REVIEW ARTICLE
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Global impact of pandemic by SARS-CoV-2 on breast cancer diagnosis and screening

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ABSTRACT

Introduction: The pandemic related to the new coronavirus is characterized by high rates of contamination, transmissibility, and mortality. The measures of social isolation adopted by the World Health Organization and corroborated by several countries, with a view to avoiding or minimizing the transmission of COVID-19, can lead to the reduction of the capacity of screening and diagnosis of diseases, such as breast cancer. **Objective:** This study aimed to analyze the diagnostic indexes and mamaria malignancy diagnosis test, such as mammogram, during the COVID-19 pandemic period. **Methodology:** Systematic review of the literature based on studies found in the PubMed, SciELO, LILACS, and ScienceDirect databases. **Results:** The six selected articles demonstrate a reduction in the diagnosis of breast cancer during the pandemic, although with discordant rates. Outcomes such as reduced number of mammograms and change in tumor stage were also analyzed. **Conclusion:** It is essential to maintain care with the screening, diagnosis, and treatment of breast cancer, in order to minimize the damage caused over more than 1 year of COVID-19 pandemic.

KEYWORDS: coronavirus; early detection of cancer; neoplasms; SARS-CoV-2.

INTRODUCTION

The SARS-CoV-2 virus infections are first recorded in December 2019 in Wuhan, China. Spreading globally, due to the inherent characteristics of the virus, there was a need to implement measures to contain viral propagation, such as social distancing and the relocation of health services, in order to meet new global demands. Therefore, many countries have chosen to temporarily suspend their screening and diagnosis programs for breast cancer, which is the world's most common neoplasm among women[1].

In Brazil, according to Bessa[2], the National Health Agency recommended that non-urgent visits, examinations, or surgeries be postponed. The State has a screening program for the diagnosis of breast cancer through the Unified Health System in women aged between 50 and 69 years. Despite government efforts, even before the pandemic, it is estimated that, together with the search for private care, only 60% of screening coverage occurs in the country.

In this context of changes in the functionality of health systems resulting from the COVID-19 pandemic, the study aimed to analyze the overall impact on the number of diagnoses of breast neoplasms and on mammograms. Through a systematic review, pre-pandemic and pandemic comparative data are described.

METHODS

This study consists of a systematic literature review so that submission to the Ethics and Research Committee was not necessary. Articles indexed in the electronic databases PubMed, SciELO, LILACS, and ScienceDirect were manually collected from August 28 to 31, 2021. Cross-sectional and retrospective observational studies were selected using the following descriptors and keywords: (Diagnosis) AND (Breast Neoplasms) AND (COVID-19), which were obtained according to the Health Science Descriptors (DeCS).

The inclusion criteria for the selection of articles for systematic review were predetermined and include relationship between the number of breast cancer diagnoses before and during the COVID-19 pandemic; articles with real data presentation; and

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articles with translation into at least one of the following languages: English, Portuguese, or Spanish. The exclusion criteria were also predetermined for the search, being excluded: editorial articles; articles whose publication has been made in languages other than those mentioned above; and articles with speculative data.

In this search for the present study, 263 results were found on the PubMed platform, 174 articles on the ScienceDirect platform, and 5 articles on the LILACS platform, with no results on the SciELO platform. Only one of the articles was duplicated, so after reading the titles, 36 studies were selected to read the abstract and, after reading the respective abstracts, 21 articles remained. These 21 studies were read in full by three reviewers and selected independently so that they met the inclusion and exclusion criteria, leaving, at the end, 6 articles.

Of the 263 articles found on the PubMed platform, 262 remained after the exclusion of the duplicate, so that 229 of them were excluded after reading the title and 12 after reading the abstract for not meeting the pre-established requirements. Of the 19 articles read in full, 10 were excluded due to the absence of the outcome of the relationship between the number of breast cancer diagnoses during the pandemic, 4 were excluded because they were guidelines or editorial letters, and 1 was excluded because it referred to simulations with unrealistic data from population models. Of the 174 studies located on the ScienceDirect platform, 171 were excluded after reading the title and 2 were excluded after reading the abstract, so the article read in full was included in the review. Of the five articles found on the LILACS platform, four studies were excluded after reading the title and one was selected to integrate the systematic review. Finally, data were extracted on the characteristics of the studies, results, and outcomes. The flowchart of the process of identification and selection of studies is presented in Figure 1.

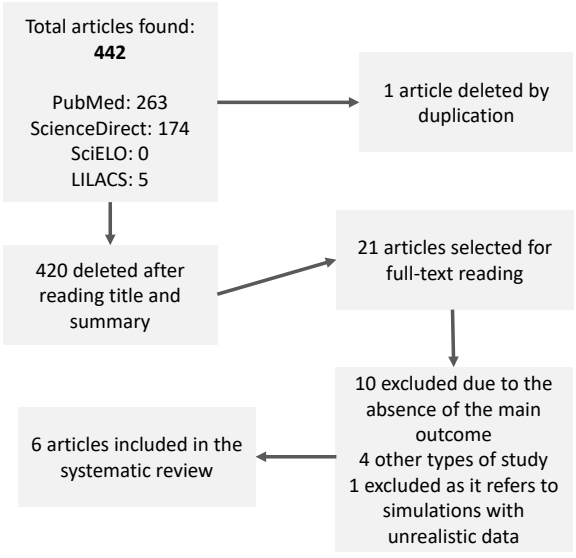

Figure 1. Search strategy flowchart. Passo Fundo (RS), 2021.

RESULTS

All articles included were published in 2020 or 2021, written in English, with impact factors ranging from 4,018 to 11,059. Regarding origin, two studies are from the Netherlands[3,4], one from Belgium[5], one from Brazil[6], one from Croatia[1], and one from Italy[7]. The outcomes addressed by the studies were decreased in breast cancer diagnoses, reduction in the number of tests performed, and changes in the stage of cancer.

In the Brazilian article, coming from Fortaleza, Ceará, mammography and breast ultrasound examinations had the greatest impact due to the pandemic, with a decrease of 95% and 100%, respectively, which led to a reduction of up to 60% of diagnoses, since the number of new cases of breast cancer was 23 in May 2019 and 8 in May 2020[6]. When comparing two distinct periods, it was noted that, in northern Italy, between May 2019 and July 2019, 15,942 mammograms were performed and 223 individuals were diagnosed with breast cancer (221 women and 2 men), but in the same quarter of 2020, only 9,052 mammograms were performed and 177 patients were diagnosed (174 women and 3 men). In addition, in 2020, there was a statistically significant reduction in the diagnosis of breast cancer in situ (from 17% of breast cancer diagnoses in 2019 to 6.8% in 2020), but the rate of cT1, cT2, and cT3 tumors diagnosed in May to July 2020 did not differ significantly from the 2019 tumors. In contrast, cT4 tumors increased from 4 (1.8%) in 2019 to 14 (7.9%) in 2020 and the number of breast cancers with metastatic lymph nodes (cN+) at the time of diagnosis increased from 28 (12.5%) in 2019 to 42 (23.7%) in 2020[7].

In the Netherlands, the incidence of breast tumors detected at screening decreased during weeks 12–13 of 2020, almost zeroed during weeks 14–25, and increased during weeks 26–35. The decrease in incidence was observed in all age groups and occurred mainly for cTis, cT1, ductal carcinoma in situ, and stage I tumors. Due to the suspension of the breast cancer screening program and its restarting with reduced capacity, the incidence of tumors detected by screening decreased by 67% during weeks 9–35 of 2020, which equates to about 2,000 possibly delayed breast cancer diagnoses. Despite this, until August 2020, there was no evidence of a transition to breast cancer at higher stages after the restart of screening[3].

A 24% reduction in newly diagnosed breast cancer cases in Croatia was seen during April, May, and June 2020 compared to the same period in 2019. However, during the whole of 2020, only 1% fewer new cases were reported than in 2019, 6% less than expected[1]. In Belgium, female breast cancer diagnoses in the screening population (50–69 years) decreased by 56% in April

2020, but it was possible to resume screening for these tumors, with only 6% of diagnoses missing by the end of 2020[5].

DISCUSSION

Breast cancer screening in the asymptomatic population leads to early diagnosis and treatment[8]. During the COVID-19 pandemic, there were problems in accessing cancer care services, which includes screening[9], raising some concerns about the delay, and decreased diagnoses of the disease[5]. This context can have deleterious long-term effects, since it was estimated that the delay of each month in diagnosis is associated with a 1.8% higher probability of a more advanced stage of cancer[1].

As can be seen in Table 1, the six articles selected for systematic review demonstrate a reduction in the diagnosis of breast cancer during the COVID-19 pandemic, although these rates present some disagreements. Lôbo et al.[6] reported a 60% reduction in diagnoses, the highest rate found, but these data are related to a restricted population, since they correspond to the city of Fortaleza (Ceará, Brazil). In addition, these rates also disagree with those presented by the National Cancer Institute[10] which demonstrates 59,700 new cases in 2019 and 66,280 in 2020, so that in Brazil, there was a 10% increase in new cases of the disease.

Toss et al.[7], Eijkelboom et al.[3], Vrdoljak et al.[1], and Eijkelboom et al.[4] demonstrated similar rates of diagnostic reduction in the first half of 2020, with 24, 37, 24, and 35% decrease, respectively. These values also disagree with those analyzed in the same studies by Vrdoljak et al.[1] and Peacock et al.[5], which demonstrate a reduction of 1 and 6%, respectively, when compared to the whole year 2019 and 2020. The explanation for these data may lie in the fact that, as cancer care services returned to work, an increase in screening volumes may have reduced the deficit in accumulated mammograms, as demonstrated in the study by Miller et al.[11], which brought up new diagnoses of the disease.

Regarding breast cancer screening tests, when analyzing the article by Lôbo et al.[6], it was evidenced a 95% decrease in the rate of mammograms in the period from March to June 2020 compared to 2019 in Brazil, while in the study by Toss et al.[7], in Italy, there was a 43% reduction in these rates from May to July 2020, compared to the previous year. The discrepancy of these data may occur due to the fact that the pandemic in Italy began earlier than in Brazil and had its peak waves of SARS-Cov-2 in different stages.

When comparing Brazilian studies, Lôbo et al.[6] with Bessa[2], there is a difference in results, because Bessa[12], based on DATASUS, showed a 42% drop in the rate of mammograms throughout the

Table 1. Outcomes found in the systematic search.

Reference	Analyzed site	Analyzed period	Breast cancer diagnostic reduction (%)	Mammography reduction (%)	Tumor stage (%)
1. Lôbo et al.[6]	Fortaleza, Ceará, Brazil	From March to June 2020, compared to the same period in 2019	60 of reduction in diagnostics	95	–
2. Toss et al.[5]	Province of Modena, northern Italy	From May to July 2020, compared to the same period in 2019	24 of reduction in diagnostics	43	IN SITU: decrease of 68 IIA: decrease of 12 Stage III: increase of 10 Stage I, IIB e IV no significant changes
3. Eijkelboom et al.[2]	Holland	From February to August 2020, compared with the same period in 2018 and 2019	37 of reduction in diagnostics	–	IN SITU: decrease of 57 Stage I: decrease of 43 Stage II: decrease of 25 Stage III: decrease of 16 Stage IV: decrease of 4
4. Vrdoljak et al.[1]	Croatia	Year 2020 compared to 2019	24 of reduction in diagnostics from April to June 2020, if compared with the same period in 2019 1 of reduction in diagnostics for the whole of 2020	–	–
5. Eijkelboom et al.[3]	Holland	From February to April 2020, compared with the same period in 2018 e 2019	35 of reduction in diagnostics	–	IN SITU: decrease of 38 Stage I: decrease of 39 Stage II: decrease of 32,5 Stage III: decrease of 38 Stage IV: decrease of 15
6. Peacock et al[4]	Belgium	2020 compared to year 2019	6 of reduction in diagnostics	–	–

country and that the most affected state was Rondônia, with 67%. However, in the study by Lôbo et al.[6], it is only in Fortaleza, Ceará, there was a 95% decrease, which is similar to the data demonstrated by Collado-Mesa et al.[12], whose decrease in mammograms was 98% in Florida, USA. From March to June 2020, the same period as evidenced by Lôbo et al.[6], the article by Song et al.[16] showed a 38% reduction in mammograms expected compared to 2019 in the United States. In another study conducted in the United States[13], from March to May 2020, the absolute deficit in the American population in breast screening associated with the COVID-19 pandemic was estimated at 87.3% compared to the same time period in 2019.

In the analysis of the selected articles, a significant reduction of 68% of the tumor in situ is found in the study by Toss et al.[7] and of 57% is found in the study by Eijkelboom et al.[3], demonstrating the proximity of the data. Already in the study by Eijkelboom et al.[4], this rate is also decreased, but with a value of 38%. Stage I had similar results in the articles by Eijkelboom et al.[3] and by Eijkelboom et al.[4], with a decrease of 43 and 39%, respectively. However, in the study by Toss et al.[7], this stage does not present significant changes, as well as IIB and IV in the same article. Stage II demonstrates a decrease of 12, 25, and 32.5% in the studies by Toss et al.[7], Eijkelboom et al.[3], and Eijkelboom et al.[4], in that order, in which the disparity of the data between the first and the other articles is perceived. Stage III shows decrease in the study by Eijkelboom et al.[3] of 16% and approximately double in the study by Eijkelboom et al.[3], with 38%. However, Toss et al.[7] presented a discrepancy in the data, with an increase of 10%. Stage IV showed a slight decrease of 4% in the study by Eijkelboom et al.[3] and a more significant percentage of 15% in the study by Eijkelboom et al.[4].

In relation to increased mortality due to delay and decrease in diagnoses, Yong et al.[14] estimated the long-term clinical impact of breast cancer screening interruptions in Canada, using a validated mathematical model, which demonstrated an increase of 110 deaths between 2020 and 2029 due to a 3-month break in the disease screening service. Another study[15] estimated the impact of COVID-19 on screening and treatment of breast cancer at Sharpless, using CISNET cancer simulation, which demonstrated an increase of more than 5,000 deaths in the next decade in the United States.

This context of reduced diagnosis and screening tests demonstrated by systematic review occurs both due to the reduced operational status of imaging clinics and due to the fear of patients seeking health services[16]. However, even in the midst of the pandemic, other pathologies, such as breast cancer, have not stopped emerging and continue to cause high morbidity and mortality. In this sense, since the COVID-19 pandemic persists for more than 1 year, it is important that breast cancer care services continue to function, with due care, in order to perpetuate care for the pathology.

Although some studies present discordant rates, this review demonstrates the reduction in the number of tests performed for breast cancer screening, as well as the decrease in diagnoses of the disease in all sites studied by the analyzed articles. In addition, it is also suggested, as a consequence of the reduction in screening, changes in the staging of breast cancer. However, more studies are needed to confirm these findings. Even so, considering the data that indicate worsening in the stage of the disease, it is essential to maintain care with the screening, diagnosis, and treatment of breast cancer, aiming to minimize the damage caused over more than 1 year of COVID-19 pandemic.

AUTHORS' CONTRIBUTION

ADDA: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. AKD: Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. GVBS: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. MB: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. VAS: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. ESG: Conceptualization, Investigation, Methodology, Validation, Writing – original draft. LLA: Conceptualization, Data curation, Investigation, Project administration, Supervision, Validation, Writing – review & editing. LMW: Conceptualization, Data curation, Investigation, Project administration, Supervision, Validation, Writing – review & editing

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