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Ductal carcinoma of the breast: morphological aspects according to the age

Carcinoma ductal da mama: aspectos morfológicos de acordo com a idade

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ABSTRACT

Introduction: Breast cancer is the most common cancer in women worldwide, and its morphological characteristics, despite the current molecular classification, also provide important information about the pattern of this disease. **Objective:** To analyze the morphological characteristics of invasive ductal breast carcinoma among women older and younger than 50 years. **Method:** 302 cases of invasive ductal carcinoma patients treated at the Division of Mastology of the Universidade Federal do Ceará, in the period 2005-2014, aged ≤ 50 years and older. The following morphological characteristics were analyzed: larger tumor diameter (TD), lymph node metastasis (MX), and histological grade (HG). **Results:** The mean age of patients was 55.6 years. The average tumor size was 3.4 cm, 40% of tumors have diameter ≤ 2 cm and 60% > 2 cm. As for the histological grade, 23.7% were grade 1, 32.1% grade 2, and 42% grade 3. Axillary metastasis were present in 66% of the cases and 34% did not. Women aged ≤ 50 years had fewer tumors grade 1 ($p = 0.002$), compared with grades 2 and 3. Women older than 50 years had more grade 3 tumors ($p = 0.002$), and more tumors larger than 2 cm diameter ($p < 0.001$). The presence of metastasis predominated in both age groups when analyzed separately ($p < 0.001$). **Conclusion:** Women older than 50 years had larger and more morphologically undifferentiated tumors. Women aged ≤ 50 years had less well-differentiated tumors. There were no differences in morphology between these two age groups when compared each other.

Key words: breast neoplasms; surgical pathology; age distribution.

INTRODUCTION

Breast cancer is the most common malignant neoplasm in women worldwide. It is currently the second leading cause of cancer death in women. The first cause of death is by lung cancer[1-3]. In Brazil, it has been observed a slight increase in the number of cases detected in recent years[4], and most of whom are elder women with advanced stage of the disease[5, 6].

Tumor morphology characteristics provide important data for the initial approach to breast cancer treatment[7]. The introduction of neoadjuvant chemotherapy, for example, is used depending on the histological grade (HG) and tumor size, as well as the presence of metastases; HG is considered a good indicator of future disease development[8-11].

In order to standardize the morphological classification of breast cancer and to refine the clinical applicability of anatomopathological reports, the histological grade of Scarff-Bloom-Richardson (SBR) system was proposed, which, later was modified by Nottingham group, in which tumors are graded 1, 2 and 3 according to the structural and cellular findings[8, 12]. In 1991, its prognostic value was demonstrated for the first time[13] and, since then, several studies have validated it, which has made it a classification system recommended worldwide[14-24].

Currently, it is also known that tumor size has high prognostic value because it is directly related to disease severity. Tumors with larger diameters are associated with axillary lymph nodes involvement, and lower disease-free interval and higher mortality[25, 26].

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Another important characteristic is the involvement of axillary lymph nodes, because it is one of the most important prognostic factors of invasive breast carcinoma, whereas patients with no axillary metastasis have a better prognosis for both overall survival and for disease-free survival. The 10 year survival is related to the number of involved lymph nodes[7, 26-28].

The age at diagnosis establishes association with disease prognosis and, in terms of age group, women who develop breast cancer before their fifth decade of life usually have more aggressive disease and poorer prognosis[29-35].

OBJECTIVE

To analyze the relationship between HG, presence of axillary lymph node metastasis (MX), and tumor diameter (TD) with the age group of women undergoing breast resection in the Mastology Division of the Universidade Federal do Ceará (UFC), Fortaleza, Brazil.

METHOD

Sample

This is a retrospective study in which were selected 302 cases of breast cancer resected by mastectomy or quadrantectomy of patients treated at Mastology service of the Maternidade Escola Assis Chateubriant (MEAC), which belongs to the hospital complex at UFC, between January 2005 to December 2014. We selected cases of invasive ductal histologic type, which had surgical resection studied by the Department of Pathology and Forensic Medicine (Departamento de Patologia e Medicina Legal [DPML]). Cases of male patients, non ductal malignant neoplasms, and cases that did not have complete reports for the variable being studied, were excluded. The initial analysis helped to confirm a loss of 28 cases for HG variable, 61 cases for MX variable, and 32 for TD variable, all due to incomplete reports. Therefore, we effectively selected for this study: HG ($n = 274$), MX ($n = 241$), and TD ($n = 270$).

Data collection and analyzed variables

Case survey and anatomopathological reports were obtained through active search in DPML database of the School of Medicine (Faculdade de Medicina [FAMED]) of the UFC. A standardized form was used for data tabulation.

The patients were divided into two groups: women aged ≤ 50 years and women older than 50 years. The categories of each variable were statistically analyzed in each age group separately.

All cases were evaluated by a pathologist of the DPML/UFC experienced in mammary tumors. The following morphological characteristics were analyzed: larger TD, MX involvement, and HG, through Scarf-Bloom-Richardson (SBR) grading system modified by Elston and Ellis[13].

Data analysis

Statistical analysis was performed using the SPSS® software version 20.0, using the Chi-square test, considering $p < 0.05$ as statistically significant. This study was approved by the Research Ethics Committee (REC) of the pro-rector for research of the UFC, through Brazil Platform, under number 651.657.

RESULTS

We collected 302 cases of invasive ductal carcinoma during the study period. The average age of patients was 55.6 years ± 13.04. The minimum age was 29 years and the maximum was 93 years. Larger TD ranged from 0.1 to 22.0 cm, with average of 3.4 cm ± 2.95.

In the studied cases, we found a predominance of women older than 50 years ($n = 181$), representing 59% of sample. Regarding HG tumors, 3 were predominant in sample ($n = 121$), representing 44,2% of the cases identified. There was a predominance of tumors that had larger diameter exceeding 2 cm ($n = 162$, 60%). In addition, 66% of cases of axillary lymph nodes studied had metastases on this site ($n = 159$).

Women aged ≤ 50 years had fewer tumors grade 1 ($p = 0.002$); women aged > 50 years, had more grade 3 ($p = 0.002$), and larger tumor diameter ($p < 0.001$). The presence of metastases predominated in both age groups when analyzed separately ($p < 0.001$) (**Table**).

Correlating these variables with age, we observed that there was a higher concentration of cases showing HG 3 (**Figure 1**), TD > 2 cm (**Figure 2**), and MX involvement (**Figure 3**) in the group of women older than 50 years.

TABLE – Statistical correlation of morphological characteristics and age-groups with x^2 test

		Age-groups		Total	*p* value
		≤ 50 years	> 50 years		
HG	1	23	42	65	0.245
	2	41	47	88	
	3	44	77	121	
Total		108	166	274	
p value		0.002	0.002	-	
MX	Absent	30	52	82	0.580
	Present	64	95	159	
Total		94	147	241	
p value		< 0.001	< 0.001	-	
TD	≤ 2 cm	47	61	108	0.389
	> 2 cm	62	100	162	
Total		109	161	270	
p value		0.348	< 0.001	---	

HG: histological grade; MX: axillary metastasis; TD: tumor diameter.

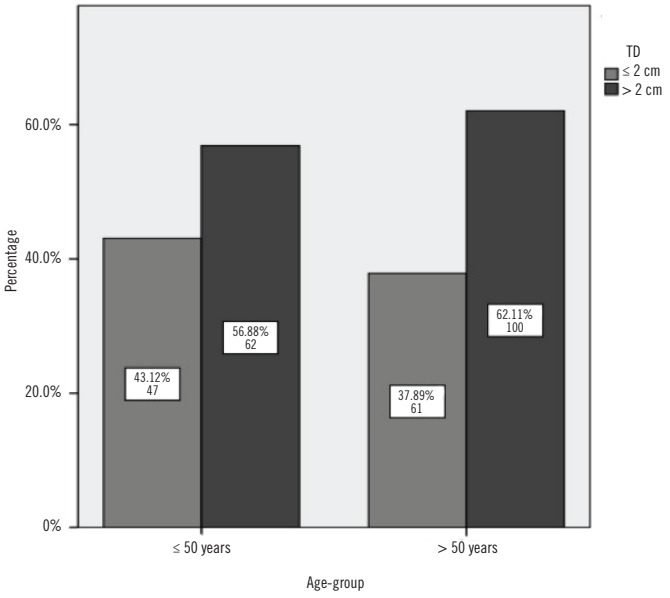

FIGURE 2 – *Frequency of TD grouped into women aged 50 years and younger or older TD: tumor diameter.*

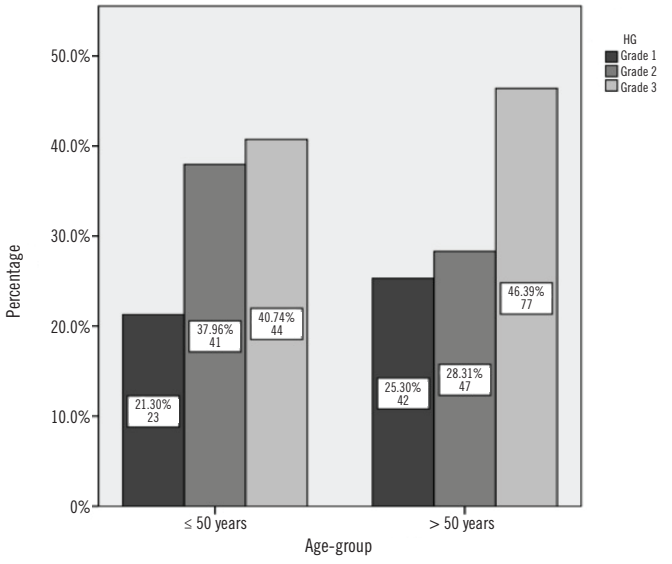

FIGURE 1 – *Frequency of HG grouped into women aged 50 years and younger or older HG: histological grade.*

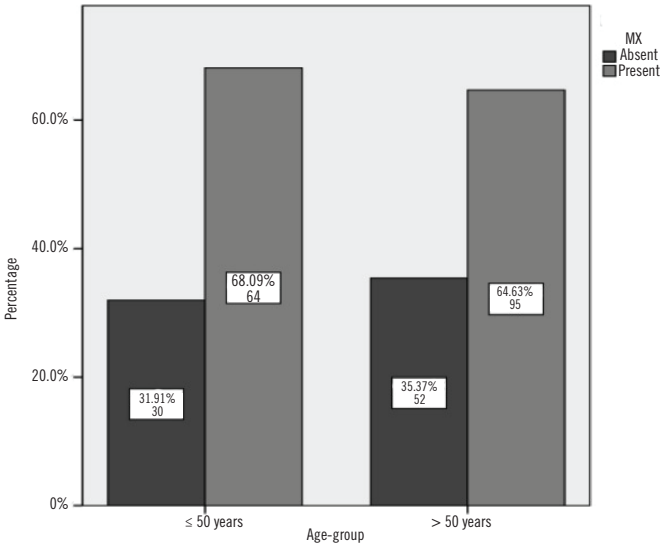

FIGURE 3 – *Frequency of MX grouped into women aged 50 years and younger or older MX: axillary metastasis.*

DISCUSSION

The current approach to breast cancer is increasingly establishing itself on the use of molecular factors and hormone receptors. However, the morphological characteristics of the tumor are still widely used for the management of appropriate treatment, such as the choice to neoadjuvant chemotherapy, for example[8-11]. Therefore, to understand even more deeply the histopathological profile in certain groups of patients may still be an important tool in decision-making.

The results showed high proportion of cases with MX involvement and HG 3, which gives quite aggressive profile and

undifferentiated tissue organization to the studied tumors. We believe that the prevalence of extensive tumors found is justified not only by the low-grade differentiation, but also for the delay to diagnose and institute the definitive therapy.

It is known that the prevalence of aggressive breast tumors is greater in younger women than in older women[29,31,36]. It has been shown that patients with HG 1 tumors have a better prognosis[8-11,17]. We also indirectly evidenced this fact when observed a few HG 1 tumors in women aged ≤ 50 years ($p = 0.002$).

Another finding which deserves attention is the large number of women aged ≤ a 50 years, diagnosed this service regardless of the morphological characteristics. When considering that in a period of ten years, more than 40% of diagnosed breast ductal carcinomas occurred in women aged ≤ 50 years, we believe it is a worrying situation that generates perspectives for future studies to justify such prevalence.

When comparing the TD between age groups, significant difference was not observed, and it was found that the sample was predominantly composed by tumor diameter > 2 cm. It is known that the high-grade of undifferentiated cancer directly contributes to the occurrence of larger tumors. However, it is important to ponder that the influence that not only late diagnosis exerts in these cases, but also the impact that the long time interval between diagnosis and surgical resection, either by social factors not addressed here, such as lack of information and access to health services, or potential resource limitations of this service, can exert in favor of such large number of extensive tumors.

When analyzed separately, women > 50 years showed prevalence of extensive tumors ($p < 0.001$). We believe that in addition to the possible limitations to diagnose and treat breast cancer previously mentioned, the prevalence of higher HG in this group ($p = 0.002$) has directly contributed to this finding.

Another determinant factor of grade of aggressiveness of the studied cases was the predominance of axils involved regardless of age group. We believe that this finding is due to the high number of large tumors in the total sample, since it is known that the size of the primary tumor has a direct correlated with MX occurrence, which has been reported in previous studies, in which patients with TD smaller than 1 cm, for example, presented 10%-20% risk of developing MX and, much higher risk in case of larger diameters[37,38]. This fact also confirms the predominance of more undifferentiated tumors found in the sample, which may have contributed to the large number of MX.

Finally, it is important to consider that the morphological characterization was obtained by histopathological reports from the medical files of this service. This limitation could impair the accuracy of the results. However, it is noteworthy that during the study period, the team that issued the reports was the same, consisting of specialized and with a high degree of expertise. In addition, it is a referral service with recognized technical quality. These facts minimize the possibility of error report and ensure the quality of the data reviewed here.

CONCLUSION

Based on the above considerations, we concluded that women aged > 50 years had larger and more undifferentiated tumors; women aged ≤ 50 years, presented less well-differentiated tumors, with no morphology difference between age groups when compared to each other.

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RESUMO

Introdução: *O câncer de mama é o câncer que mais acomete mulheres no mundo, e suas características morfológicas, a despeito da atual classificação molecular, ainda fornecem informações importantes sobre o comportamento desta doença.* ***Objetivo:*** *Analisar as características morfológicas dos carcinomas ductais invasivos da mama em mulheres acima e abaixo de 50 anos de idade.* ***Métodos:*** *Trezentos e dois casos de carcinoma ductal de pacientes do serviço de Mastologia da Universidade Federal do Ceará (UFC), no período de 2005 a 2014, com idade ≤ 50 anos e acima de 50 anos. Foram analisadas as seguintes características morfológicas: maior*

diâmetro do tumor (DT), presença de metástase axilar (MX) e grau histológico (GH). ***Resultados:*** *A idade média das pacientes foi de 55,6 anos; o tamanho médio dos tumores, de 3,4 cm. Quarenta por cento dos tumores possuíam diâmetro ≤ 2 cm e 60%, > 2 cm. Quanto ao grau histológico, 23,7% eram grau 1, 32,1%, grau 2 e 42%, grau 3. Sessenta e seis por cento dos casos apresentaram metástase axilar e 34% não. Mulheres com idade ≤ 50 anos apresentaram menos tumores grau 1 (*p = *0,002) em relação aos graus 2 e 3. Mulheres acima de 50 anos apresentaram mais tumores grau 3 (*p = *0,002) e mais tumores com mais de 2 cm de diâmetro (*p < *0,001). A presença de metástase predominou nas duas faixas etárias quando analisadas isoladamente (*p < *0,001).* ***Conclusão:*** *Mulheres acima de 50 anos apresentaram tumores maiores e de morfologia mais indiferenciada; mulheres com idade ≤ 50 anos, menos tumores bem diferenciados. Não houve diferença da morfologia entre as faixas etárias quando comparadas entre si.*

Unitermos: *neoplasias da mama; patologia cirúrgica; distribuição por idade*

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