

# Analysis of delayed core biopsy results during COVID-19 pandemic: the experience of a single public center

Marina Ávila Ferrari<sup>1\*</sup> , Nadhine Feltrin Ronsoni<sup>1</sup> , Gustavo Alberto Ozol de Ávila<sup>1</sup> ,  
Paula Cechella<sup>1</sup> , Adriana Freitas<sup>2</sup> , Rebeca Heinzen<sup>3</sup> 

## ABSTRACT

**Introduction:** To observe and analyze the waiting time for breast biopsy and the impact of this time on the early diagnosis of breast cancer in Santa Catarina. **Methods:** Observational cohort study. Data collection was performed through direct observation with the application of a questionnaire and subsequent quantitative analysis. A convenience sample was used, in which data were computed through a questionnaire administered to patients in cases where a breast biopsy with a thick needle was requested due to the existence of a suspicious lesion in the physical examination or in imaging examinations requested as breast cancer screening. Data from the collection instrument were extracted through direct interviews with patients in the office and completion of a questionnaire, after their correct guidance and signing of an informed consent form. The percentage of malignant versus benign lesions and the pain scale during core biopsy were evaluated. **Results:** The questionnaire was submitted to 71 women who attended the mastology outpatient clinic at the Hospital Regional de São José – Dr. Homero de Miranda Gomes (HRSJ-HMG) between October 2021 and May 2022. Of these, 7 did not undergo breast biopsy due to the lesion not being identified, 39.1% resulted in malignant neoplasia and 60.9% in benign lesion. Regarding the assessment of pain during core biopsy, 57.8% experienced mild or no pain, 21.8% moderate pain and 10.9% severe pain. **Conclusions:** Through this study, it was possible to diagnose malignant lesions and treat patients who had the chance of early follow-up.

**KEYWORDS:** breast neoplasms; core biopsy; descriptive epidemiology; referred pain; menopause; early diagnosis.

## INTRODUCTION

Breast cancer is among the most common malignant neoplasms in women in several countries, including Brazil, where, excluding non-melanoma skin cancers, it is the most common type of cancer in women, with the highest number in the South and Southeast regions<sup>1,2</sup>. Data from the National Cancer Institute<sup>2</sup> show breast cancer as the leading cause of death from malignant neoplasms in women in all regions of Brazil, with the exception of the North region, where it is second only to cervical cancer. Additionally, 73,610 new cases of breast cancer were estimated in Brazil in 2023, with an estimated risk of 66.54 cases per 100,000 women. The mortality rate in 2021 was 11.71 deaths/100,000 women<sup>2</sup>.

According to Concord-3<sup>4</sup>, there was a drop in the five-year survival rate for women with breast cancer, falling to 76.9% (75.5–78) from 2005 to 2009 and 75.2% (73.9–76.5) from 2010 to 2014<sup>3,4</sup>.

These data reflect the speed with which these women are able to access early diagnosis, which includes access to medical care, screening mammograms (MMG) and biopsies of lesions detected as suspicious, as well as the conditions of systemic treatment.

In recent years, the COVID-19 pandemic has led to a reduction in routine consultations for the prevention of female cancer. A questionnaire distributed among specialists in Santa Catarina estimated that there was a reduction of more than 50% in consultations and screening examinations during this period<sup>5</sup>. National estimates show that more than 40,000 cases of breast cancer were not diagnosed in 2020.

It is extremely important that, as soon as a lesion suspected of malignancy is detected, patients are able to undergo a breast biopsy procedure in a timely manner for pathological and immunohistochemical analysis, followed by appropriate referral and

<sup>1</sup>Hospital Regional de São José Dr. Homero de Miranda Gomes – São José (SC), Brazil.

<sup>2</sup>Larmony Santa Catarina – Florianópolis (SC), Brazil.

<sup>3</sup>Universidade do Sul de Santa Catarina – Palhoça (SC), Brazil.

\*Corresponding author: [avilaamarina@gmail.com](mailto:avilaamarina@gmail.com)

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admission to specialized centers for treatment. Such consultations and procedures were also hindered by the COVID-19 pandemic<sup>6</sup>.

The most commonly used procedures for breast biopsies are: fine-needle aspiration biopsy (FNA), percutaneous core biopsy, vacuum-assisted biopsy (mammotomy), and surgical, incisional or excisional biopsy. The method chosen will depend on a clinical and imaging evaluation of the lesion and the patient's clinical analysis<sup>6,7</sup>. Image-guided biopsy has brought greater practicality and reduced morbidity for patients, similar to the efficacy and precision seen with surgical biopsy<sup>8</sup>. Currently, less than 9% of core needle biopsies diagnose high-grade lesions; however, this number tends to increase with the improvement of breast imaging techniques<sup>3</sup>.

A comprehensive review of the literature assesses the conduct of high-grade lesions and observes the diversity of existing results, demonstrating the importance of increasing the number of core biopsies for lesions suspected in imaging tests or clinically so that strategies can be defined and there is a reduction in the incidence of cancers or an improvement in cure and survival rates<sup>9</sup>.

Institutional differences in excision rates for high-grade lesions, once diagnosed in the core biopsy, demonstrate the need for further studies and improvements in the number of lesions detected for the appropriate indication of these biopsies<sup>10</sup>.

The role of the mastologist includes strategies for surveillance and risk reduction, as well as defining methods for screening and diagnosing these lesions<sup>6</sup>. In this scenario, MMG and core biopsy, which are essential for monitoring patients, are allies in the diagnosis of high-grade or malignant lesions.

In view of this, the present study aimed to analyze the results of breast biopsies of patients recruited because of suspicious lesions after the COVID-19 pandemic. In addition, the objective was to assess the waiting time between the request and the performance of the core needle biopsy and the degree of discomfort with the procedure.

## METHODS

A retrospective cohort study was conducted. Data collection was performed through direct observation with the administration of a questionnaire and subsequent quantitative analysis.

The study took place at the Mastology Service of the Maternity Ward of the Dr. Homero de Miranda Gomes Regional Hospital of São José (HRSJ-HMG), in the city of São José, state of Santa Catarina.

Data were computed through a questionnaire applied to patients who underwent breast biopsy with a thick needle due to the existence of a suspicious lesion in the physical examination or in imaging tests, requested as breast cancer screening, according to the BI-RADS classification by the Basic Health Unit (UBS). All patients were referred from primary care for biopsy

at a tertiary service with mastology care, as shown in the flowchart presented in Figure 1.

During a six-month period, data from patients on the SUS waiting list for breast biopsy in 18 cities in Santa Catarina were evaluated. The primary objective was to evaluate the pathological results of the core needle biopsy and the waiting time for the biopsy from the time the request was made by the primary care physician. The secondary objectives were to analyze the pain related to the procedure, as well as the epidemiological characteristics. To perform the breast biopsies, the BARD needle, models MN1413 and MN1410, and the BARD Magnum gun were used.

After authorization by the HRSJ and approval by the institution's Research Ethics Committee (CEP), a questionnaire was administered to patients seen at the HRSJ-HMG mastology outpatient clinic.



**Figure 1.** Flowchart of patient care.

The collected data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS), version 20.0, and Minitab 16. Statistical tests were performed with a significance level of  $\alpha=0.05$  and, therefore, a confidence level of 95%. Qualitative variables were expressed as frequencies and percentages using Microsoft Excel, version 2010.

## RESULTS

In a seven-month period between October 2021 and May 2022, 185 women were waiting for a breast biopsy through SUS, in a corresponding list of 18 municipalities in the state of Santa Catarina, because of suspicious changes in breast imaging examinations, BI-RADS category 4 or 5, or through physical examination by the UBS. During this period, of the total of 185 patients, only 71 (38.4%) chose to be seen in the HRSJ-HMG Mastology Outpatient Clinic to undergo the procedure through active recruitment. There was no information on the progress of the situation of the remaining 114 patients. Of the women treated, 6 did not undergo a breast biopsy because the lesion designated as suspicious was not identified in screening examinations. Of the 64 patients who underwent the examination, the biopsy of 25 (39.1%) resulted in malignant breast neoplasm and 39 (60.9%) presented with a benign lesion in the histopathological result (Figure 2). Of the 39 benign lesions, 2 were categorized as risk lesions such as flat epithelial atypia, atypical ductal hyperplasia, papillary lesions with atypia, radial scar with atypia, atypical lobular hyperplasia and lobular carcinoma *in situ*.

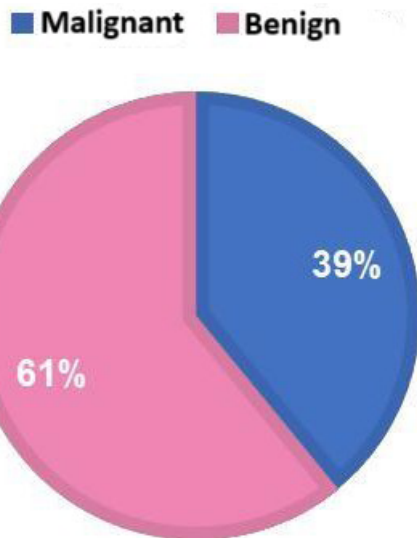
After the procedure, patients were asked about their pain, using a visual analogue scale from 0 to 10 to measure each patient's pain level. Of these, 40 (62.5%) had mild or no pain, 17

(26.5%) had moderate pain, and only 7 patients (11%) reported severe pain, as shown in Figure 3.

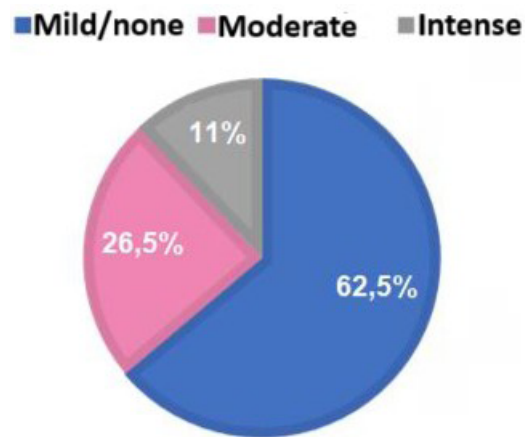
In the group of patients who had pain during core biopsy, 35% had a malignant result in the pathological examination and 65% had a benign result.

Table 1 shows the relationship between the variables analyzed during the administration of the questionnaire to the patients. Comparing age groups, a total of 28 women aged 50 or younger obtained 22 (78.6%) benign results and 6 (21.4%) malignant results. In women over 50 years of age, 16 (47%) biopsies with benign lesions and 18 (53%) with malignant lesions were obtained. Age over 50 years was a statistically significant factor for the presence of malignancy ( $p=0.006$ ).

Also in Table 1, the relationship between the result obtained and the menopausal status at the time of perception of the breast lesion can be noted. This variable was found in 35 patients after the onset of menopause, of which 16 (45.7%) were benign lesions and 19 (54.3%) were malignant lesions. A total of 28 women reported being in menacme, with 22 (78.6%) showing benign results and 6 (21.4%) malignant results of the biopsied lesion.



**Figure 2.** Histopathological result of biopsies performed because of suspicious changes.



**Figure 3.** Pain scale in core biopsy procedure.

**Table 1.** Clinical profile of patients undergoing breast biopsy at a tertiary care facility.

	PE – Benign	PE – Malignant	p-value
	n (%)	n (%)	
Age (years)			
≤50	22 (78.6)	6 (21.4)	0.006
>50	16 (47)	18 (53)	
Menopause			
Yes	16 (45.7)	19 (54.3)	0.006
No	22 (78.6)	6 (21.4)	
Palpable			
Yes	10 (50)	10 (50)	0.13
No	28 (65.1)	15 (34.9)	

PE: result of the pathological examination.

Table 1 also sought to relate the pathological results found with the presence of palpable lesions or by finding in screening examination. The study included 20 women with palpable lesions at the time of biopsy; of these, 50% obtained malignant results. There were 43 patients with suspicious non-palpable changes in the breast; of these, 28 (65.1%) showed benign lesions and 15 (34.9%) were diagnosed malignant. Within the group of non-palpable breast lesions, in which the biopsy was guided by imaging, with MMG and breast USG being available for this study, a total of 30 were guided by USG, of which 63.3% had benign lesions and 36.7% had malignant lesions. A total of 13 patients underwent MMG-guided biopsy, of which 69.2% were benign and 30.8% were malignant. There was no statistical correlation between the malignancy result and the type of malignant lesion, whether palpable or a finding on physical examination ( $p=0.13$ ).

The time between the identification of the suspicious lesion and the time the biopsy was performed was analyzed. Most patients (31–47%) had access to the biopsy more than 90 days after the lesion was found, either through clinical examination of the breasts or through imaging. It was noted that 12 (18.2%) patients had their lesion biopsied between 30 and 90 days and 23 patients (34.8%) in less than 30 days. Of the 20 palpable lesions, 40% of the women were over 50 years of age. It was recorded that 45% had palpable lesions and were in menopause, while 55% were in menarche. Among the 43 patients without palpable lesions on clinical examination, 37.2% were 50 years of age or younger, while 11.4% of postmenopausal patients were 50 years of age or younger and 88.6% were over that age.

Six patients were lost to follow-up, did not return with the results for management and were not found in the active search. One patient, of the 71 referred for a suspicious lesion, did not attend the outpatient clinic.

## DISCUSSION

Several studies conducted in recent years have shown that breast cancer in young women under 40 years old accounts for approximately 7% of all cases of the disease<sup>11</sup>. A retrospective study demonstrated a more severe prognosis for breast cancer in patients under 40 years of age. This makes early diagnosis necessary, since these are usually more aggressive tumors that grow more rapidly<sup>11</sup>.

On the other hand, it is worth noting that, with regard to age, the present study addresses the occurrence of breast cancer in patients over 50, who account for the majority of cases, and whose samples have a highly significant p-value compared to younger women. Likewise, it is noted that cases of breast cancer are more prevalent after menopause, with 54.3% of diagnoses for breast cancer occurring in this scenario and 21.4% before this period. Regarding the clinical finding of palpable lesions, no

association was found between palpable nodules or alterations in screening tests and the diagnosis of malignancy in the pathological examination.

It was noted in the present study that the majority of patients who presented to the service with a palpable lesion (60%) were under 50 years of age, in addition to the finding of 55% in the menarche period, which is in agreement with the current literature that indicates that young women have more palpable breast nodules<sup>12</sup>.

We observed that 47% of patients presented to the service for biopsy after 90 days from the moment of detection of the suspicious lesion, a period whose compliance is crucial for the success of the treatment and the respective achievement of cure. Since the time until the beginning of treatment for malignant breast neoplasia is directly related to the cure rates, it is of utmost importance that it begin as soon as possible.

In view of this, it is important to emphasize that palpable lesions can be biopsied simply and efficiently in an outpatient setting, with appropriate training and equipment. In other words, a total of 10 (14%) patients in this study — who had palpable lesions and were diagnosed with breast cancer — would have had access to definitive treatment services more quickly and earlier if they had been available. For this reason, it is extremely important that UBS teams be familiar with the types of procedures available and their indications, as well as providing the necessary information to the pathologist<sup>6</sup>.

One of these procedures is the core biopsy, a method appropriate for nodules, architectural changes or breast density<sup>6</sup>. FNA is indicated for cystic lesions that are well defined on imaging as benign or malignant, in cases of suspected recurrence in the chest wall or for analysis of lymph node metastasis<sup>6,13</sup>. A meta-analysis demonstrated that USG-guided core biopsy was superior to FNA in the axillary staging of breast cancer<sup>14</sup>.

One of the justifications for performing FNA instead of core biopsy is the less discomfort of the fine needle compared to the thick needle and the lower operating cost. However, we demonstrated that 54 patients reported mild or moderate pain. Furthermore, none of the biopsied lesions had insufficient material, which could frequently occur when cytological analysis alone was performed.

Therefore, immediate performance of a thick needle biopsy ensured that the waiting time for diagnosis — in most cases, more than three months — was not delayed by insufficient material or inconclusive examination generated by cytology.

Furthermore, delays in diagnosis, especially of palpable lesions, could be reduced by training primary care teams to perform core needle biopsies in these cases — which, in this sample, corresponded to 20 patients treated at a tertiary hospital for the procedure. This would reduce the cost of patient care and travel, as well as delays in diagnosis.

Among the limitations found in FNA, we have the underestimation of invasion, as well as the failure to recognize components of ductal carcinoma in situ in cases of papillary and atypical lesions<sup>8,13</sup>. Cases like these may be alleviated as the core biopsy procedure becomes more routine, with the training of professionals qualified to perform it.

In comparison with open surgical biopsy, biopsy guided by imaging methods, such as USG, MMG or magnetic resonance imaging, is equally accurate and has a complication rate of less than 1%, such as infection, hematoma and pneumothorax. In addition, image-guided biopsies generate lower final costs, since they imply fewer surgical procedures necessary to obtain adequate free margins<sup>7</sup>.

It is noted that there are lesions that need to be surgically removed, based on diagnosis in breast biopsies, due to the high risk of progression to breast cancer. These are: atypical ductal hyperplasia, flat epithelial atypia, papillary lesions with atypia, radial scar with atypia, atypical lobular hyperplasia and lobular carcinoma in situ<sup>9,10,13</sup>.

Studies show that these lesions can underestimate breast cancer, especially when they are large and when a small-gauge needle is used for biopsy<sup>6,9</sup>. In this study, we found 5.1% of high-risk benign lesions, which were referred for surgical excision.

Although clinical protocols are highly effective and briefly guide the techniques to be used, knowing the work environment, the patient, her limitations, her traumas and her expectations is essential when trying to reduce the potential pain impact inherent to a biopsy experience.

Furthermore, it is essential to pay attention to the presence of physical disabilities, which may make it difficult to position the patient during the examination, and other limitations for the correct planning of the method, which will result in greater practicality, safety and efficacy in the final result<sup>7</sup>.

It is important to conduct further studies comparing the cure and survival rates between women with palpable lesions who had them biopsied at the UBS and those who need to travel to another service to undergo the examination. Research is also suggested that relates the fear of pain when performing a core biopsy to the speed of diagnosis, as well as the waiting time in the SUS line to reach the referral service.

## CONCLUSION

This study is the result of a seven-month follow-up period, between October 2021 and May 2022, during a period of high relevance due to the COVID-19 pandemic. Since breast cancer is highly sensitive to the time it takes to evolve, especially from the discovery of the lesion to the biopsy followed by

treatment, it was convenient to analyze the results of the core needle examinations in this pandemic scenario. It is worth mentioning that the study involved 71 women, all of whom were previously awaiting a breast biopsy through SUS, either because of suspicious changes in breast imaging examinations (BI-RADS category 4 or 5) or because of physical examinations performed at the UBS. The 71 women were seen at the mastology outpatient clinic at the Hospital Regional de São José – Dr. Homero de Miranda Gomes to undergo the procedure through active recruitment.

In terms of the main results of the core biopsy itself, a high propensity for malignant lesions was found in women over 50 years old (53% of cases), while only 21.4% for women under 50. Furthermore, it was understood that these lesions are more frequent in postmenopausal patients, compared to menstruating patients, with the incidence of malignant lesions being 54.3 and 21.4%, respectively.

The above results were in fact expected, given the history of the neoplasm. However, an important analysis regarding the time between the identification of the suspicious lesion and the performance of the biopsy is noteworthy: 47% of the patients had access to the biopsy more than 90 days after the lesion was found; 18.2% in a period between 30 and 90 days; and 34.8% in less than 30 days. It is important to note that six patients were lost to follow-up and did not return with the result for the management. Therefore, this study demonstrates the importance of preparing UBS teams to perform core biopsies of breast lesions suspected of malignancy, aiming at early diagnosis and direct referral to centers for oncological treatment. Although the COVID-19 pandemic has been greatly mitigated, other similar critical scenarios could require greater diagnostic agility in UBS in a similar way, since the present study highlighted possible losses that delayed results could cause in terms of delaying the start of treatment — consequently, reducing the chance of cure.

In addition, the study reinforces the need to carefully outline the concerns and limitations of each patient, with the aim of reducing fear of undergoing breast biopsy, so that treatment is not delayed.

## AUTHORS' CONTRIBUTION

MAF: Conceptualization, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft. NFR: data curation, formal analysis, Writing – original draft. GAOA: Data curation, Formal analysis, Writing – original draft. PC: Data curation, Formal analysis, Writing – original draft. AF: Methodology, Validation, Writing – revision & editing. RH: Project administration, Supervision, Validation, Visualization, Writing – revision & editing.

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