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Repercussions of the COVID-19 pandemic on breast cancer treatment in a referral hospital in Santos-SP, Brazil

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ABSTRACT

Objective: Considering that breast cancer has the fifth highest mortality rate in the world, this study aims to evaluate the repercussions of the COVID-19 pandemic on the treatment, both surgical and systemic, of patients with cancer in general and those with breast cancer at Hospital Guilherme Álvaro (Santos, Brazil), between March 1st, 2019 and February 28, 2021. **Methods**: For this purpose, data were collected from both the hospital's surgery record book and electronic medical records of patients who were followed up in the Mastology and Oncology sectors at Hospital Guilherme Álvaro. This information was tabulated, estimating the total number of surgeries, whether: benign elective surgeries, diagnostic surgeries, surgeries of cancer in general, surgeries exclusive to mastology, of cancer in mastology, benign surgery in mastology, and plastic reconstructive surgery. The percentage ratio between these numbers was calculated. **Results**: A 49% reduction in total surgeries was observed, comparing the period prior to the pandemic (2019–2020) with the pandemic period (2020–2021), with a decrease of 24.6% in the number of general cancer surgeries except for mastology, and 19.6% of surgeries exclusive to mastology. In other words, there was a total reduction of 22.9% in all oncological surgeries. Moreover, there was a decrease of 11.5% in the total number of patients treated with chemotherapy. In 2020, of the 214 new cases, 116 (54.2%) were mastology patients, being 45.8% of other oncology clinics. **Conclusion**: Thus, it is concluded that the reduction in the number of aesthetic, benign, and reconstructive surgeries was expected, as observed in the decrease in the number of chemotherapies, which could be due to a limitation on medical appointments. The number of diagnostic surgeries remained stable, which could lead to positive outcomes for oncology patients. It is not possible to predict the next repercussions of the COVID-19 pandemic on breast cancer treatment while the pandemic endures, requiring more studies on this topic.

KEYWORDS: COVID-19; breast neoplasms; neoadjuvant therapy.

INTRODUCTION

Breast cancer is the fifth with the highest mortality rate worldwide and has a high incidence among young women in Brazil[1,2]. Recently, it became the most diagnosed type of cancer, surpassing lung cancer[1]. Its early diagnosis, in addition to advances in treatment, has shown better results and greater survival for patients[3]. However, in December 2019, a new disease called COVID-19, caused by the SARS-CoV-2 virus, was detected in Wuhan, China. A pandemic was declared by the World Health Organization (WHO) in March 2020. Faced with this new situation, breast cancer screening and treatment were hampered[4,5].

Although breast surgery is of great importance in the treatment, as it aims to remove the entire tumor with free margins, neoadjuvant chemotherapy (NC) has gained prominence during the pandemic, and there is a decrease in the probability of recurrence and increase in the survival of patients who undergo this procedure[6,7]. The purpose of NC is to reduce mass in locally-advanced tumors and to allow the use of efficient surgical and radiotherapy treatments[7].

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Until recently, the indication for NC was based on inoperable T3-T4/N2-N3 tumors (inflammatory breast cancer; inoperable tumor due to invasion of the skin or thoracic structures; clinically coalesced and/or fixed axillary lymph nodes; lymph node metastases beyond the axillary chain) or operable tumors in need of reduction to perform conservative surgery (tumor greater than 5 cm or between 2 and 5 cm with an unfavorable tumor/breast ratio for conservative surgery)[6,8,9].

However, after the beginning of the pandemic, the recommendation for breast cancer treatment has changed. For new cases diagnosed after this period, it has been recommended to start systemic treatment with neoadjuvant endocrine therapy or neoadjuvant chemotherapy with anti-HER2 blockade, if the disease was positive for HER2[10]. As HER2 and triple negative tumors are more aggressive molecular subtypes, there are discussions for starting the treatment with chemotherapy and target therapy (HER2 subtype) before surgery in tumors larger than 1 cm, whereas in tumors smaller than 1 cm, surgery should not be postponed[11]. In addition, this should be considered in three situations: if the disease progresses during NC; if it is a malignant phyllodes tumor; or breast sarcoma[10]. It should be noted that, according to a systematic literature review and meta-analysis published in July 2021, the ideal time to perform breast surgery after the completion of the NC is four to eight weeks[12].

Both the chemotherapy and radiotherapy used in the treatment and the cancer itself have immunosuppressive effects, making cancer patients vulnerable to infections[13]. Therefore, the recommendations for such patients also include limiting their exposure to SARS-CoV-2, encouraging telemedicine appointments whenever possible and restricting visits to wards with immunocompromised patients[4,13].

Another important measure implemented to contain the advance of the new coronavirus was to consider many of the breast cancer treatment surgeries as elective[8]. Nevertheless, the choice to postpone such therapy is only possible when the patient is not at risk of life, or when it is possible to use less invasive methods such as chemotherapy and radiotherapy[14]. Thus, as in other services, the Mastology Department of Hospital Guilherme Álvaro, located in Santos (state of São Paulo, Brazil), expanded the indications for neoadjuvant care, restricted surgeries, and maintained outpatient care only for emergencies[15].

Even though it is proven that these noninvasive methods can delay definitive surgical treatment for a period of time, the duration of restrictive measures during the pandemic remains indetermined[14]. The impact of postponing tumor resection and the administration of invasive therapies for an extended period of time on the outcome and survival of these patients is still uncertain[13]. Furthermore, in this context, the impact that cancer illness has on the physical and mental health of patients can have psychological effects such as anxiety, depression, anguish, and acute stress[16]. This situation, in addition to the fear of infection with the new coronavirus or the waste of health resources, would favor the reduction of diagnoses and the quality of cancer treatment[16].

Hence, this study aims to assess the repercussion of the COVID-19 pandemic on the number of elective and oncological surgeries and chemotherapy treatments performed at Hospital Guilherme Álvaro, a major oncology reference center in Baixada Santista, state of São Paulo, Brazil.

METHODS

This is a cross-sectional and retrospective study, based on surgeries performed at Hospital Guilherme Álvaro, a public tertiary hospital located in the city of Santos, Brazil, from March 1st, 2019 to February 28, 2021. Data were obtained from the hospital's surgery record book, whose content was based on information such as date of surgery, patient's name, age, anesthetic risk, underlying pathology, surgical procedure, type of anesthesia, name of anesthesiologist, name of surgery resident, name of surgeon, time of the surgery, and destination of the patient after the surgical procedure; and electronic medical records of patients who were followed up in the Mastology and Oncology Departments of the institution.

These data were transcribed into a table on the computer, using the Microsoft Excel Office 2016 program, and the statistical analysis was later performed in the same program.

The analyzed variables were: benign elective surgeries, diagnostic surgeries, general cancer surgeries, and surgeries exclusive to mastology. In the latter group, it was observed which surgeries were related to breast cancer and whether adjuvant or neoadjuvant chemotherapy were administered.

Among the inclusion criteria, it is worth highlighting patients treated by the mastology team during the period stipulated by the research; patients treated by the surgical team of Hospital Guilherme Álvaro during the same period; and patients with breast diseases treated by the Oncology Clinics of *Rede Hebe Camargo de Combate ao Câncer* [Hebe Camargo Network for Combating Cancer], at Hospital Guilherme Álvaro. Patients whose data in the medical records were incomplete for the study, or patients treated outside the stipulated period, were not evaluated.

Data were monthly tabulated, estimating the total number of surgeries, as well as how many of them were benign, diagnostic, of cancer in general, exclusive to mastology, of cancer in mastology, benign surgeries in mastology, and plastic reconstructive. In addition, it was verified how many patients underwent chemotherapy, considering the patients who were already being treated prior to the pandemic and the new cases that emerged during that period. The percentage ratio between these numbers was estimated and the Z-test, a null hypothesis statistical calculation based on the Z statistics, was applied, which establishes whether

the difference between the sample mean and that of the population is large enough to be statistically significant.

The pre-pandemic period was considered to be that between March 1st, 2019 and February 28, 2020; and the pandemic period, as that between March 1st, 2020 and February 28, 2021.

This study was submitted and approved by the Research Ethics Committee of Hospital Guilherme Álvaro and Fundação Lusíada (UNILUS), approved by Plataforma Brasil (Certificate of Presentation for Ethical Consideration — CAAE: 51960121.6.0000.5436), and complied with the code of ethics of the 1964 Declaration of Helsinki and all its subsequent updates. Furthermore, the study has own funding and the authors have no conflicts of interest to declare.

RESULTS

After data collection, tables were monthly compiled to obtain the results. During the analyzed period, from March 1st, 2019 to February 28, 2020, 3,118 general surgeries were performed; and from March 1st, 2020 to February 28, 2021, 1,591 general surgeries, totaling a sample of 4,709 (Table 1).

By analyzing the data on general surgery, an association with statistical significance can be observed in the number of surgeries performed for benign pathologies, cancer in general, and plastic reconstructive procedures when comparing the pre-pandemic period with the pandemic period ($p<0.01$). Meanwhile, with regard to surgeries performed by the mastology sector, there was an association with statistical significance for surgeries performed for breast cancer and breast reconstructions when correlating the pre-pandemic and the pandemic periods ($p<0.01$) (Table 1).

According to data obtained from the Hebe Camargo Network, the number of cases undergoing treatment and new cases of chemotherapy, before and during the pandemic, can be verified. However, it was not possible to establish an association with statistical significance between the obtained results (Table 2).

DISCUSSION

After the beginning of the COVID-19 pandemic, the recommendation for breast cancer treatment has changed. The new indication is based on initiating neoadjuvant systemic or endocrine therapy whenever possible, in addition to having medical appointments via telemedicine, thus restricting visits to wards with immunocompromised patients. Elective surgical treatment would only be indicated again if there was a decrease in infection rates for at least two consecutive weeks in the hospital region[17]. A problem faced by the patients treated at Hospital Guilherme Álvaro was the lack of structure for some of these changes such as the impossibility of arranging medical appointments via telemedicine.

Thus, a 49% reduction in total surgeries at the hospital was observed when comparing the pre-pandemic period (2019–2020) with the pandemic period (2020–2021), with a 24.6% drop in the number of oncological surgeries except for mastology and 19.6% in the number of oncological surgeries in mastology. Therefore, there was a total reduction of 22.9% in all oncological surgeries. Likewise, a study conducted in England also observed a 16.4% decrease in the number of patients receiving

Table 1. Total number of general and mastology surgeries in periods prior to and during the pandemic.

	Pre-pandemic	During the pandemic	Z-test (p-value)	Difference between proportions	Confidence Interval	
	Surgery of cancer in general				-95%	+95%
Total surgeries	3,118	1,591				
Benign	2,471 (79.25%)	1,143 (71.84%)	<0.01	7.41%	4.90	10.00
General diagnostic	131 (4.20%)	93 (5.85%)	0.01	-1.64%	-2.90	-0.40
Cancer in general	272 (8.72%)	205 (12.88%)	<0.01	-4.16%	-6.00	-2.30
Plastic reconstructive	24 (0.77%)	0 (0.00%)	<0.01	0.77%	0.30	1.20
	Mastology					
Cancer	138 (4.43%)	113 (7.10%)	<0.01	-2.68%	-4.00	-1.30
Benign	19 (0.61%)	4 (0.25%)	0.09	0.36%	-0.10	0.80
Diagnostic	35 (1.12%)	28 (1.76%)	0.07	-0.64%	-1.30	0.10
Reconstructive	19 (0.61%)	1 (0.06%)	<0.01	0.55%	0.20	0.90
Cancer + immediate reconstructive	5 (0.16%)	3 (0.19%)	0.8241	-0.03%	-0.30	0.20
Non-oncological aesthetic	4 (0.13%)	1 (0.06%)	0.5143	0.07%	-0.10	0.30

Source: Prepared by the authors.

Table 2. Total number of chemotherapies in periods prior to and during the pandemic.

	Pre-pandemic	During the pandemic	Z-test (p-value)	Difference between proportions	Confidence Interval	
	Chemotherapy				-95%	+95%
Undergoing treatment	3,719 (94.1%)	3,283 (94%)	0.8555	0.10%	-0.98	1.18
New cases	233 (5.9%)	214 (6%)	0.8555	-0.10%	-0.98	1.18

Source: Prepared by the authors.

treatment in the first half of 2020 after breast cancer diagnosis compared with 2019, and the authors expected an even greater reduction[18]. This scenario had repercussions on the treatment of cancer patients during the pandemic, mainly because cancer is a progressive chronic disease and, in its initial phase, it can be controlled or even cured by surgical treatment[17].

When analyzing the surgeries performed by the mastology team of Hospital Guilherme Álvaro, there was a decrease in their absolute number during the pandemic period (31.8%). However, if only oncological surgeries are considered, there is an increase of 2.67% ($p<0.01$). This is probably due to the fact that surgeries performed for aesthetic and benign purposes are not being prioritized during the pandemic period, after considering their risks and benefits[4].

Another relevant finding was the sharp decrease of 94.7% of reconstructive surgeries in the 2020–2021 period compared with 2019–2020, a decrease proportional to the number of total surgeries, 0.55% ($p<0.01$). As in Brazil, Walter et al. found, in a study conducted in the United States of America, that 19% of physicians reported the suspension of immediate breast reconstruction surgeries during the pandemic at their institutions[19]. This situation reflects the recommendations of medical entities and societies, which indicate the careful selection of patients eligible for surgical treatment during this pandemic period[18].

Consequently, not performing this procedure can be harmful to patients, as it is proven that immediate reconstruction has benefits both in improving self-image and in the quality of life and mental health in the long term. Another advantage would be not to subject the patient to more than one procedure, given the anesthetic risks inherent in the surgical process itself[20,21].

Furthermore, in a research conducted in Londrina (state of Paraná, Brazil), the authors observed that women diagnosed during the pandemic had lower emotional and physical scores when compared with previously diagnosed patients[22]. We must also consider the effects of the psychological factor on those who have had treatment suspended due to fear of the progression of the disease while awaiting a new date for their definitive treatment.

As the recommendation of health agencies was to perform neoadjuvant therapy to reduce tumor size and postpone surgery during the peak of the pandemic, an increase in the number of this procedure was expected[7,15]. Nevertheless, there was a decrease of 11.5% in the total number of patients treated with chemotherapy during the pandemic[13,15]. One factor that may have contributed to this finding is that, although the indications and protocols for NC are well-established in the literature, in Brazil there are some barriers, especially in the public sector, related to the delay in diagnosis, the difficulty of infrastructure, and the incorporation of medicines[23]. Nonetheless, as the data were not statistically significant ($p=0.85$), further studies are necessary for a reliable and accurate interpretation.

In 2020, of the 214 new cases, 116 (54.2%) were from mastology patients, whereas 45.8% were from other oncology clinics. This predominance of new mastology cases in the chemotherapy sector could constitute a good prognostic factor, considering that it would reduce the likelihood of recurrence of the disease and increase survival[7]. One of the limitations found for the analysis of this information was the fact that the Instituto Hebe Camargo did not divide chemotherapy data by sector, which began to be done in 2020. Thus, it became difficult to compare the number of breast cancer chemotherapies from the periods prior to and during the pandemic. In addition, medical records were unavailable and could not be computed.

In comparison, a study conducted at Hospital Central da Aeronáutica in Rio de Janeiro (state of Rio de Janeiro, Brazil) evaluated surgeries in mastology during the pandemic period compared with the pre-pandemic period. The authors verified a decrease in the number of surgeries in mastology (28.6%) and an increase in the indications for neoadjuvant care (133%) in the same period[15,24]. These results can be compared with our findings, as both studies showed a total decrease in the number of surgical interventions. While in the present study it was not possible to obtain statistically significant results with regard to neoadjuvant chemotherapy, the research carried out in Rio de Janeiro reached a result that confirms the hypothesis of a possible increase in the number of NC[15,24].

In view of these results, we can assess that the reduction in the number of aesthetic, benign, and reconstructive (elective) surgeries was expected due to the orientation to patients to avoid unnecessary visits to the hospital, once the risks and benefits were analyzed. Nevertheless, we also observed a decrease in the number of chemotherapies, which may be due to the limitation of outpatient care. Meanwhile, the number of diagnostic

surgeries remained stable and may bring positive results to the prognosis of cancer patients.

Another beneficial aspect is due to the fact that the Hospital Guilherme Álvaro maintained a number of breast cancer surgeries, during the pandemic period, similar to that of the analyzed pre-pandemic period. However, it is worth mentioning that at the end of March 2021 the elective surgeries at the institution were suspended, and only those deemed urgent and emergency cases were performed, in exceptional situations. This change can be explained by the fact that, so far, March was the month with the worst repercussions of the pandemic in the State of São Paulo, with a mortality of 9.1 thousand people until March 23[25].

The psychological factor of patients who had treatment suspended and were unable to undergo reconstructive surgery must also be considered, as they remain anxious and afraid of the disease while waiting for a new date for their definitive treatment. Therefore, even though it is proven that these non-invasive methods can delay definitive surgical treatment for a period of time, the duration of restrictive measures during the pandemic remains indetermined[14]. The impact of postponing tumor resection and the administration of invasive therapies over an extended period of time on the outcome and survival of these patients is still uncertain, in such a way that further studies on this topic are necessary[13].

CONCLUSIONS

We verified a reduction in the number of aesthetic, benign, and reconstructive surgeries, as well as in the number of chemotherapies, which may be due to the limitation of outpatient care. Moreover, the number of diagnostic surgeries remained stable and may bring positive results to the prognosis of cancer patients. As long as the pandemic continues, it will not be possible to fully predict the next repercussions of COVID-19 on the treatment of breast cancer, which indicates the need for more long-term research on this topic.

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AUTHORS' CONTRIBUTION

MAK, EBLS, TCM, RCTR: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing — original draft, Writing — review & editing. MFHP: Data curation, Formal analysis, Investigation, Supervision, Writing — review & editing.

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