J Bras Patol Med Lab. 2020; 56: 1-8.

10.5935/1676-2444.20200018

Ductal carcinoma *in situ* of the breast: correlation of architectural, cytological, IHC findings and recurrence analysis

Carcinoma ductal in situ *da mama: correlação dos achados arquiteturais, citológicos e IHQ e análise de recorrência*

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ABSTRACT

Objective: This study evaluated the histopathological features of ductal carcinoma *in situ* (DCIS), including cytological grade, architectural pattern and immunohistochemistry (IHC) in pure DCIS and DCIS associated with invasive carcinoma of no special type (ICNST). **Methods:** We evaluated a series of 232 cases of pure DCIS and DCIS associated with ICNST from a total of 399 breast carcinomas from a population consisting by women diagnosed with breast cancer and submitted to breast surgery from 2011 to 2015. **Results:** DCIS presented a mixed architectural pattern in most cases (56%); the solid subtype was the most common morphology (30%). High-grade DCIS was identified in 84/221 cases (38%), and comedonecrosis was present in 106/221 cases (48%). High-grade was more common in the solid subtype (61/155 cases, 39%, $p < 0.001$). Tumor size was greater in the presence of comedonecrosis than in the absence (mean 27 vs 20 mm, $p = 0.009$). Estrogen receptor (ER) was positive in 81% of cases with a cribriform pattern ($p = 0.013$). Greater locoregional recurrence was found in the comedonecrosis (15%) and micropapillary (19%) subtypes in DCIS associated with ICNST. **Conclusion:** We observed a greater relationship of ER with the low nuclear grade, while Ki-67 was related to the high-grade. DCIS presented a higher nuclear grade compared to ICNST. The less common pure pattern was the micropapillary, and the most common, the solid. Comedonecrosis was more frequent in the solid pattern. Our results showed that high-grade was more common in the solid and comedo subtype, and low-grade was more frequent in the cribriform.

Key words: non-infiltrating intraductal carcinoma; breast cancer; immunohistochemistry.

RESUMO

Objetivo: *Este estudo avaliou as características histopatológicas do carcinoma ductal* in situ *(CDIS), incluindo grau citológico, padrão arquitetural e imuno-histoquímica (IHQ) em CDIS puro e associado a carcinoma invasivo tipo não especial (CI-TNE).* ***Métodos:*** *Avaliamos uma série de 232 casos de CDIS puro ou associado ao carcinoma mamário invasivo de um total de 399 carcinomas mamários provenientes de uma população constituída por mulheres diagnosticadas com câncer de mama e submetidas à cirurgia mamária, entre 2011 e 2015.* ***Resultados:*** *O CDIS apresentou um padrão arquitetural misto na maioria dos casos (56%); o subtipo sólido foi a morfologia mais comum (30%). O CDIS de alto grau foi identificado em 84/221 casos (38%), e comedonecrose estava presente em 106/221 casos (48%). O alto grau foi mais comum no subtipo sólido (61/155 casos, 39%;* $p < 0,001$*). O tamanho do tumor foi maior na presença de comedonecrose do que na ausência (média 27* vs. *20 mm;* $p = 0,009$*). O receptor de estrogênio (RE) foi positivo em 81% dos casos com padrão cribriforme (*$p = 0,013$*). Maior recorrência locorregional foi encontrada nos subtipos comedonecrose (15%) e micropapilar (19%) no CDIS associado ao CI-TNE.* ***Conclusão:*** *Observamos uma maior relação do RE com o baixo grau nuclear, enquanto o Ki-67 relacionou-se com o alto grau. O CDIS apresentou mais alto grau nuclear em comparação com o CI-TNE. O padrão puro menos comum foi o micropapilar, e o mais comum, o sólido. A comedonecrose foi mais frequente no padrão sólido. Nossos resultados mostraram que o alto grau foi mais comum nos subtipos sólido e comedonecrose, e o baixo grau, mais frequente no cribriforme.*

Unitermos: *carcinoma intraductal não infiltrante; câncer de mama; imuno-histoquímica.*

First submission on 07/01/19; last submission on 08/20/19; accepted for publication on 08/20/19; published on 03/03/20

RESUMEN

Objetivo: *Este estudio evaluó las características del carcinoma ductal* in situ *(CDIS), incluyendo grado citológico, patrón arquitectural y inmunohistoquímica en CDIS puro y asociado a carcinoma invasivo tipo no especial (CI-TNE).* ***Métodos:*** *Evaluamos una serie de 232 casos de CDIS puro o asociado a carcinoma mamario invasivo procedentes de una población de mujeres diagnosticadas con cáncer de mama y sometidas a cirugía mamaria, entre 2011 y 2015.* ***Resultados:*** *El CDIS presentó un patrón arquitectural mixto en la mayoría de los casos (56%); el subtipo sólido fue la morfología más común (30%). El CDIS de alto grado fue identificado en 84/221 casos (38%), y comedonecrosis estaba presente en 106/221 casos (48%). El alto grado fue más común en el subtipo sólido (61/155 casos, 39%;* $p < 0.001$*). El tamaño del tumor fue más grande en presencia de comedonecrosis de lo que en su ausencia (promedio 27* vs. *20 mm;* $p = 0.009$*). El receptor de estrógeno (RE) fue positivo en el 81% de los casos con patrón cribiforme (*$p = 0.013$*). Se encontró mayor recidiva locorregional en los subtipos comedonecrosis (15%) y micropapilar (19%) en el CDIS asociado al CI-TNE.* ***Conclusión:*** *Observamos mayor relación del RE con bajo grado nuclear, mientras Ki-67 se relacionó con alto grado. El CDIS presentó grado nuclear más alto de lo que el CI-TNE. El patrón puro menos común fue el micropapilar, y el más común, el sólido. La comedonecrosis fue más frecuente en el patrón sólido. Nuestros resultados mostraron que el alto grado fue más común en los subtipos sólido y comedonecrosis, y el bajo grado, más frecuente en el cribiforme.*

Palabras clave: *carcinoma intraductal no infiltrante; cáncer de mama; inmunohistoquímica.*

INTRODUCTION

Ductal carcinoma *in situ* (DCIS), formerly an uncommon disease, now represents up to 10%-30% of all newly diagnosed breast cancers. This results largely from the detection of DCIS by mammography screening[1]. Due to the increase in the number of cases available for study, it has become clear that DCIS is a heterogeneous group of lesions with different characteristics[2, 3] and with different clinical outcomes[4, 5], reinforcing the need for a relevant histological classification system. The traditional system classifies DCIS according to the architectural patterns, the presence or absence of necrosis and the nuclear grade[6].

Many cases show more than one architectural pattern[2, 5, 7]. Among the DCIS characteristics, the architectural pattern and its prognostic value have been controversial[8]. Regarding grade, it is universally accepted that nuclear grade is an essential characteristic present in all classification systems already proposed and currently in use[9]. There is an association, though not consistent, between the nuclear grade and the architectural growth pattern. It is generally accepted that most of the micropapillary and cribriform *in situ* carcinomas are low nuclear grade and relatively indolent[10]. The DCIS comedo seems to be a more aggressive lesion. However, micropapillary DCIS was found associated with ipsilateral and contralateral recurrence of malignancy in multivariate analysis in a publication by Fisher *et al*. (2007)[11].

The aim of this study was to determine the frequencies of architectural subtypes and nuclear grade of a series of DCIS pure and associated to invasive breast cancer, in our reality, to correlate with clinical and histopathological characteristics and to evaluate the degree of agreement between *in situ* and invasive components in DCIS cases associated with invasive carcinoma, besides analyzing the recurrence of the disease in the studied groups.

PATIENTS AND METHODS

Study design and patient inclusion criteria

We selected 232 cases of DCIS pure or associated to invasive carcinoma of a series 399 consecutive mammary carcinomas from a population composed by women diagnosed with breast cancer and submitted to surgery and histopathological and immunohistochemical (IHC) study of the surgical specimen at the Laboratory of Pathology of São Rafael Hospital in Salvador, Brazil, from January 2011 to June 2015. Only women with a complete immunohistochemical panel and surgical and clinical treatment performed at the hospital were selected for this study. Ethics Committee approved protocol no. 1.400.421.

Data collection and study variables

The data were collected through an active search of medical records and IHC reports, based on the study variables. The following variables were collected: date of surgery, age at diagnosis (in years); type of surgery and lymph node involvement; tumor size measured in the surgical specimen by the pathologist; histological type; nuclear grade and histological grade; architectural pattern

of carcinoma *in situ*; surgical margin (categorized as free when ≥ 2 mm, close when < 2 mm, but no ink, and compromised when ink on tumor cells are present); IHC markers [estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2), Ki-67] evaluated in pure DCIS and in the invasive component when associated with DCIS; locoregional recurrence (LRR) disease, defined as a clinically and histologically documented ipsilateral breast relapse, and a regional recurrence as ipsilateral lymph node involvement, obtained from data collection performed until June 2016. The patients were followed up clinically after surgical treatment and were followed every three months in the first year and every six months thereafter. All cases were blind reviewed by one pathologist with practice in breast cancer.

Histology and IHC

The criteria defined by the World Health Organization (WHO) (2012)[12] and the College of American Pathologists (CAP) protocol 2012[13], were used for histopathological diagnosis and classification of DCIS and invasive carcinoma. DCIS nuclear grade was classified as low, intermediate or high based on nuclear size, chromatin pattern, pleomorphism, presence of nucleoli and mitotic activity. The histological grade of invasive carcinoma was assessed according to the Elston-Ellis modified by Bloom Richardson system[14, 15] and classified as low, intermediate or high based on an assessment of nuclear pleomorphism, tubule/gland formation, and mitotic count[12].

The architectural and cytological aspects of DCIS, the presence or absence of necrosis were evaluated. The main types of DCIS, according to the architectural growth pattern (micropapillary, cribriform, papillary, comedo and solid) were evaluated. DCIS was architecturally divided into pure/single, when > 90% of the *in situ* tumor presented only one architectural pattern, and mixed when the dominant pattern constituted < 90% of the *in situ* carcinoma.

The evaluation of ER and PR was performed using criteria adopted by the CAP during the period of time the reactions were performed. When 1% or more of the tumor cells showed marked nuclei, the tumor was considered positive[16]. In the assessment of HER2, the criteria proposed in the hercep test manual and accepted by the literature during the period of the tests were considered[17, 18]. Positive results are those with a score of 3+ (strongly positive) value and those with 2+ (weakly positive) value by IHC staining and showing HER-2 amplification based on fluorescence *in situ* hybridization (FISH)[17]. The Ki-67 labeling (clone MIB-1) on tumors classification was considered as a high proliferative index (tumors with labeled nuclei greater than 20%), and low proliferative index (tumors with less than 20%)[19, 20]. The antibodies used were clone 1D5 (ER), clone PgR636 (PR), clone SP3+5 (HER2).

Statistical methods

Statistical analyses were performed with SPSS, version 21.0 (SPSS, Inc., Chicago IL, 2012). The χ^2 test and, when necessary, Fisher's exact test were used to evaluate the association between architectural subtypes and grades of DCIS and the clinicopathological characteristics of prognostic importance. The *t*-test was used to compare age between groups. The weighted kappa test was used to assess the agreement between the nuclear grade of DCIS and the nuclear and histological grade of invasive carcinoma. Kappa values in the range of 0.21 to 0.40 showed a fair agreement[21]. All tests were conducted considering the significance level α of 0.05 and power (1-β) of 0.80.

RESULTS

Pure DCIS was detected in 51/232 cases (21.9%) and 181/232 (78%) was associated with invasive carcinomas of no special type (ICNST). There was no significant difference between the age at diagnosis in pure DCIS (51 ± 10.7 years) and DCIS associated with ICNST (53 ± 11.8 years) ($p = 0.669$). There was a significant difference on mean size between pure DCIS and DCIS associated with ICNST, mean 14.5 ± 11.4 mm vs 26.4 ± 21.6 mm ($p = 0$), and between DCIS size in the absence and presence of comedonecrosis (19.9 ± 16.6 mm vs 27.1 ± 23.1 mm) ($p = 0.009$).

As expected, there was a higher frequency of mastectomy compared to conservative surgery in the DCIS group associated with invasive 36.9% versus 20.5% in the pure DCIS group ($p = 0.039$). One hundred twenty-eight (71%) DCIS associated to ICNST and 5 (11%) in pure DCIS (five patients submitted to neoadjuvant QT) were submitted to chemotherapy; 128 (71%) DCIS associated to ICNST and 29 (66%) in pure DCIS to hormone therapy; 19 (16%) DCIS associated to ICNST and 1/20 (5%) in pure DCIS (patient submitted to neo-QT) to the trastuzumab; 153 (85%) DCIS associated to ICNST and 33 (75%) in pure DCIS to the radiotherapy.

Lymph node involvement was more frequent in the pure comedo pattern subtype with 60% vs 33.3% in the micropapillary subtype ($p = 0.882$) and was more frequent on high nuclear grade DCIS than on low grade, 46.8% vs 36.4% ($p = 0.357$). We found greater impairment of the surgical margin in pure DCIS (11.4%) compared to the margin of invasive associated with DCIS (6.1%)

($p = 0.308$). Nuclear grade and architectural patterns were not associated with margin status.

Architectural pattern in histological components of pure carcinoma *in situ* and associated with invasive carcinoma

DCIS with single architectural growth pattern was presented in 97 (44%) and 124 (56%) showed a mixed growth pattern. The DCIS with a single growth pattern was solid in 67 (30%), cribriform 15 (7%), micropapillary three (1%), papillary zero (0%) and comedo 12 (3%). Architectural pattern was mixed with solid in 171 (77%), cribriform in 129 (58%), micropapillary in 33 (15%), papillary in 21 (9%) and comedo in 106 (48%). A micropapillary component was presented in 11 cases of pure DCIS, all mixed with other growth patterns, and 24 cases of DCIS associated with ICNST. We observed that the solid pattern is the one that is most related to the invasive component with 131/165 (79%) ($p = 0.702$). The pattern least related to invasive was the micropapillary 21/32 (66%) ($p = 0.041$) (**Table 1**).

IHC and architectural pattern

Architectural pattern types of pure DCIS showed relationship only between the cribriform type and the ER-positive in 80.6% of cases ($p = 0.013$) and Ki-67 that presented low positivity (< 20%) in 74.2% ($p = 0.044$). We observed a higher frequency of hormone receptor positivity in the presence of the solid subtype ($p < 0.05$). The HER2 positivity presented higher frequencies in the micropapillary and comedonecrosis subtypes. High positivity for Ki-67 was present in higher frequency in the solid and comedonecrosis ($p < 0.05$) subtypes.

Cytological grade

DCIS associated with ICNST were high-grade in 65/160 (41%) and low-grade in 11/160 (7%) cases. DCIS without an invasive component were high grade in 44.2% (19/43) and low grade in 4.7% (2/43) cases ($p = 0.162$). Among the architectural patterns of DCIS, high-grade was more common in the solid (42%, $p < 0.001$) and comedonecrosis (57%, $p = 0$) subtype. Comedonecrosis was present in 106/221 (48%) DCIS cases, of which 37/67 (55.2%) cases in pure DCIS with solid pattern, 4/15 (26.7%) in cribriform, 1/3 (33.3%) in micropapillary ($p = 0.002$). Comedonecrosis was present in 57% of the high-grade tumors and only in 1% of the low-grade tumors ($p = 0$).

Recurrence analysis

The LRR frequency found was 1/44 (2.3%) in pure DCIS and 16/179 (8.9%) in DCIS associated with ICNST ($p = 0.077$). In initial tumors (TNM I-IIIA), the recurrence rate of DCIS was 1/32 (3.1%) and DCIS associated with ICNST was 10/150 (6.7%) ($p = 0.289$). Systemic recurrence in the initial tumors showed in DCIS was 1/32 (3.1%) and DCIS associated with ICNST was 15/150 (10%) ($p = 0.349$).

The analysis of locoregional recurrence in the different architectural patterns showed a higher frequency of recurrence in the micropapillary architectural pattern in DCIS associated with ICNST (**Table 2**). In DCIS associated with ICNST, LRR was 4/84 (5%) in the intermediate-grade and 9/65 (14%) in the high-grade, in the low-grade, meanwhile, 0/11 (0%) ($p = 0.207$).

Comparing the status of the surgical margin, we identified LRR in DCIS associated with ICNST in 13/151 (9%) cases with free margin, in 2/17 (12%) cases with close margin, and 1/11 (9%) with compromised margin ($p = 0.908$). In pure DCIS there was only 1/37 (3%) case of LRR in patients with free margin ($p = 0.927$).

DISCUSSION

In our series, we evaluated features which are well established as predictors of DCIS behavior[12, 22, 23] and may predict the risk of recurrence in women with DCIS including age, tumor size, linear

TABLE 1 – Correlation of the different pure and mixed architectural patterns of DCIS in the groups DCIS and DCIS associated with ICNST – number/total (%)

	Architectural patterns	Solid	Cribriform	Micropapillary	Papillary	Comedonecrosis
DCIS	Pure	12/67 (18%)	2/15 (13%)	0/3 (0%)	0/0 (0%)	3/12 (25%)
DCIS + ICNST	Pure	55/67 (82%)	13/15 (87%)	3/3 (100%)	0/0 (0%)	9/12 (75%)
DCIS	Mixed	34/165 (21%)	31/123 (25%)*	11/32 (34%)*	6/19 (32%)	24/105 (23%)
DCIS + ICNST	Mixed	131/165 (79%)	92/123 (75%)*	21/32 (66%)*	13/19 (68%)	81/105 (77%)

DCIS: ductal carcinoma in situ*; ICNST: invasive carcinomas of no special type;* *p < 0.05.*

TABLE 2 – LRR in different architectural patterns for DCIS and DCIS associated to ICNST – number/total (%)

LRR	Solid	Cribriform	Micropapillary	Papillary	Comedonecrosis
DCIS	1/32 (3%)	0/31 (0%)	0/11 (0%)	0/6 (0%)	0/22 (0%)
DCIS + ICNST	12/131 (9%)	4/91 (4%)*	4/21 (19%)	2/13 (15%)	12/81 (15%)*

LRR: locoregional recurrence; DCIS: ductal carcinoma in situ*; ICNST: invasive carcinomas of no special type;* *p < 0.05.

extent of resection margin, tumor grade, architectural subtype, IHC, and the presence of comedonecrosis[24, 25]. The age < 40 years was demonstrated as an independent prognostic factor for local recurrence, used in the Van Nuys-Silverstein Prognostic Index[23]. In our study, we did not observe an age difference between patients with pure DCIS or DCIS associated with invasive carcinoma.

It has been shown that DCIS without invasive carcinoma ER weak or negative occurs more frequently[26] when compared to DCIS associated with invasive carcinoma. The reason for this is unclear, it is speculated that it is possible that ER levels in DCIS may be increased only when the invasion develops in the surrounding tissues[27]. Poller *et al.* (1993)[28] reported that among 151 pure DCIS, 48 (32%) were ER-positive. The ER positivity was significantly associated with non-comedo type architectural patterns, low histological grade, small cell size, and lack of overexpression of HER2. On the other hand, micropapillary and cribriform carcinomas, characterized mainly by low or intermediate cytological grade, are commonly ER and PR positive[29]. We detected a relationship of the micropapillary with positive ER in 75%, whereas the cribriform presented ER positivity in 84%.

In our study, patients with high-grade DCIS were younger (50 ± 10.5 years) compared to patients with low-grade DCIS (58.7 ± 11.5 years). Patients with comedonecrosis tumors were younger (51 ± 11 years) compared to patients with non-comedonecrosis tumors (53.9 ± 11.3 years), agreeing with that found by Perez *et al.* (2014)[30]. The presence of a higher rate of high nuclear grade DCIS in the younger patients group may represent an increased risk of local recurrence when undergoing conservative surgical therapy[11].

We classified DCIS grade as high in 84 (38%) cases, intermediate in 106 (48%), and low in only 13 (6%) cases. Scripcaru *et al.* (2012)[31], found high and intermediate nuclear grade DCIS, respectively, in 45% and 41% of their 157 cases, and Perez *et al.* (2014)[30] in, respectively, 73% and 15% of 403 cases. Kim *et al.* (2013)[32], in a study with 1751 ICNST with DCIS in 79% of the cases, observed that patients with high-grade DCIS had worse survival (86%) than patients with low-grade DCIS or pure ICNST (97% and 93%, respectively, $p = 0.001$), presenting a 2.5 fold higher probability of local or distant recurrence. Studies have shown that nuclear classification was the most significant predictor of recurrence than the architectural pattern[33, 34]. In the different nuclear grades of DCIS associated with ICNST we identified LRR in 9/65 (14%) high grade and 0/11 (0%) low-grade ($p = 0.207$).

The nuclear grade of DCIS was correlated with the nuclear and histological grade of invasive carcinoma in the same tumor to evaluate the agreement between *in situ* and invasive components in cases of DCIS that were associated with invasive carcinoma. Significant agreement (0.61-0.80) was observed between *in situ* and invasive components in relation to nuclear grade (weighted kappa = 0.64), and moderate agreement (0.41-0.6) between the nuclear grade of *in situ* and histological grade of invasive (weighted kappa = 0.41), $p = 0.000$. Finding higher than that described by Perez *et al.* (2014), (weighted kappa = 0.23) in 403 cases of DCIS, with a high-grade identified in 293/403 cases (72.7%).

Among the pure architectural patterns, the solid subtype was the most common (30%), and the least common was micropapillary in 1.3% of the cases. According to Scripcaru *et al.* (2012)[31] the macropapillary type is the rarest, occurring as a pure form in less than 3% of all cases of DCIS and the most common is the solid pattern (67%). Perez *et al.* (2014)[30] observed the solid pattern as the most common (42%) and papillary as less common (3%). Micropapillary tumor and ductal comedonecrosis were found to be independent high-risk factors for recurrence of ipsilateral breast tumor and contralateral breast cancer by Fisher *et al.* (2007)[35]. In this study, the micropapillary pattern in DCIS associated with ICNST presented a higher LRR with 4/21 (19%). Castellano *et al.* (2010)[36] showed that high nuclear grade micropapillary DCIS frequently overexpress HER2 and has a higher rate of proliferation, necrosis, and microinvasion. In this study, we found the micropapillary pattern in pure DCIS with HER2 positive in 36%.

The presence of comedonecrosis was more frequent in the solid architectural pattern (55%) than in the others ($p = 0.002$). Scripcaru *et al.* (2012)[31] and Perez *et al.* (2014)[30] also identified a statistically significant difference between the presence of comedonecrosis in morphological subtypes, most often in the solid subtype in both with 59% and 79%, respectively. The relationship that we found between the presence of comedonecrosis and nuclear grade of DCIS was also reported by Harrison *et al.* (1996)[37]. Although rates of ipsilateral tumor recurrence are generally higher for tumors with comedonecrosis than tumors without necrosis, the presence of necrosis may be a weaker predictor of ipsilateral

recurrence than cell architecture and nuclear grade, regardless of therapies adjuvants[38]. However, the grade of nuclear atypia and intraluminal necrosis are the main factors used as criteria in most classification systems[39].

Our results showed that high-grade was more common in the solid subtype (39%, $p < 0.001$) and comedo type (57%; $p < 0$), similar finding to that described by Scripcaru *et al.* (2012)[31] and Perez *et al.* (2014)[30]. Pure solid DCIS with low nuclear grade is quite rare, 5% in our study, contrasting with 36% cribriform. Fisher *et al.* (2007)[11] found comedo and micropapillary subtypes as independent risk factors for the recurrence of ipsilateral and contralateral breast tumors. We also found a greater LRR in the comedo (15%) and micropapillary (19%) subtypes in DCIS associated with ICNST.

Emma J. Groen (2017)[40] analyzed a cohort of 10,090 women with a primary diagnosis of DCIS. In total, 5.8% developed ipsilateral invasive recurrence after treatment for DCIS (conservative or mastectomy) after a median follow-up of 11.6 years. Wallis *et al.* (2012)[41] recently reported that the DCIS grade affects the type of recurrence and time for invasive recurrence and high-grade DCIS has early recurrence (six months), while low and intermediate-grade DCIS may recur after 60 months (mostly noninvasive events) with an average time of 131 months.

Although free DCIS excision margins are clearly important to the prognosis for local recurrence of the disease[42], there is no broad agreement as to the width of the resection margin at which DCIS is considered to be "completely excised". Patients with tumor positive margins often need to undergo subsequent surgery. In the literature, reoperation rates range from 10.6% to 48%[43]. A panel of experts from St. Gallen 2015 consensus[44] endorsed the conclusions of Houssami and Morrow (2014)[45] which reinforced the importance of obtaining negative margins, defined as the absence of ink on invasive cancer or DCIS, to optimize the local control[46, 47].

In this study, the presence of relapses was detected in only one case of pure DCIS and the remaining 16 cases of DCIS associated to invasive carcinoma, possibly due to the short follow-up time for DCIS lesions (maximum 5.5 years), since the DCIS takes longer to recur and the greater probability of recurrence of the invasive component in the lesions in which the DCIS was associated with the invasive ones. When we analyzed only the initial tumors (TNM I-IIIA), the recurrence of DCIS was 1/32 (3%) and the DCIS associated with ICNST was 10/142 (7%) ($p = 0.289$).

CONCLUSION

We corroborated that younger patients showed DCIS with morphological characteristics more frequently related as a risk factor for recurrence. The low-grade was more related to ER, while high-grade to Ki-67. We did not detect the relationship of the micropapillary architectural pattern with the higher ER positivity, neither the relationship of the comedo type pattern with the younger age. We obtained greater agreement in the comparison of the nuclear grade of DCIS and ICNST in the same tumor. Our results showed that the high-grade was more common in the solid and comedo subtype and the low-grade most frequent in the cribriform subtype. We also found a greater locoregional recurrence in the comedo and micropapillary subtypes.

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