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Evaluation of the histological and immunohistochemical subtype of breast cancer patients from a referral hospital in the inland of the state of São Paulo

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ABSTRACT

Introduction: The immunohistochemical markers used in breast cancer cases allow the classification of tumors into four subtypes: luminal A (1), luminal B (2), HER2 positive (3), and triple-negative or basal-like (4). This study aimed to evaluate the histological and immunohistochemical profile of breast cancer patients from a referral hospital in the inland of the state of São Paulo and understand the particularities of the prognosis based on the tumor-node-metastasis staging. **Methods:** This retrospective observational epidemiological cohort study was carried out at Hospital Regional de Presidente Prudente, with the first half of 2020 as the time frame. The research target population was women diagnosed with breast cancer who underwent immunohistochemical examination. We excluded patients with breast carcinoma *in situ* and incomplete medical records, which made data analysis impossible. After classifying the cases into four molecular subtypes based on immunohistochemistry, identifying the histological grade, and verifying the pathological staging criteria, we gathered the data and addressed the pathological-prognostic staging to investigate the prognosis of each patient. **Results:** We analyzed 49 patients with a complete immunohistochemical profile. Among them, luminal A (44.9%) was the most prevalent molecular subtype, followed by luminal B (36.7%). The least prevalent subtypes were triple-negative (16.8%) and HER2 (2%). Pathological-prognostic staging was possible in 73.5% of cases. **Conclusions:** The molecular subtype is important for tumor evaluation and has direct implications for the staging of breast cancer patients.

KEYWORDS: breast neoplasms; immunohistochemistry; histology.

INTRODUCTION

Breast cancer is the most common neoplasm in women worldwide, totaling 24.2% of cancer cases in 2018[1]. In Brazil, it is the second most prevalent type of cancer among women, behind only non-melanoma skin cancer[2]. Over the past few years, the significant increase in the incidence of breast cancer in populations of both developed and developing countries has attracted attention[3]. Moreover, breast cancer stands out for its high mortality rate, holding second place in the number of deaths among women with malignant tumors, as well as for the impact produced by its locoregional and systemic treatment[2,4].

Immunohistochemical (IHC) markers for breast tumors are based on a panel of antibodies that provide a breast cancer prognosis and help determine the treatment[5]. IHC analyses allow defining the tumor molecular profile and determining the type of genetic mutation and expressed proteins, which facilitates the elaboration of the therapeutic approach[6]. These markers include: progesterone receptor (PR), estrogen receptor (ER), human epidermal growth factor receptor 2 (HER2), and Ki-67 protein, in addition to tumor size and grade[3,5].

PR and ER are hormone receptors expressed by less aggressive tumors, used to evaluate the indication for hormone therapy, have a better prognosis, and are found in most breast carcinomas[7,8]. HER2 overexpression is relatively common in breast cancer cases, with significant importance in tumor growth. It is associated with malignant tumors of high histological grade and high proliferation index and is closely related to the likelihood of disease relapse and patient survival[7,9,10].

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In turn, the Ki-67 protein is the main involved in tumor proliferation marking, although not evaluated as an isolated marker. Still, it is a determinant for the molecular differentiation of breast tumors defined as luminal A and luminal B[7,11,12].

Invasive breast cancer can be classified into the molecular subtypes: luminal A, luminal B, HER2 positive, and triple-negative or basal-like. They allow discriminating patients and improving therapeutic management[7,13]. Each subtype was correlated with the following factors: incidence, prognosis, organ preference of metastasis, response to treatment, recurrence, or survival[11].

Luminal carcinomas, classified as luminal A and luminal B, are the most frequent[2]. The luminal A subtype (LAS) is the most common, with low histological grade and low mitotic activity. Its IHC study reveals the presence of ER and/or PR, with HER2 negative and Ki-67 index less than 14%, meaning less invasive tumors responsive to targeted therapy[13,14].

The luminal B subtype (LBS) has a more aggressive phenotype and, unlike LAS, presents a high histological grade and greater mitotic activity, defined from an IHC perspective by the presence of ER, with HER2 negative and high Ki-67 index (above 14%) or ER and HER2 positive[13].

Tumors classified as HER2 positive are defined by the presence of HER2 and absence of ER and PR, with high histological grades and a great propensity for metastasis[13]. The basal-like subtype or triple-negative tumor does not have ER, PR, and HER2, expressing several genes in basal cells with high histological grade and mitotic index levels. It can be positive for the epidermal growth factor receptor and represents three out of four breast cancer cases with mutation in the *BRCA1* gene[13].

The molecular definition of breast cancer is often used in clinical practice[15,16]. However, IHC markers cannot establish a subtype intrinsic in any cancer. An effective marker should determine the prognosis (risk of recurrence or metastasis) and predictive factors (the benefit of treatment)[13,14].

In Brazil, the Southeast Region has the highest mortality rate from the disease (14.76 deaths/100 thousand women), exceeding the national mean of 13.84 deaths/100 thousand women in 2018[1].

Elaborating a treatment plan and establishing the prognosis of cancer patients are important steps that affect their survival[13]. Understanding the extent of the disease regarding molecular level, tumor aggressiveness, and predictive factors of breast cancer have proven to be a promising way to better define the patient's treatment and evaluate the risks of recurrence and relapse.

Considering these factors, as well as the high breast cancer incidence — which is increasing in economically active women — and mortality, the present study carried out an analytical retrospective assessment to understand the epidemiological profile of breast cancer patients in the west of São Paulo, Brazil. To that end, we adopted the IHC classification of invasive tumors, using as a prognostic evaluation factor the pathological tumor-node-metastasis (TNM) staging, described in the eighth edition of the American Joint Committee on Cancer (AJCC) manual[17].

This work aimed to evaluate the histological and IHC profile of breast cancer patients from a referral hospital in the inland of the state of São Paulo and understand the particularities of the prognosis based on the TNM staging.

METHODS

This retrospective observational epidemiological cohort study was carried out at Hospital Regional de Presidente Prudente (HRPP), located in the inland of the state of São Paulo, in the first half of 2020.

The research target population was women diagnosed with breast cancer followed at the mastology service of the hospital. The total number of patients with ICD10 C50 (malignant neoplasm of breast) followed was 950.

The proportion used to calculate the study sample was p=0.8545, a value based on the study by Peruzzi and Andrade (2016), in which 85.45% of patients could be classified according to IHC. The chosen sample has a 98% confidence level and a 3% margin of error, with 419 medical records to evaluate[18].

The inclusion criteria were females with breast cancer, who underwent IHC examination, diagnosed by core biopsy or surgery to remove the neoplasm with anatomopathological study. The exclusion criteria were defined as patients with breast carcinoma *in situ* and incomplete medical records that made data analysis impossible.

Data were collected from electronic records of patients treated in the determined time frame. Anatomopathological and IHC reports were prepared by a third-party laboratory that provides service to the hospital.

Following data collection and evaluation of IHC findings, four molecular subtypes were identified: luminal A (ER+ and/or PR+, HER2-, and Ki-67<14%); luminal B (ER+ and/or PR+ and/or HER2+, and Ki-67≥14%), triple-negative (ER-, PR-, and HER2-), and HER2 (ER-, PR-, and HER2+). After detecting the histological grade, classifying the molecular subtype, and verifying the pathological staging criteria, we gathered the data and addressed the pathological-prognostic staging to investigate the prognosis of each patient. We applied the criteria established by the eighth edition of the AJCC to determine all patients' anatomic and pathological-prognostic staging.

Microsoft Excel and RStudio were used to treat and analyze the data. The tests used to compare variables among the groups were: χ^2 for categorical ones, Kendall's Tau-b correlation coefficient for ordinal ones, and ANOVA for quantitative ones. The significance level adopted in all tests was 5%, and the results were expressed as frequency distribution for categorical variables and summary measures for quantitative ones.

RESULTS

The study population sample comprised women diagnosed with breast cancer at Hospital Regional de Presidente Prudente/São Paulo from January to June 2020, retrieved from the hospital system using the filter ICD C50 (n=950). Nonetheless, the system could not accurately quantify and retrieve the number of patients. During the study, the analysis of medical records revealed that only 73 cases had a diagnosis with anatomopathological confirmation; 30 of them were diagnosed by core biopsy — the biopsy type was not evaluated in this study —, and only 13 had a complete IHC profile, and thus were included in the study. In 15 cases, the IHC profile was incomplete (HER2 and/or Ki-67 absent), preventing molecular classification, and the remaining two cases corresponded to ductal carcinoma *in situ*. A total of 43 patients were diagnosed by surgery, of whom 36 had a complete IHC profile and met the inclusion criteria of this study. Five cases were diagnosed with ductal carcinoma *in situ*, one with phyllodes tumor, and one could not be classified because the HER2 result was unreliable and the fluorescence *in situ* hybridization (FISH) test that could confirm it was not found in the medical records, leading to the patient's exclusion from the study.

Thus, the study included 49 cases (n=49) (Table 1). The total population was female, and the mean age was 58.1 years (standard deviation ±10.5), with a median of 55 years. In 38 records (77.5%), the patients were aged 50 years or older, and 11 (22.5%) were under 50 years.

In 13 cases (26.5%), the anatomopathological diagnosis was established by biopsy, while 36 (73.5%) were performed after surgery.

Another item analyzed was the type of surgery, of which the most prevalent was breast-conserving surgery, performed in 20 patients (55.6%), followed by mastectomy in 16 (44.4%). Although the molecular subtypes were quite proportional regarding the type of surgery, cases with triple-negative and HER2 tumors were more frequent in mastectomies (Figure 1). Most surgeries were performed in January (nine — 25%), February (seven — 19.4%), March (nine — 25%), and June (six — 16.7%) 2020. On the other hand, the number of these procedures dropped in April, with four (11.1%) surgeries registered, and in May, with only one (2.8%).

The most prevalent histological differentiation grade was G3 (high combined differentiation grade), with 17 cases (35.4%), followed by G2 (intermediate combined differentiation grade), with 14 (29.2%), G1 (low combined differentiation grade), with 10 (20.8%), and in seven cases (14.6%), the differentiation grade could not be assessed.

As for histological classification, the most common type was invasive carcinoma of no special type (NST), recorded in 39 cases (79.6%), followed by five cases (10.2%) of invasive lobular carcinoma, three (6.1%) of invasive papillary carcinoma, one (2%) of mixed invasive carcinoma (ductal and lobular), and one (2%) of microinvasive carcinoma.

Table 1. Participant characteristics regarding histological and immunohistochemical classification.

	Category	n (%)
Histological grade	G1 (low combined grade)	10 (20.8)
	G2 (intermediate combined grade)	14 (29.2)
	G3 (high combined grade)	17 (35.4)
	GX (could not be assessed)	7 (14.6)
Molecular classification	HER2	1 (2)
	Luminal A	22 (44.9)
	Luminal B	17 (36.7)
	Triple-negative	8 (16.3)
Progesterone receptor	Positive	39 (79.6)
	Negative	10 (20.4)
Estrogen receptor	Positive	40 (81.6)
	Negative	9 (18.4)
HER2[a]	Positive	2 (4.1)
	Negative	47 (95.9)
Ki-67[b]	High	27 (55.1)
	Low	22 (44.9)
Histological classification	Microinvasive carcinoma	1 (2)
	Invasive carcinoma of no special type	39 (79.6)
	Invasive papillary carcinoma	3 (6.1)
	Mixed invasive carcinoma	1 (2)
	Invasive lobular carcinoma	5 (10.2)
Age	Mean ± standard deviation	58.1±10.5
	Median (min–max)	55 (44–81)
	<50 years	11 (22.5)
	≥50 years	38 (77.5)

[a]HER2: human epidermal growth factor receptor 2. [b]Ki-67: proliferation index

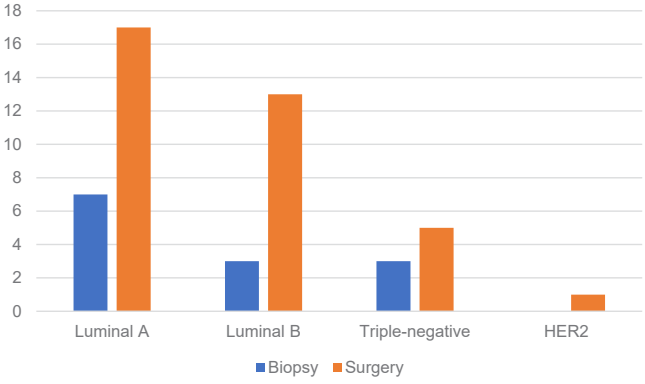

Figure 1. Distribution of subtypes regarding the type of diagnosis.

PR was positive in 39 cases (79.6%) and negative in ten (20.4%), while ER was positive in 40 (81.6%) and negative in nine (18.4%); HER2 was positive in two (4.1%) and negative in 47 (95.9%); and the Ki-67 protein had a high differentiation grade in 27 cases (55.1%).

Regarding the IHC classification, the predominant molecular subtype was luminal A, recorded in 22 cases (44.9%), followed by luminal B in 17 (36.7%), triple-negative in eight (16.3%), and HER2 in one (2%).

In findings resulting from biopsy, the luminal A subtype was the most common — identified in seven patients (53.8%) —, followed by luminal B in three (23.1%) and triple-negative in three (23.1%). In cases diagnosed by surgery, the main subtype was luminal A, found in 17 women (47.2%), followed by luminal B in 13 (36.1%), triple-negative in five (13.9%), and HER2, the least incident, detected in one patient (2.8%) (Figure 2).

The TNM evaluation, also called pathological staging, occurred after the surgical procedure. Thus, 36 cases (73.5%) could be evaluated as to tumor size, involvement of lymph nodes, and presence of distant metastasis by anatomopathological study, following the criteria described in the eighth edition of the American Joint Committee on Cancer (AJCC) manual (Table 2).

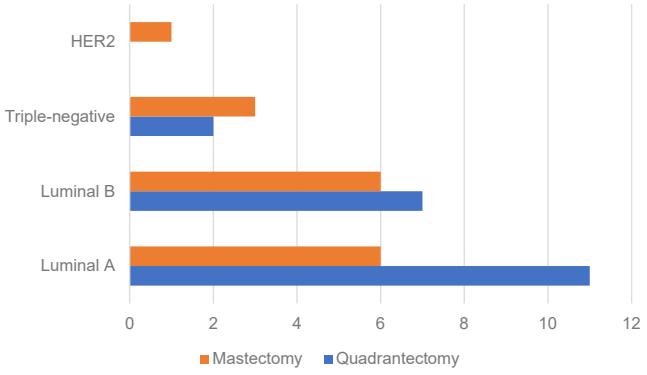

Figure 2. Distribution of subtypes regarding the type of surgery.

Table 2. Distribution of the findings as to tumor-node-metastasis (n=36).

TNM	Categories	n (%)
pT[a]	T1	15 (41.7)
	T2	13 (36.1)
	T3	2 (5.6)
	T4	6 (16.7)
pN[b]	N0	20 (55.6)
	N1	7 (19.4)
	N2	2 (5.6)
	N3	7 (19.4)
pM[c]	M0	31 (86.1)
	M1	1 (2.8)
	MX	4 (11.1)

[a]pT: tumor; [b]pN: node; [c]pM: metastasis.

The remaining 13 cases could not be analyzed because they were diagnosed by biopsy, which would compromise the assessment of the above criteria.

With respect to the extent of the primary tumor, 15 cases (41.7%) were in T1; 13 (36.1%) in T2; two (5.6%) in T3; and six (16.7%) in T4. Concerning lymph node involvement, 20 patients (55.6%) were in stage N0, seven (19.4%) in N1, two (5.6%) in N2, and seven (19.4%) in N3. Only one case (2.8%) had distant metastasis at diagnosis, while another 31 (86.1%) had no distant metastasis, and four (11.1%) could not be assessed.

The anatomic staging could be evaluated in the 36 cases (73.5%) to which TNM was applied, revealing 12 (33.3%) cases in stage IA; one (2.8%) in stage IB; seven (19.4%) in stage IIA; five (13.9%) in stage IIB; one (2.8%) in stage IIIA; three (8.3%) in stage IIIB; six (16.7%) in stage IIIC; and one (2.8%) in stage IV.

The prognostic staging (Table 3) by TNM analysis was possible in 35 cases (71.4%); one case could not have its histological grade assessed, leading to the non-classification of its prognostic staging. Of the 35 records, 17 (48.6%) were classified as stage IA, with a prevalence of low (41.2%) and intermediate (41.2%) combined histological grade (p=0.002) and LAS (76.5%; p=0.005), as described in Table 3.

Five cases (14.3%) were categorized into stage IB, with a preponderance of high combined histological grade (60%; p=0.002) and LBS (80%; p=0.005), and one (2.9%) into stage IIA, with high combined histological grade (100%; p=0.002) and triple-negative subtype (100%; p=0.005). One case (2.9%) was also recorded in stage IIB, with intermediate combined histological grade (100%; p=0.002) and LAS (100%; p=0.005).

In three cases (8.6%), the stage found was IIIA, with a predominance of intermediate combined histological grade (two — 66.7%; p=0.002) and LAS (two — 66.7%; p=0.005). The three stage IIIB cases (8.6%) had high combined histological grade (three — 100%; p=0.002) and LBS (three — 100%; p=0.005).

Stage IIIC had four cases (11.4%), with a prevalence of high combined histological grade (three — 75%; p=0.002) and triple-negative subtype (three — 75%; p=0.005). Only one case (2.9%) was classified into stage IV, with a high combined histological grade (one — 100%; p=0.002) and LBS (one — 100%; p=0.005).

DISCUSSION

Prior to the incorporation of the Ki-67 index by the St. Gallen consensus (2011) as a criterion to differentiate molecular subtypes of breast cancer, luminal A showed a significant prevalence compared to luminal B. Previous studies had a predominance of LAS (from 50% to 60% of cases), while the prevalence of luminal B ranged from 10% to 20%[19].

LAS and LBS remained the most common in breast cancer cases, but the number of tumors classified as luminal B increased with the addition of the Ki-67 index[20]. This could be noted in some

Table 3. Correlation between pathological-prognostic staging and type of surgery, tumor histological grade, and molecular subtype (n=35).

	Prognostic staging								p-value*
	IA (%)	IB (%)	IIA (%)	IIB (%)	IIIA (%)	IIIB (%)	IIIC (%)	IV (%)	
Type of surgery									
Mastectomy	4 (23.5)	3 (60)	0 (0)	0 (0)	2 (66.7)	2 (66.7)	4 (100)	0 (0)	0.095
Quadrantectomy	13 (76.5)	2 (40)	1 (100)	1 (100)	1 (33.3)	1 (33.3)	0 (0)	1 (100)	
Histological grade									
G1[a]	7 (41.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.002
G2[b]	7 (41.2)	2 (40)	0 (0)	1 (100)	2 (66.7)	0 (0)	1 (25)	0 (0)	
G3[c]	1 (5.9)	3 (60)	1 (100)	0 (0)	1 (33.3)	3 (100.0)	3 (75)	1 (100.0)	
GX[d]	2 (11.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Subtype									
HER2[e]	1 (5.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Luminal A	13 (76.5)	1 (20)	0 (0)	1 (100)	2 (66.7)	0 (0)	0 (0)	0 (0)	0.005
Luminal B	3 (17.6)	4 (80)	0 (0)	0 (0)	0 (0)	3 (100)	1 (25)	1 (100)	
Triple-Negative	0 (0)	0 (0)	1 (100)	0 (0)	1 (33.3)	0 (0)	3 (75)	0 (0)	

*p-value of the tests: X^2 for categorical variables; Kendall's tau-b correlation coefficient for ordinal variables; and ANOVA for quantitative variables. [a]G1: low combined grade; [b]G2: intermediate combined grade; [c]G3: high combined grade; [d]GX: could not be assessed; [e]HER2: human epidermal growth factor receptor 2 positive.

regional studies published after the change in classification[21,22]. Our study sample showed a higher prevalence of LAS, with 44.9% of cases, followed by LBS, which corresponded to 36.7% of records. A weakness of this research is the sample size for restricting the comparison with other data from the literature.

A multicenter study in Brazil evaluated the IHC classification in the country's five geographic regions to identify the predominance of hormonal subtypes. The prevalence varied among the subtypes: luminal A, from 24.1% to 30.8%; luminal B, from 30.8% to 39.5%; triple-negative, from 14% to 20.3%; and HER2, from 6.7% to 13.5%[22]. Carvalho et al. also used a triple-positive category, which we included in LBS, with a variable prevalence between 9.7% and 12.9%[22]. Some particularities found refer to the South and Southeast regions, which had a higher number of luminal A cases. The population of the Southeast region showed a profile with a prevalence of LBS and the second highest proportion of luminal A and ER/PR positivity[22]. The research highlighted that this region has the second-largest white population in the country. Still, this comparison is irrelevant to our investigation since we did not evaluate the population's race and skin color[22].

Cintra et al. found a predominance of LBS, while triple-negative had the second highest incidence (Table 4), which the authors associated with cases of younger women[21]. In that study, the authors adopted two classifications for LBS, dividing it into luminal B HER2 positive and luminal B HER2 negative, both included in LBS[21]. Therefore, the findings disagree with those of Carvalho et al., but we can still identify that the prevalence of luminal subtypes is higher in both[21,22].

Table 4. Relationship between studies.

	Authors		
	Carvalho et al.	Cintra et al.	This study
Mean age	55.5	57.4	58.1
Distribution (%)			
Luminal A	28.8	17.1	44.9
Luminal B	53.5	52.6	36.7
HER2	7.9	6	2
Triple-negative	9.7	24.2	16.3

HER2: human epidermal growth factor receptor 2.

A problem in differentiating luminal subtypes results from the difficulty in defining an optimal cut-off value for Ki-67. There is a discussion that the index value should range from 20% to 29%[23]. This value was tested in the study by Haarbeck et al., who adopted a 20% cut-off value to evaluate the repercussion of Abemaciclib use on adjuvant breast cancer therapy, considering ≥20% a high proliferation index and <20% a low proliferation index. The results showed prognostic value because the treatment indicated for patients with high proliferation (≥20%) improved invasive disease-free survival[24]. Establishing an optimal cut-off value is relevant for clinical routine since defining the molecular subtype classification directly impacts the treatment. LAS has a higher endocrine response, low cell proliferation, and progresses with a good prognosis, while LBS presents a lower endocrine response, high cell proliferation, and a worse prognosis compared to luminal A[13,16,22].

A question to be raised would be the use of the Ki-67 index. Looking for a more accurate evaluation method for the differentiation index, Horii et al. found that these rates are often subjective and rater-dependent[25]. The same image analyzed by an image evaluation system and compared with the conclusions of three pathologists had different results[25]. The analysis system showed a mean proliferation index of around 12.8%, while, according to the pathologists' evaluation, the rates varied in 15.1%, 19%, and 22.7%[25]. These variations are important findings that may change the molecular classification and explain the high proportion of LBS in studies such as those by Carvalho et al. And Cintra et al.[21,22,25].

More modern tests with greater sensitivity are available, ensuring treatment against breast cancer. These markers are Oncotype DX® and MammaPrint®[26,27]. The TAILORx study used the Oncotype DX® molecular test, with 21 genes, in about 10 thousand breast cancer patients from several countries and, according to their findings, 70% of women with primary breast cancer, negative axillary lymph nodes, and intermediate recurrence score could avoid chemotherapy[26]. The MINDACT study screened patients diagnosed with early-stage breast cancer and HER2 negative, evaluating 70 genes; after screening these patients, the study found that chemotherapy was unnecessary in about 46% of cases[27]. Nonetheless, given the economic profile of the Brazilian population and the high cost of these markers for the public health system, the definition of these subtypes must be more accurate. A better-defined cut-off value and better analysis of the proliferation index by the pathologist can improve the indication of an optimal treatment for these patients[23].

The incidence of ER and PR was close in percentage levels — positive in 81.6% and 79.6%, respectively. The high expression of these markers was also found in the study by Carvalho et al., who detected an 82.8% prevalence in the Southeast Region[22]. In our study, the HER2 marker corresponded to 4.1% of the sample, while Carvalho et al. found a 17.6% rate[22]. The incidence of this marker is lower in the population; however, the small result found in this investigation is directly related to the sample size. Thus, analyzing a larger number of patients is necessary for a more effective comparison.

The mean age at diagnosis was 58.1 years, similar to that of the study by Cintra et al., whose mean age at diagnosis was 57.4 years, and Carvalho et al., with a mean age of 55.5 years. In addition, most patients in our research were in the age group from 50 to 59 years, corroborating estimates that describe a higher incidence of breast cancer in women over 50 years in Brazil[21,22].

The predominant histological types were NST (79.6%) and invasive lobular carcinoma (10.2%), data similar to those found in the study by Cintra et al., which presented 73.3% of NST cases, followed by invasive lobular carcinoma (9.8%)[21].

The number of surgeries decreased in April and May compared to January, February, and March 2020. This period was marked by the beginning of the COVID-19 pandemic in Brazil.

The study by Ribeiro et al. investigated the effects of the pandemic on cancer diagnosis and treatment in Brazil, detecting a reduced number of surgeries in cancer patients in 2020 compared to 2019 data. In the Southeast Region, this reduction reached 15%. However, the present research only focused on data from January to June 2020, so we cannot confirm this decrease[28]. In Hospital Regional de Presidente Prudente, the demand for oncological care, which was maintained, and surgeries decreased.

The analysis of pathological-prognostic staging revealed that the study population presents less advanced stages of the disease. The study by Knutsvik et al. compared patient survival according to tumor molecular subtypes, and the findings showed that, since diagnosis, LAS had better patient survival over time, while the HER2 subtype was associated with the worst survival rate[29].

This comparison is irrelevant to our research; nevertheless, most LAS cases recorded staging between IA and IB, and no case had a stage greater than IIIB. LBS was related to more advanced stages of the disease in patients in stages IIIB, IIIC, and IV.

On the other hand, the HER2 subtype, which usually has a higher cell differentiation grade and a greater propensity to metastasis, was related to a lower prognostic stage (IA)[13,30]. In this case, we underline that this result was limited by the number of cases found in the study, that is, the small sample, which prevents its confirmation.

In our investigation, the type of surgery had no impact on disease prognosis, but the rate of radical surgery was lower in the population involved. Kang et al. found a reduced number of mastectomies in the population of South Korea in 2020 compared to the total recorded in the pre-pandemic period. We cannot confirm this finding, as we would need to compare it with the total surgeries in the same period in 2019[31].

A difference was detected in findings related to anatomic staging and pathological-prognostic staging (Figure 3). This difference occurs because the anatomic staging involves characteristics such as lesion size and presence of lymph node or distant metastases. In addition, the prognostic staging assesses

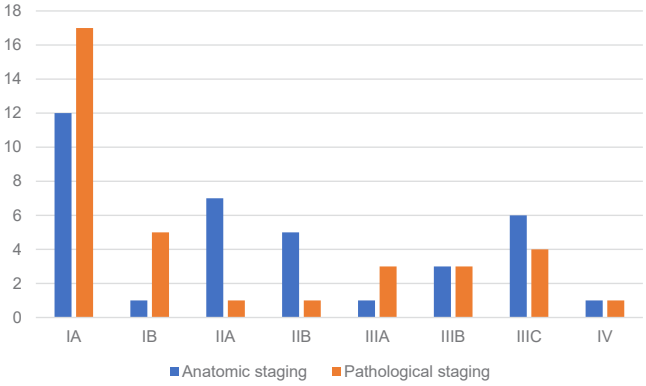

Figure 3. Distribution of findings related to anatomic and pathological-prognostic staging.

the histological grade of the tumor and the presence or absence of hormone receptors (ER and PR) and HER2. Currently, the Oncotype Dx® genomic test can also be evaluated[32].

Prospective studies have shown greater accuracy when evaluating the pathological-prognostic staging to define patient management[32]. Yet, as the objective of this study was only to investigate whether molecular subtypes influenced the disease staging, no adjuvant therapy was analyzed; thus, no further statements on the subject are pertinent.

We found a variation in the prevalence of tumors in Brazil. Hospital Regional de Presidente Prudente is a reference in the care of breast cancer patients for the population of the western region of the state of São Paulo. Although regional studies of the Brazilian population revealed a prevalence of LBS, the analysis of this population based on the evaluation of tumor molecular types shows that most of the population assessed herein is in the age group above 50 years, which is expected, as neoplasms tend to be more prevalent after the fifth decade of life[2]. Having said that, LBS has an important relationship with breast cancer cases in younger women, mainly because they have higher cellular activity. The lower prevalence of LBS compared to LAS is in line with what is found in the literature, given the lower incidence of the disease in women under 50 years in this study[13].

However, because the sample of this study is small, we would need more time and a larger population sample to make a statement about the profile of these patients with more accurate results, in addition to evaluating the relationship between tumor type and its impact on disease-free survival, considering that knowing the epidemiological profile of breast cancer leads to the formulation of better treatment strategies for patients.

CONCLUSIONS

Analyses of IHC markers are relevant for the classification of the neoplasm molecular subtype and influence the staging of breast cancer patients. The molecular subtype is significant to the pathological-prognostic staging. Understanding these analyses enables more appropriate clinical management of these patients.

AUTHORS' CONTRIBUTION

ICS: Conceptualization, Data curation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. GAAF: Conceptualization, Data curation, Methodology, Writing – original draft. TRM: Conceptualization, Data curation, Methodology, Writing – original draft. SUS: Formal Analysis, Investigation, Methodology, Software, Writing – original draft. RSS: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

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