ORIGINAL ARTICLE
https://doi.org/10.29289/2594539420210012

Impact of the immunohistochemical panel on patients with breast cancer diagnosis cared for in a referral hospital in the state of Amazonas

Hilka Flávia Barra Espírito Santo Alves Pereira[1,2,3]*, Roberto Alves Pereira[2], Thais Cristina Fonseca da Silva[2], Henrique Vieira Pereira[2], Lucas Barbosa Arruda[4], Valbécia Tavares de Aguiar[4], Maiara Magri Pereira Olenchi[4], Moysa Marquez Serruya[4], Valéria Santos da Costa[4]

ABSTRACT

Objective: To demonstrate the time between the diagnosis of the disease, the result of the immunohistochemical panel and the beginning of specialized treatment in patients diagnosed with breast cancer seen at the Foundation Center of Oncology of the State of Amazonas, from June to November 2018 and in the same period of 2019. **Methods:** The study was part retrospective, based on data from medical records, and part prospective, based on data from patients, and we evaluated the time between diagnosis from the immunohistochemical panel and the beginning of specialized treatment in breast cancer patients. **Results:** 170 patients diagnosed with breast cancer were included, 71 from June to November 2018 and 99 breast cancer patients seen from June to November 2019. The median time between diagnosis and immunohistochemistry results of all patients was 36 days, and comparing the two groups of patients, it was observed that for half of the 2018 patients, the time was less than 105 days, while for half of the 2019 patients, it was less than 27 days. If the times between the result of the immunohistochemical panel and the start of personalized treatment in both groups were compared, it was seen that the median time until the start of treatment was longer for patients in 2018, 94.5 days versus 79 days for patients in 2019. **Conclusion:** There was a decrease in the time between the diagnosis and the result of the molecular panel in 2019 compared to 2018. Achieving this result more quickly provided the choice of personalized treatment for each patient, having an important impact on survival in that population.

KEYWORDS: prognosis; survival; breast cancer; immunohistochemistry; time-to-treatment.

INTRODUCTION

Breast cancer is the most common cancer in women worldwide, accounting for 24.2% of all cases in 2018, with 2.1 million new cases[1]. It is estimated for each year of the 2020/2022 triennium, the diagnosis of 66,280 new cases of breast cancer, with an estimated risk of 61.61 cases per 100,000 women[2].

The increased incidence of cancer is related to the increase in life expectancy, improvement of diagnostic methods and the expansion of screening programs[3]. Most tumors have a slow progression and, if diagnosed early, show a considerable increase in the possibility of cure or improvement in survival[4].

The immunohistochemical study has been used in different situations of breast pathology. Hormone receptors, namely estrogen receptors (ER) and progesterone receptors (PR) and the overexpression or amplification of human epidermal growth factor receptor-2 (HER2), are predictive factors among breast cancer patients[5] and are used to define the treatment and establishment of the disease prognosis associated with clinical and pathological variables, as well as lymph node involvement, tumor size, histological type, tumor grade and surgical margins[6].

The time interval between diagnosis and the start of treatment is important to guide resolving measures[7], since delay can worsen prognosis in breast cancer. There is an association

[1]Post-graduation in Obstetrics and Gynecology, Botucatu School of Medicine, Universidade Estadual Paulista "Júlio de Mesquita Filho" – São Paulo (SP), Brazil.
[2]Universidade Federal do Amazonas – Manaus (AM), Brazil.
[3]Fundação Centro de Oncologia do Estado do Amazonas – Manaus (AM), Brazil.
[4]Universidade Nilton Lins – Manaus (AM), Brazil.
***Corresponding author:** hilkaespiritosanto@me.com
Conflict of interests: nothing to declare.
Received on: 02/18/2021. **Accepted on:** 06/28/2021.

between delayed diagnosis and treatment with worse disease-free survival, occurrence of lymph node metastasis, tumor size and late staging, but early detection is related to higher cure rates[8].

Therefore, in Brazil, Law No. 12.732, of November 2012 guarantees cancer patients the right to start treatment within 60 days or less after confirmed diagnosis[9].

Accordingly, the aim of our study was to demonstrate the time between the diagnosis of the disease, result of the immunohistochemical panel and beginning of personalized treatment in patients treated at the Foundation Center of Oncology of the State of Amazonas (FCECON) with a diagnosis of breast cancer, in the period from June to November 2018 and in the same period during 2019.

METHODS

This was an observational, cross-sectional and epidemiological study, composed of a retrospective part based on data from medical records, and a prospective part based on patient data, evaluating the time between the diagnosis according to the immunohistochemical panel and the beginning of specialized treatment in patients diagnosed with breast cancer. General data such as age, clinical stage at diagnosis, histological type, immunohistochemical panel, time between diagnosis and the start of treatment and time between diagnosis and the definitive result of the immunohistochemical panel were evaluated.

The 2017 FCECON management report was used as the basis to define a sample, which says that in one year, 131 patients were diagnosed with breast cancer. Therefore, our sample includes information collected from the medical records of patients diagnosed with breast cancer in the period from June to November 2018. Only records with complete information were entered in the study. In the prospective part, data were collected from patients diagnosed with breast cancer in the period from June to November 2019, with a questionnaire being filled out at the time of the consultation at the start of treatment. A total of 169 patients were evaluated, part retrospective, part prospective, referring to the period from June to November 2018 and 2019.

In 2019, FCECON became part of Roche Laboratory's Roche Testing program, enabling the complete and rapid assessment of the immunohistochemical panel for breast cancer. Previously, the examination was performed in a laboratory outside the city of Manaus, which involved a delay that sometimes exceeded 90 days, so there was an important gain for the institution. Thus, the study aimed to determine whether there was a change in the time between the diagnosis of the disease, the result of the immunohistochemical panel and the start of specialized treatment, comparing the 2018 part and 2019 part, since the institution did not yet have this support in 2018.

The immunohistochemical study was based on the identification of markers: ER, PR, HER2 and ki-67 protein. The classification is performed according to: luminal A (ER- and/or PR-positive, HER2-negative and ki-67 index less than 14%), luminal B (ER- and/or PR-positive, HER2-negative and ki-67 index greater than 14%), overexpressed HER2 (HER2-positive, regardless of the presence of PR and ER), triple-negative (ER-, PR- and HER2-negative) and hybrid luminal (luminal B and HER2 overexpression).

The study was approved by the Research Ethics Committee on June 30, 2019, under No. 3.477.033 and CAAE 16400519.2.0000.0004. In the prospective evaluation, all patients signed an informed consent form.

RESULTS

A total of 170 breast cancer patients were included, 71 from June to November 2018 and 99 from June to November 2019. Most patients were between 40 and 69 years old, accounting for 80% of the women included in the study.

Regarding the histological type of patients, the ductal type was the most frequent among those interviewed in both periods. In assessing the immunohistochemical panel, luminal type A was the most common among patients, while the hybrid luminal type was the least frequent.

Regarding the initial treatment chosen in both periods, surgery was the most frequent; however, there was a significant increase in the percentage of patients who had chemotherapy as initial therapy in 2019, that is, 49.5% of patients in 2019 versus 28.2% in 2018.

The data for all variables listed above are presented in Table 1.

Regarding clinical staging, stage IIA was the most frequent in both periods. The most frequent Breast Imaging Reporting and Data System (BIRADS) classification was class IV, also in the two periods studied (Table 2).

In addition to the clinical characteristics of these patients, the time interval between diagnosis and the immunohistochemical results was analyzed. The median time between diagnosis and immunohistochemistry for all patients was 36 days (median absolute deviation or MAD of 28.9 days). Comparing the two groups of patients, it was observed that for half of the patients in 2018 the time was below 105 days (median), while for half of the patients in 2019 it was below 27 days (Figure 1). According to the non-parametric Mann-Whitney test, it can be concluded that there was a significant difference in time interval from diagnosis to immunohistochemical panel results between the two groups ($P \leq 0.05$).

Regarding the time between the result of the immunohistochemical panel and the beginning of personalized treatment, the median time was 86 days (MAD=74.1). When comparing the times in the two groups, the median time to start of treatment was longer for the 2018 patients – 94.5 days versus 79 days for the 2019 patients. The non-parametric Mann-Whitney test was not statistically significant; however, in the exploratory analysis,

Table 1. Profile of patients according to age, histological type, initial treatment and immunohistochemical panel.

Variable	Total n = 170 (%)	Group	
		Patients from 2018 n = 71 (%)	Patients from 2019 n = 99 (%)
Age (years)			
< 40	19 (11.2)	7 (9.9)	12 (12.1)
40–69	136 (80.0)	59 (83.1)	77 (77.8)
≥ 70	15 (8.8)	5 (7.0)	10 (10.1)
Histological type			
Ductal	149 (87.6)	57 (80.3)	92 (92.9)
In situ	7 (4.1)	7 (9.9)	0
Lobular	7 (4.1)	5 (7.0)	2 (2.0)
Medullary	2 (1.2)	0	2 (2.0)
Other	2 (1.2)	1 (1.4)	1 (1.0)
Papillary	3 (1.8)	1 (1.4)	2 (2.0)
Initial treatment			
Surgery	101 (59.4)	51 (71.8)	50 (50.5)
Chemotherapy	69 (40.6)	20 (28.2)	49 (49.5)
Immunohistochemical panel			
HER2 overexpression	36 (21.2)	8 (11.3)	28 (28.3)
Luminal A	72 (42.4)	36 (50.7)	36 (36.4)
Luminal B	38 (22.4)	15 (21.1)	23 (23.2)
Hybrid luminal	4 (2.4)	4 (5.6)	0
Triple-negative	20 (11.8)	8 (11.3)	12 (12.1)

Table 2. Profile of patients according to clinical staging and Breast Imaging Reporting and Data System classification.

Variable	Total n = 170 (%)	Group	
		Patients from 2018 n = 71 (%)	Patients from 2019 n = 99 (%)
Stage			
IA	8 (4.7)	5 (7.0)	3 (3.0)
IB	14 (8.2)	4 (5.6)	10 (10.1)
IIA	56 (32.9)	26 (36.6)	30 (30.3)
IIB	38 (22.4)	15 (21.1)	23 (23.2)
IIIA	25 (15.3)	10 (15.5)	15 (15.2)
IIIB	25 (14.7)	10 (14.1)	15 (15.2)
IV	3 (1.8)	0	3 (3.0)
BIRADS			
I	1 (0.6)	0	1 (1.0)
II	6 (3.5)	3 (4.2)	3 (3.0)
III	9 (5.3)	6 (8.5)	3 (3.0)
IV	105 (61.8)	46 (64.8)	59 (59.6)
V	49 (28.8)	16 (22.5)	33 (33.3)

BIRADS: Breast Imaging Reporting and Data System.

there was a difference in the interval between the result of the molecular panel and the start of personalized treatment in the 2018 compared to 2019 period (Figure 2).

DISCUSSION

The average age of the women analyzed in the study was close to that reported in other studies with Brazilian patients diagnosed with breast cancer, demonstrating an average age of 51.8 and higher frequency between 41 and 60 years[10]. In the present study, most patients were between 40 and 69, totaling about 80% of the women included.

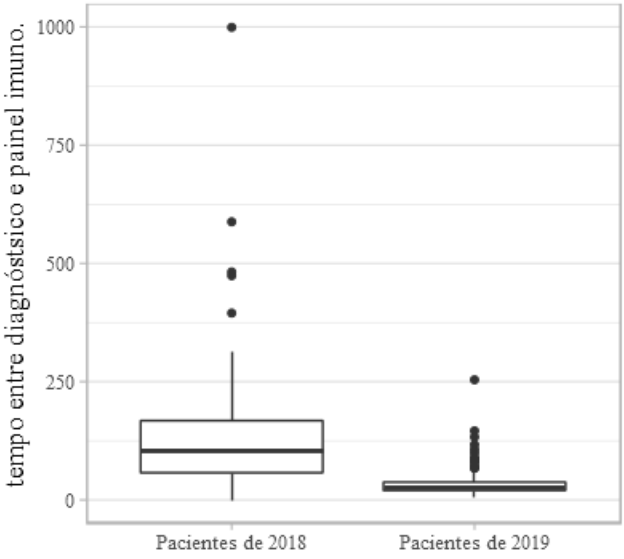


Figure 1. Distribution of time between diagnosis and immunohistochemical results, in days.

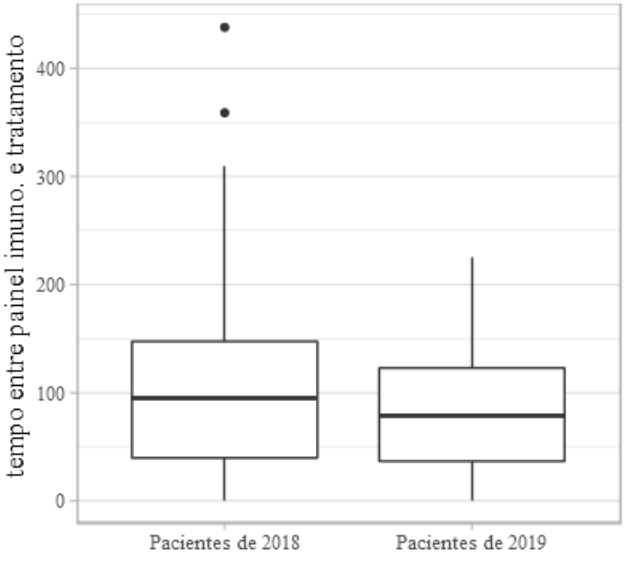


Figure 2. Distribution of time between immunohistochemical results and start of treatment, in days.

Regarding the clinical staging of patients, our data agree with an earlier study that showed a prevalence of clinical stage II in patients[11], as seen in both periods analyzed in our study.

In the BIRADS classification of patients, there was a prevalence of classification IV in both periods, data that agree with what was described in a study in which 34.7% of patients were classified as having BIRADS IV[12].

Regarding the histological type, our finding is similar to that published in another study that demonstrated that 76.9% of the patients analyzed had the invasive ductal histological type[13]. In the present study, 87.6% had this same histological type. Data referring to the immunohistochemical panel of the patients analyzed are in agreement with a study that demonstrated that most of the patients analyzed had luminal A[14].

The prevalent elapsed time interval between diagnosis and immunohistochemical results in the 2018 period agreed with an earlier finding that most of the patients analyzed had a time interval between diagnosis and immunohistochemical examination greater than 90 days[15]. In the 2019 period, most patients obtained their immunohistochemical results within 27 days after diagnosis, a reflection of the integration of FCECON in the Roche Laboratory Roche Testing program, enabling the complete evaluation of the immunohistochemical panel for breast cancer.

In 2019, most patients started treatment within an average interval of 85.8 days after the immunohistochemical results. These data agree with a study that demonstrated that most patients started treatment more than 60 days after immunohistochemical diagnosis[15].

This decrease in the time interval between diagnosis and the result of the immunohistochemical panel in 2019 compared to what was observed in 2018 contributed to the choice of personalized treatment for each patient, which before was often not possible, In 2018, obtaining the immunohistochemical panel was greatly delayed, exceeding the 90-day interval, so treatment was based on the staging of each patient.

In 2018, most patients underwent initial surgical treatment (71.8%), because of this large time interval to obtain the molecular panel results. Thus, many patients who had a triple-negative panel or overexpressed HER2, for example, did not benefit from the appropriate initial treatment for their molecular types. In 2019, with the possibility of obtaining immunohistochemical information sooner, there was a significant increase in patients who received chemotherapy as initial therapy (49.5%), a result of the molecular evaluation that enabled the identification of patients who would benefit from this initial therapy and thereby receive personalized treatment.

CONCLUSION

Immunohistochemical diagnosis is a very important factor in the appropriate choice of initial treatment for breast cancer patients, ensuring personalized treatment for these women. The present study demonstrates the importance of the public-private partnership in improving the times for the diagnosis and treatment of breast cancer.

AUTHORS' CONTRIBUTIONS

H.P.: Writing — original article.
R.P.: Writing — original article.
T.S.: Writing — original article.
H.P.: Writing — original article.
L.A.: Writing — original article.
V.A.: Writing — original article.
M.O.: Writing — original article.
M.S.: Writing — original article.
V.C.: Writing — original article.

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