in cancer patients [3]. Patients who received chemotherapy within 14 days are described as a particularly high-risk group [4]. Both because these patients are highly affected by changes in the functioning of the healthcare system and because they are in the high-risk group for the COVID-19, the pandemic may have a more significant emotional impact on patients living with cancer and other vulnerable groups. Studies on the psychological effects of COVID-19 in patients with cancer have had controversial results [6-9].

Globally, breast cancer is the most frequently diagnosed malignancy in women, and it is also the leading cause of cancer death in women worldwide [10]. Moreover, breast cancer patients are noted in the literature to experience increased anxiety, distress, fear and depression [11,12]. Almost all of this patient group consists of females, and the disease appears at a younger age than other types of cancer, both of which contribute to higher anxiety levels [13,14]. Although anxiety levels in cancer patients during the pandemic period varies according to the cancer type, treatment status and sociodemographic factors [6,8], anxiety levels of females and breast cancer patients tend to be higher when the subgroups are examined [7,9]. Also, it is known that emotional distress has a negative effect on compliance with oncological treatment and patients' overall quality of life; it is also related to increased risk of mortality [15]. Therefore, evaluating breast cancer patients' psychological situation, known as a patient group prone to anxiety, is of great importance for appropriate support and optimal oncological treatment.

In this study, we aimed to assess the effect of COVID-19 in breast cancer patients' anxiety levels according to the treatment status and the disease stage.

## Materials & methods

### Study design and patients

In this cross-sectional study, eligible breast cancer patients followed up in the medical oncology outpatient clinic were consecutively enrolled for 4 months. Between 1 April and 1 August 2020, 382 breast cancer patients were admitted to the medical oncology clinic; 347 eligible patients were informed about the questionnaires, and 298 volunteer patients were included in the study (Figure 1). The inclusion criteria were as follows: breast cancer diagnosis of any stage (metastatic/nonmetastatic) and any treatment status (chemotherapy/hormonotherapy/no treatment), able to read/speak Turkish and understand/answer the questionnaires, age over 18 years and good performance status (Eastern Cooperative Oncology Group [ECOG] performance status 0-1). Patients with ECOG  $\geq 2$  or who were unable to understand or answer the questionnaires were excluded. All participants completed the Spielberger State-Trait Anxiety Inventory (STAI) form, including 40 questions, a sociodemographic data form produced for this study and the Visual Analogue Scale for Anxiety (VAS-A) and Visual Analogue Scale for Anxiety in COVID-19 (VAS-CoV) scales to evaluate their anxiety levels during the pandemic. Participants were divided into two groups

according to the stage of the disease: metastatic or nonmetastatic. Three groups were established according to treatment status: chemotherapy – patients receiving chemotherapy in a neoadjuvant/adjuvant/metastatic setting; hormonotherapy – patients receiving hormonotherapy in a neoadjuvant/adjuvant/metastatic setting; and no treatment – patients who had completed treatment or in whom the disease was under control and thus were not currently undergoing treatment. The data collection process was completed following the Declaration of Helsinki. The local ethics committee approved the study (16/330). All patients signed informed consent forms.

### Sociodemographic and descriptive data form

With the descriptive data form created for the study, we collected patients' sociodemographic information: age in years, marital status, education level, working status and whether patients live alone. Additionally, we obtained clinical information on their health status, including disease stage, oncological treatment status, history of COVID-19, smoking and alcohol habits, antidepressant medication use and postponed oncology appointment.

### State-Trait Anxiety Inventory

The STAI is used to evaluate occasional and permanent anxiety levels [16]. Oner and Le Compte adapted and validated the STAI test to Turkish in 1977 [17], and it is widely used in cancer patients [18–20]. Two components of anxiety are assessed: State Anxiety (STAI-S), in which temporary life events are believed to cause stress, and Trait Anxiety (STAI-T), in which there is a personal predisposition to stress. Forty questions were answered in two parts consisting of 20 questions; participants were asked to score on how much the sentences reflect their emotional situation on a 4-point scale of 1 (not at all) to 4 (very much so). Scores in each section were added separately, and a score between 20 and 80 was obtained. We described a cutoff level of  $>39$  as high anxiety category and  $\leq 39$  as a low anxiety category in the STAI test, as shown in previous studies [21,22].

### VAS for Anxiety (VAS-A and VAS-CoV)

VAS-A is a single-question test to assess anxiety [23], widely used in cancer patients [24]. In the VAS-A test, patients were asked to score their general anxiety levels from 0 (no anxiety) to 10 (maximum anxiety). Additionally, we adapted VAS-A to COVID-19 (VAS-CoV) to briefly evaluate COVID-19-related anxiety. Patients were asked to score their pandemic-related anxiety levels from 0 (no anxiety) to 10 (maximum anxiety).

### Statistical analysis

SPSS 20 program (Statistical Package for Social Sciences, IBM Inc., IL, USA) was performed to analyze this study's data. The normal distribution of the sample was shown with skewness and kurtosis values and the Kolmogorov-Smirnov test. To evaluate the correlation between variables Pearson's and Spearman's tests were performed according to data distribution. Two independent groups with normal distribution were compared with independent samples t-test. Mann-Whitney U-test was used for comparison of the groups without normal distribution. A multivariate analysis of covariance (MANCOVA) was applied to evaluate whether the scores of STAI-S, STAI-T, VAS-A and VAS-CoV were related to the disease stage and treatment status while correcting for possible factors affecting the psychopathological situation. For evaluating variables with nonnormal distribution, the Box-Cox transformation was used. The equality of variances was assessed with Leneve's test. A post hoc Bonferroni test was performed in cases where there is a significant difference between more than two groups. All sociodemographic dimensions that were found to be clinically significant for breast cancer patients were introduced as covariates. The statistical significance level was accepted as  $p < 0.05$ . There were no missing data because among all eligible patients, only patients with complete questionnaires were included in the study.

### Results

Our study group consisted of 298 women with breast cancer (mean age  $53.2 \pm 10.79$  years); 17% ( $n = 52$ ) were geriatric patients aged over 65 years. Clinical and sociodemographic characteristics of patients are shown in Table 1.

When we classified the patients according to the disease stage in two groups, metastatic and nonmetastatic, mean age in the metastatic group was  $55.56 \pm 10.14$  and  $52.54 \pm 10.9$  in the nonmetastatic group ( $p = 0.026$ ). Mean scores of STAI-S, STAI-T, VAS-A and VAS-CoV, according to these groups, were presented in Table 2. In the study group, 144 (48.3%) patients were in the high-anxiety category for STAI-S, and 202 (67.8%) patients were in the high-anxiety category for STAI-T. STAI-T score was  $46.10 \pm 1.05$  in the metastatic group and  $43.21 \pm 0.54$  in the nonmetastatic group, so it was significantly high in the metastatic group than the nonmetastatic group

**Table 1. Sample characteristics.**

Characteristic (n = 298)	n (%) / mean ± standard deviation
Age (years)	53.2 ± 10.79
Geriatric:	
– >65 years	52 (17)
– <65 years	246 (83)
Stage of the disease:	
– Metastatic	67 (22.5)
– Nonmetastatic	231 (77.5)
Education level (years)	7.45 ± 4.65
Treatment status:	
– Chemotherapy	96 (32.2)
– Hormonotherapy	155 (52)
– Surveillance	47 (15.7)
Marital status:	
– Married	233 (78.1)
– Single	65 (21.8)
Smoking	46 (15.5)
Alcohol use	3 (1)
Antidepressant medication use	65 (22)
Postponed oncology appointment	97 (32.8)
Living with family	266 (89.6)
Living alone	31 (10.4)
Working status:	
– Employed	19 (6.4)
– Unemployed	277 (93.6)
COVID-19:	
– Positive (n)	0
– Negative (n)	298
VAS-A	4.06 ± 2.73
VAS-CoV	6.34 ± 2.77
STAI-S	40.78 ± 10.79
STAI-T	43.9 ± 8.5

STAI-S: State Trait Anxiety Inventory – State; STAI-T: State Trait Anxiety Inventory – Trait; VAS-A: Visual Analogue Scale for Anxiety (VAS-A); VAS-CoV: Visual Analogue Scale for Anxiety in COVID-19.

**Table 2. STAI and VAS-A scores of breast cancer patients (n = 298) according to metastatic or nonmetastatic status.**

STAI and VAS-A scores	Metastatic patients (n = 67)	Nonmetastatic patients (n = 231)	p-value
VAS-A	4.52 ± 0.35	3.94 ± 0.18	0.143
VAS-CoV	6.43 ± 0.35	6.31 ± 0.18	0.768
STAI-S	42.29 ± 1.36	40.28 ± 0.71	0.195
STAI-T	46.10 ± 1.05	43.21 ± 0.54	0.017

Data are mean ± standard deviation.  
 STAI-S: State Trait Anxiety Inventory – State; STAI-T: State Trait Anxiety Inventory – Trait; VAS-A: Visual Analogue Scale for Anxiety (VAS-A); VAS-CoV: Visual Analogue Scale for Anxiety in COVID-19.

(p = 0.017). When the MANCOVA method was applied for metastatic–nonmetastatic groups, there were no statistically significant differences between the groups on the STAI-S, STAI-T, VAS-A and VAS-CoV scores after controlling for age, being geriatric, education years, marital and employment status, smoking and alcohol habits and living alone covariates (p > 0.05).

Three groups were conducted according to the treatment status, chemotherapy, hormonotherapy and no treatment. Mean age was 54.06 ± 10.85 years for the chemotherapy group, 53.01 ± 11.56 years for the hormonotherapy group, and 51.57 ± 10.14 years for the no treatment group. Comparison STAI-S, STAI-T, VAS-A and VAS-CoV of breast cancer patients according to treatment status are shown in Table 3. VAS-CoV scores were 6.63 ± 2.78, 6.28 ± 2.85 and 5.55 ± 2.49 in the hormonotherapy, chemotherapy and no treatment groups, respectively. VAS-CoV score in the hormonotherapy group was significantly different among the treatment status groups (p = 0.028).

**Table 3. STAI and VAS-A scores of breast cancer patients (n = 298) according to treatment status.**

STAI and VAS-A scores	Treatment status			p-value <sup>†</sup>
	Chemotherapy (n = 96)	Hormonotherapy (n = 155)	No treatment (n = 47)	
VAS-A	4.10 ± 2.65	4.08 ± 2.74	3.87 ± 2.90	NS
VAS-CoV	6.28 ± 2.85	6.63 ± 2.78	5.55 ± 2.49	0.028
STAI-S	41.96 ± 10.79	39.81 ± 10.63	41.55 ± 11.27	NS
STAI-T	45.36 ± 8.59	43.05 ± 6.67	43.77 ± 7.48	NS

Data are mean ± standard deviation.

<sup>†</sup> 0.023 for hormonotherapy vs. no treatment (post hoc Bonferroni test was applied).

STAI-S: State Trait Anxiety Inventory – State; STAI-T: State Trait Anxiety Inventory – Trait; VAS-A: Visual Analogue Scale for Anxiety (VAS-A); VAS-CoV: Visual Analogue Scale for Anxiety in COVID-19.

When the post hoc Bonferroni test was performed, the VAS-CoV score in the hormonotherapy group was significantly higher than the no treatment group ( $p = 0.023$ ). When the MANCOVA test was conducted by taking into consideration age, being geriatric, education years, marital and employment status, smoking and alcohol habits and living alone or with family covariates in the comparison of the STAI-S, STAI-T, VAS-A and VAS-CoV scores according to treatment status, no significant difference was found.

In correlation analysis, there was a positive and strong correlation between VAS-CoV and VAS levels ( $r = 0.708$ ,  $p < 0.001$ ). Also, there was a positive correlation between VAS-CoV and STAI-S and STAI-T scores ( $r = 0.402$ ,  $p < 0.001$ ;  $r = 0.185$ ,  $p = 0.001$ , respectively) and a negative correlation between education years and STAI-T scores ( $r = -0.172$ ,  $p = 0.003$ ).

## Discussion

Our study evaluated anxiety levels of breast cancer patients who were followed up in our clinic during the COVID-19 pandemic. We demonstrated that STAI-T scores were higher in the metastatic group compared with the nonmetastatic group. However, no significant difference was found between the groups in terms of anxiety levels when controlling for sociodemographic characteristics affecting patients' psychological situation. Although some studies have shown high anxiety in metastatic breast cancer patients [13,25], it has been found that cancer patients' anxiety levels are affected more by sociodemographic than medical variables [26]. Similarly, when we considered the sociodemographic factors of the patients, there was no significant difference in anxiety levels between the metastatic and nonmetastatic groups.

Most studies on COVID-19 have focused on clinical features, epidemiology and treatment of the disease, and few have addressed the psychological effects of COVID-19, such as depression, anxiety, psychotic symptoms and stress-related disorders. Vulnerable groups such as patients with chronic diseases are particularly affected emotionally by COVID-19 [6,9,27]. Moreover, studies from Turkey have shown that female gender and chronic disease are risk factors for anxiety during the pandemic [2,28]. It has been shown that cancer itself, as a life-threatening chronic disease, causes anxiety in 17–46% of patients [29]. According to the literature review, a comparison of cancer patients' anxiety levels with a healthy population had controversial results [30–33]. Most studies have shown lower anxiety levels in cancer patients compared with individuals without cancer diagnosis in non-cancer-related stressful situations [32,33]. It has been shown that patients' treatment compliance is negatively affected by symptoms related to anxiety, which is important for cancer patients [34,35]. COVID-19 has devastating effects for cancer patients due to uncertainties including the lack of treatment, economic loss and other concerns and restrictions, causing anxiety and fear. However, studies about the psychological effects of COVID-19 in cancer patients are limited. In the study reported by Wang *et al.* from China, the anxiety levels measured at the onset of the pandemic and after 4 weeks were compared; even though the anxiety scores remained above the cutoff value, it was observed that the anxiety scores decreased despite the increase in the number of cases over the 4 weeks [8]. In another study from Poland by Sigorski *et al.*, 306 cancer patients were included, 86 of whom were breast cancer patients. They reported that being under 65 years of age, female gender and having breast cancer were associated with the highest anxiety levels, and cancer-related anxiety levels were higher than COVID-19-related anxiety levels [7]. In another study from France, Baffert *et al.* investigated COVID-19-related anxiety in cancer patients and showed low-anxiety levels post-lockdown. The contribution of the well-organized healthcare system to these low anxiety levels was highlighted in the study [6]. Consistent with these studies, we found the percentage of patients with high trait anxiety was higher than the percentage of those with high state anxiety. Recent studies and oncology guidelines recommended

a careful assessment of the treatment priority and the potential risk of COVID-19 infection to avoid the risk of suboptimal cancer care [36–38]. Although there were a few postponed appointments, the follow-up and treatment processes of the patients continued in accordance with the oncology guidelines of our clinic, which could be a possible explanation for the relatively low state anxiety levels. Another explanation maybe that cancer patients with a life-threatening disease getting used to living with anxiety, so they adapted more quickly to COVID-19, which, like cancer, had high morbidity and mortality.

It has been shown that cancer patients' sociodemographic characteristics, such as marital status, educational status and age, affect anxiety levels more than disease-related characteristics [26,39]. Merz *et al.* indicated that low education level was correlated with high anxiety levels of cancer patients during the COVID-19 pandemic [40]. Similarly, there was a negative correlation between educational status and STAI-T scores in our study, whereas the STAI-S score was not affected by sociodemographic characteristics. This could be explained by the fact that highly educated patients have more advanced coping mechanisms because they have more access to information about their disease and treatment methods to evaluate their situation rationally. Additionally, they could express themselves better and communicate more effectively with their physicians, making them feel less uncertain and anxious.

Studies have shown that VAS-A effectively evaluates anxiety in cancer patients [41,42]. Furthermore, considering that single-question tests can eliminate the difference in education level between patients, we used VAS-A and VAS-CoV test, which we adapted to assess COVID-19-related anxiety. The mean score of VAS-A was <5, and the mean score of VAS-CoV was >5 in our study. The scores of VAS-A and VAS-CoV tests were positively correlated with each other. Both were also positively correlated with STAI-S and STAI-T. This finding suggests that after validation, the VAS-CoV test could be used for a brief evaluation of COVID-19-related anxiety in cancer patients. Furthermore, the VAS-CoV score in the hormonotherapy group was significantly higher than the no treatment group. Studies have shown that several endocrine signaling pathways in hormone-related cancers interact with 5-HT receptors, causing depression and anxiety in patients [43,44]. Additionally, hormone receptor status and endocrine treatment were related to emotional distress, depression and anxiety in breast cancer patients [45–47]. The high score of VAS-CoV in the hormonotherapy group in our study could be explained by all of the preceding possibilities. Some limitations of the study should be noted. It was conducted in a single center, which could be considered a limitation. Additionally, we did not assess all patient sociodemographic factors, such as economic status, social media use and exercise habits, that might affect psychological status. We did not have a control group but we compared the groups of patients according to disease stage and treatment status. The strength of our study was the large and homogenous sample consisting of female breast cancer patients.

## Conclusion

The COVID-19 pandemic is related to rapidly rising anxiety levels worldwide. Cancer patients are among the most affected population in this situation. The high mortality of COVID-19 in cancer patients, changing treatment routines and disruptions to the healthcare system are leading causes of the high anxiety observed in these patients. Our study demonstrates that changes in anxiety levels may occur during the pandemic, especially in patients with metastatic cancer. However, continuing oncological follow-up and treatment and easy access to health services contributed to the prevention of anxiety in breast cancer patients. It is crucial to provide psychological support to breast cancer patients to improve both treatment and follow-up processes during the pandemic. There is a need for more comprehensive studies with larger sample sizes using various scales to evaluate different psychological dynamics.

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## Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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### Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

### Summary points

- The COVID-19 pandemic has changed daily life in many ways. Restriction of social life, concerns about health status and economic issues increased anxiety and other psychological disorders.
- The high mortality of COVID-19 in cancer patients, changing treatment routines and disruptions to the healthcare system are leading causes of the anxiety.
- Anxiety of females and breast cancer patients tend to be high, although anxiety levels in cancer patients during the pandemic period varies according to the cancer type, treatment status and sociodemographic factors.
- This study assessed the effect of COVID-19 pandemic in breast cancer patients' anxiety levels according to treatment status and stage of disease.
- Breast cancer patients (n = 298) completed the State-Trait Anxiety Inventory (S – anxiety for state scale, T – anxiety for trait scale), Visual Analogue Scale for Anxiety (VAS-A), and Visual Analogue Scale for Anxiety in COVID-19 (VAS-CoV).
- VAS-CoV is a single-question test to assess anxiety adapted by us from VAS-A for this study to evaluate anxiety levels during the pandemic.
- Results demonstrated that the percentage of patients with high trait anxiety was higher than the percentage of those with high state anxiety. Besides, trait anxiety was significantly higher in the metastatic group than the nonmetastatic group. When controlling for sociodemographic characteristics affecting patients' psychological situation, there was no significant difference between groups. Additionally, COVID-19 pandemic-related anxiety in the hormonotherapy group was significantly higher than in the no treatment group.
- This study highlighted the importance of intensive assessment and close monitoring of breast cancer patients' psychological status. It is crucial to provide psychological support to breast cancer patients to contribute to both treatment and follow-up processes and to avoid the risk of suboptimal cancer care during COVID-19 pandemic.

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