Axillary management of breast ductal carcinoma *in situ* with microinvasion: experience from a single institution

Ahmed Gaber[a], Islam M. Miligy[b,c], Alaa Elsisi[a], Ahmed Fawzy[a,d]

Departments of [a]General Surgery, [b]Histopathology, Faculty of Medicine, Menoufia University, Menoufia, Egypt, [c]Department of Histopathology, School of Medicine, University of Nottingham, Nottingham, UK, [d]Department of General Surgery, Faculty of Medicine, Taibah University, Taibah, Kingdom of Saudi Arabia

Correspondence to Ahmed Fawzy, MD, Department of General Surgery and Surgical Oncology, Menoufia University, Menoufia 32511, Egypt.
e-mail: drahmedfawzy9@gmail.com

Received: 16 October 2022
Revised: 15 November 2022
Accepted: 26 November 2022
Published: 28 April 2023

The Egyptian Journal of Surgery 2023, 41:1524–1531

Introduction
The decision regarding the surgical management of the axilla in ductal carcinoma *in situ* (DCIS) with microinvasion (DCISM) remains a controversial issue for surgeons. We aimed to define the clinicopathological parameters linked to axillary lymph node (LN) metastasis and the role of axillary staging in these cases.
Patients and methods
All cases of DCISM diagnosed from 2008 to 2016 in Menoufia University Hospitals, Egypt, were identified. The clinicopathological, surgical management, and outcome data were retrieved.
Results
A total of 48 cases of DCISM were included. Axillary surgery was performed for 37 (77.1%) cases. Only two (5.4%) cases showed positive LN metastasis, and those cases were above the age of 50 years, with a tumor size of more than 2 cm, estrogen receptor negative, high grade, and associated with comedo necrosis. A significant correlation was identified between human epidermal growth factor receptor 2 positivity and the presence of LN metastasis (P=0.033). No significant association was detected between the surgical modality, axillary surgery, or presence of nodal metastasis and overall survival (P=0.494, P=0.097, and P=0.711, respectively).
Conclusion
DCISM has a similar outcome as pure DCIS with low rate of LN metastasis. Axillary staging for DCISM should not be done as a routine, and only high-risk patients could be offered axillary surgery after discussion in the MDT.

Keywords:
ductal carcinoma in situ, lymph node metastasis, microinvasion

Egyptian J Surgery 41:1524–1531

1110-1121

Introduction

Ductal carcinoma *in situ* (DCIS) is defined as a mammary carcinoma that originates from abnormal proliferation of epithelial cells without invasion beyond the basement membrane of the breast ductal system and represents one-fifth of the newly diagnosed breast cancers worldwide [1].

DCIS, as a noninvasive lesion, is widely recognized as a precursor of invasive ductal carcinoma [2,3]. DCIS with microinvasion (DCISM) is an uncommon pathological diagnosis, which comprises ~1% of all breast cancer [4,5].

The American Joint Committee on Cancer (AJCC) has defined DCISM as DCIS with microscopic foci of tumor cells extending beyond the basement membrane into the adjacent stroma with a maximum invasive focus diameter of no more than 1 mm. DCISM is considered a subset of T1 disease, and the term 'T1mic' has been added to the TNM staging system [6,7]. DCISM is commonly encountered in large, palpable, multifocal DCIS lesions [8,9].

Screening mammography and other advanced imaging modalities are the reasons behind the significant increase in the proportion of early breast cancer including DCIS and DCISM [10,11].

DCIS has no potential for axillary lymph node (LN) spread, and so axillary staging in the form of sentinel lymph node biopsy (SLNB) is only required for mastectomy or breast-conserving surgery (BCS) for selected lesions with high risk of invasion, such as lesions with large mass-forming (5 cm or greater) or highly suspicious lesions on radiology [12].

Owing to the rarity of DCISM, questions remain regarding the risk factors, surgical management of the axilla, and patients' overall outcome. The incidence of axillary LN metastasis in the literature has a wide range. This is probably owing to the wide

spectrum of the definition of DCISM over the years and to the different pathological technique used to interpret the involved LNs[13]. Many studies have not been able to identify the predictive factors for axillary LN involvement, and there is no definitive surgical management for the axillary LNs[14–18].

Identifying patients at high risk for nodal metastasis will help in tailoring axillary staging to avoid unnecessary axillary surgery in lower risk patients. In the current study, we aimed to highlight the factors that might contribute to axillary LN metastasis and the role of axillary staging in this uncommon pathological entity.

Patients and methods

A well-characterized cohort of 495 patients with DCIS diagnosed between 2008 and 2016 at Menoufia University Hospitals, Egypt, was included, of whom 48 patients with DCISM were identified after having the triple assessment, including the core biopsy, and it was confirmed by the final pathology report. Patients' demographic data and clinicopathological characteristics were collated. Surgical management of the cases was in the form of mastectomy or BCS with or without axillary surgery in the form of SLNB or axillary clearance. All patients then were referred to medical oncology team to complete their assessment and receive their appropriate locoregional and systemic treatment protocols.

Local recurrence-free survival was defined as the time (in months) between 6 months after the first DCIS surgery and the occurrence of ipsilateral local recurrence (either as DCIS or invasive). Cases undergoing re-excision within the first 6 months owing to close surgical margins or presence of residual disease were not considered as recurrence. Patients who developed contralateral disease following DCIS diagnosis were censored at the time of development of contralateral cancer. Within a median follow-up period of 64 months (range, 6–138), no patient with DCISM developed ipsilateral local recurrence.

Former written informed consent was obtained from all participants included in this study to use their tissue materials in research. It was approved by the ethical and research committees in Faculty of Medicine, Menoufia University, Egypt. All samples and data were used fully anonymized. The research was carried out following Helsinki declaration of using human tissue in research.

Additionally, data on estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) were available and included. For ER, a 1% cut-off value was used to dichotomize the cases into positive and negative [19]. HER2 status was considered negative if the immunohistochemical score was 0 or 1+, equivocal if the score was 2+, and positive if the score was 3+ [20].

Statistical analyses were performed using SPSS, v26 (SPSS Inc., Chicago, Illinois, USA) for Windows. Association between different clinicopathological parameters in DCISM was performed using χ^2 for the categorized data. Survival rates were determined using the Kaplan–Meier method and compared by the log-rank test. All tests were two-tailed, and a P value of less than 0.05 was considered as statistically significant.

Results

A total of 48 cases of DCIS associated with microinvasion were assessed. Approximately 85% of patients were above the age of 50 years. DCIS of high grade and comedo-type necrosis morphology constituted 64.6 and 81.4%, respectively. ER-positive cases represented 61.3%, whereas HER2 positivity was observed in 32.1%.

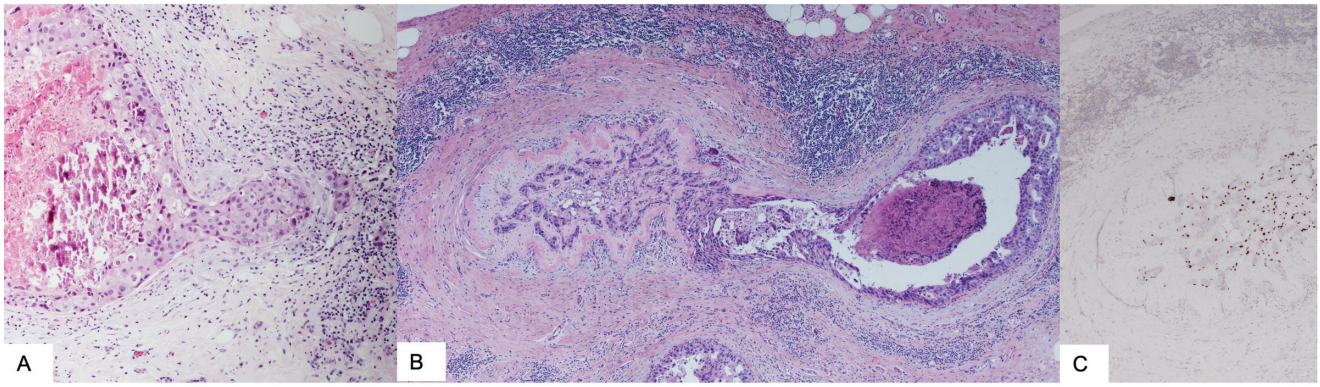
Microinvasion was either a single focus (77.1%) or multiple foci (22.9%) (Fig. 1). There was a significant correlation between the presence of a single focus of MI and smaller size of the tumor less than or equal to 2 cm (P=0.039). Most single-focus cases tend to be ER positive and HER2 negative (P=0.041 and 0.010, respectively) (Table 1).

Cases with tumor size more than 2 cm were reported in 37 (77.1%) patients, whereas only 11 (22.9%) patients had tumor size less than 2 cm. Tumor grade and comedo necrosis showed a significant correlation with larger tumor size (P=0.028 and 0.047, respectively) (Table 2).

Mastectomy was the predominant surgical modality (62.5%), and it was significantly correlated with multiple foci of microinvasion (P=0.003). Wide local excision was the chosen surgical modality for small DCIS size less than 2 cm ($P<0.001$) and HER2-negative disease (P=0.035) (Table 3). A total of 37 (77.1%) cases underwent axillary surgery, whereas 11 (22.9%) cases underwent breast surgery only without axillary surgery (Table 4).

Only two (5.4%) cases showed positive LN metastasis, and these cases were above the age of 50 years, ER-

Figure 1



Microscopic appearance of microinvasion: (a) hematoxylin and eosin (H&E)-stained section of a case of DCIS with microinvasive focus of less than 1 mm. Another case of DCIS with microinvasion-like foci with staining of H&E (b) and immunohistochemical staining of myoepithelial cell marker p63 (c). DCIS, ductal carcinoma *in situ*.

Table 1 Association between the number of microinvasive foci (single or multiple) and the different clinicopathological variables

Variables	*n* (%)	Number of MI foci		χ^2 (*P* value)
		Single focus	Multiple foci	
Age (years)				
≤50	7 (14.6)	4 (57.1)	3 (42.9)	1.845 (0.174)
>50	41 (85.4)	33 (80.5)	8 (19.5)	
DCIS grade				
Low	2 (4.2)	1 (50.0)	1 (50.0)	1.757 (0.415)
Intermediate	15 (31.3)	13 (86.7)	2 (13.3)	
High	31 (64.6)	23 (74.2)	8 (25.8)	
DCIS size				
≤2 cm	11 (22.9)	11 (100.0)	0	4.243 (0.039)
>2 cm	37 (77.1)	26 (70.3)	11 (29.7)	
Comedo necrosis				
Absent	8 (18.6)	8 (100.0)	0	2.978 (0.084)
Present	35 (81.4)	25 (71.4)	10 (28.6)	
ER/PR				
Negative	12 (38.7)	6 (50.0)	6 (50.0)	4.178 (0.041)
Positive	19 (61.3)	16 (84.2)	3 (15.8)	
HER2				
Negative	19 (67.9)	17 (89.5)	2 (10.5)	6.604 (0.010)
Positive	9 (32.1)	4 (44.4)	5 (55.6)	
Surgical procedure				
WLE	18 (37.5)	18 (100.0)	0	8.652 (0.003)
Mastectomy	30 (62.5)	19 (63.3)	11 (36.7)	
Axillary surgery				
Yes	37(77.1)	28 (75.7)	9 (24.3)	0.181 (0.670)
No	11(22.9)	9 (81.8)	2 (18.8)	
LN status				
Negative	35 (94.6)	26(74.3)	9(25.7)	0.867 (0.352)
Positive	2 (5.4)	1 (50.0)	1 (50.0)	

DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; MI, microinvasion; PR, progesterone receptor; WLE, wide local excision.

negative tumor, tumor size more than 2 cm, high grade, associated with comedo necrosis, and were treated with mastectomy (Table 5). A significant correlation was observed between the HER2-positive status of those tumors and the presence of LN metastasis (*P*=0.032). Survival analysis revealed no significant association between the surgical modality (BCS vs. mastectomy) and the overall survival of patients with DCISM (*P*=0.494). Surgical management of the axilla did not affect the survival of patients (*P*=0.097). There

Table 2 Association between the size of ductal carcinoma *in situ* and the different clinicopathological variables

Variables	*n* (%)	DCIS size		χ^2 (*P* value)
		≤2 cm	>2 cm	
Age (years)				
≤50	7 (14.6)	1 (14.3)	6 (85.7)	0.346 (0.557)
>50	41 (85.4)	10 (24.4)	31 (75.6)	
DCIS grade				
Low	2 (4.2)	0	2 (100.0)	7.144 (0.028)
Intermediate	15 (31.3)	7 (46.7)	8 (53.3)	
High	31 (64.6)	4 (12.9)	27 (87.1)	
Comedo necrosis				
Absent	8 (18.6)	4 (50.0)	4 (50.0)	3.939 (0.047)
Present	35 (81.4)	6 (17.1)	29 (82.9)	
ER/PR				
Negative	12 (38.7)	1 (8.3)	11 (91.7)	0.880 (0.348)
Positive	19 (61.3)	4 (21.1)	15 (78.9)	
HER2				
Negative	19 (67.9)	4 (21.1)	15 (78.9)	2.211 (0.137)
Positive	9 (32.1)	0	9 (100.0)	
Number of MI foci				
Single	37 (77.1)	11 (29.7)	26 (70.3)	4.243 (0.039)
Multiple	11 (22.9)	0	11 (100.0)	
Surgical procedure				
WLE	18 (37.5)	9 (50.0)	9 (50.0)	11.959 (<0.001)
Mastectomy	30 (62.5)	2 (6.7)	28 (93.3)	
Axillary surgery				
Yes	37(77.1)	8 (21.6)	29(78.4)	0.153 (0.695)
No	11(22.9)	3(27.3)	8(72.7)	
LN status				
Negative	35 (94.6)	8 (22.9)	27(77.1)	0.620 (0.431)
Positive	2 (5.4)	0	2 (100.0)	

DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; MI, microinvasion; PR, progesterone receptor; WLE, wide local excision.

was a trend toward shorter overall survival in patients with larger DCIS size, high tumor grade, presence of comedo necrosis, and presence of multiple MI foci, but this did not reach statistical significance (*P*=0.755, 0.831, 0.292, and 0.172, respectively) (Fig. 2).

Discussion

DCISM is an uncommon clinical entity, and because it is rare, its surgical management of axilla is controversial [18]. DCISM represents an intermediate state between DCIS and invasive carcinoma, with the final definition as an invasive focus diameter of less than or equal to 1 mm. The current literature is variable regarding the prognosis of DCISM [18].

In this study, we found that DCISM was frequently detected in DCIS tumors with large size, high nuclear grade, and comedo necrosis, and this finding was in line with some other studies [21–23]. Regarding biomarker expression, microinvasive DCIS frequently showed ER positivity (61.3%) and HER2 negativity (67.9%), which was compatible with the findings shown in the study by Zhang *et al.* [24]. A wide range of results in terms of HER2 expression have been reported by different studies. Wang *et al.* [10] showed similar rates of HER2 positivity between DCIS and microinvasive carcinoma. However, Margalit *et al.* [25] described a significant overexpression of HER2 in microinvasive carcinoma than in DCIS and invasive carcinoma.

BCS is the surgical choice for patients with unifocal and small breast lesions in comparison with the breast size. In the current study, only 18 (37.5%) patients underwent BCS, whereas 30 (62.5%) patients underwent mastectomy. Possible explanations are the presence of multiple foci of microinvasion, large tumor size, and in some instances, patient preference. This finding has been observed by Pu *et al.* [22], who recorded 26 (10.7%) and 216 (89.3%) patients undergoing BCS and mastectomy, respectively, in their study. Champion *et al.* [26] have also reported a high mastectomy rate in DCISM (43.5%) in

Table 3 Association between the surgical modality (breast-conserving surgery vs. mastectomy) and the different clinicopathological variables

Variables	*n* (%)	Surgical procedure		χ^2 (*P* value)
		BCS	Mastectomy	
Age (years)				
≤50	7 (14.6)	2 (28.6)	5 (71.4)	0.279 (0.598)
>50	41 (85.4)	16 (39.0)	25 (61.0)	
DCIS grade				
Low	2 (4.2)	0	2 (100.0)	1.792 (0.408)
Intermediate	15 (31.3)	7 (46.7)	8 (53.3)	
High	31 (64.6)	11 (35.5)	20 (64.5)	
DCIS size				
≤2 cm	11 (22.9)	9 (81.8)	2 (18.2)	11.959 (<0.001)
>2 cm	37 (77.1)	9 (24.3)	28 (75.7)	
Comedo necrosis				
Absent	8 (18.6)	2 (25.0)	6 (75.0)	0.423 (0.516)
Present	35 (81.4)	13 (37.1)	22 (62.9)	
ER/PR				
Negative	12 (38.7)	1 (8.3)	11 (91.7)	3.122 (0.077)
Positive	19 (61.3)	7 (36.8)	12 (63.2)	
HER2				
Negative	19 (67.9)	7 (36.8)	12 (63.2)	4.421 (0.035)
Positive	9 (32.1)	0	9 (100.0)	
Number of MI				
Single	37 (77.1)	18 (48.6)	19 (51.4)	8.562 (0.003)
Multiple	11 (22.9)	0	11 (100.0)	
Axillary surgery				
Yes	37(77.1)	7 (18.9)	30 (81.1)	1.769 (0.184)
No	11(22.9)	11(100.0)	0	
LN status				
Negative	35 (94.6)	7 (20.0)	28 (80.0)	1.252 (0.263)
Positive	2 (5.4)	0	2 (100.0)	

BCS, breast-conserving surgery; DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; MI, microinvasion; PR, progesterone receptor; WLE, wide local excision.

comparison with DCIS or invasive cancer, and they contributed it to the possibility of extensive *in situ* disease surrounding the microinvasion foci.

Although the guidance on surgical axillary staging in DCIS is well established, which is only offered with mastectomy or selected cases of BCS with high risk of invasion [17], it is not well defined and remains a debatable issue for surgeons to decide in cases of DCISM.

SLNB has a much lower rate of complications in comparison with axillary lymph node dissection (ALND). Patients who underwent ALND had a significant higher risk of developing shoulder stiffness, axillary cording or axillary web syndrome, arm pain, and lymphedema, especially in the early postoperative period, which slightly improved with time after 6 months, but even then, SLNB still had much better values [27].

There is a wide range for the incidence of LN metastasis in DCISM (0–20%) [21,22,28,29]. It was elucidated that the staging of axilla in DCISM is mandatory [8].

In invasive breast cancer, there is a correlation between the volume of invasive disease and the multifocality with increased incidence of LN metastasis [30,31]. Kim *et al.* have reported a significant correlation between multifocality and axillary node metastasis in DCISM [21]. However, the current study did not show any significant correlation between the number of microinvasive foci and the rate of LN metastasis. Similar finding has been reported by Matsen *et al.* [32], who could not find any correlation between the multiple foci of microinvasion and LN metastasis, and they concluded that patients with microinvasive carcinoma either unifocal or multifocal have a very low risk of nodal metastasis. Another study by Kapoor *et al.* [16] showed a trend toward LN metastasis in patients with multiple microinvasive foci in comparison with patients with unifocal disease, but this correlation did not reach statistical significance.In the current study, 37 (77.1%) patients with DCISM had axillary staging

Table 4 Association between the axillary surgery and the different clinicopathological variables

Variables	*n* (%)	Axillary surgery		χ^2 (*P* value)
		Absent	Present	
Age (years)				
≤50	7 (14.6)	1 (14.3)	6 (85.7)	0.346 (0.557)
>50	41 (85.4)	10 (24.4)	31 (75.6)	
DCIS grade				
Low	2 (4.2)	0	2 (100.0)	0.813 (0.666)
Intermediate	15 (31.3)	3 (20.0)	12 (80.0)	
High	31 (64.6)	8 (25.8)	23 (74.2)	
DCIS size				
≤2 cm	11 (22.9)	3 (27.3)	8 (72.7)	0.153 (0.695)
>2 cm	37 (77.1)	8 (21.6)	29 (78.4)	
Comedo necrosis				
Absent	8 (18.6)	2 (25.0)	6 (75.0)	0.017 (0.897)
Present	35 (81.4)	8 (22.9)	27 (77.1)	
ER/PR				
Negative	12 (38.7)	3 (25.0)	9 (75.0)	2.549 (0.110)
Positive	19 (61.3)	1 (5.3)	18 (94.7)	
HER2				
Negative	19 (67.9)	1 (5.3)	18 (94.7)	1.836 (0.175)
Positive	9 (32.1)	2 (22.2)	7 (77.8)	
Number of MI foci				
Single	37 (77.1)	9 (24.3)	28 (75.7)	0.181 (0.670)
Multiple	11 (22.9)	2 (18.2)	9 (81.8)	
Surgical procedure				
WLE	18 (37.5)	11 (61.1)	7(38.9)	1.769 (0.184)
Mastectomy	30 (62.5)	0	30 (100.0)	

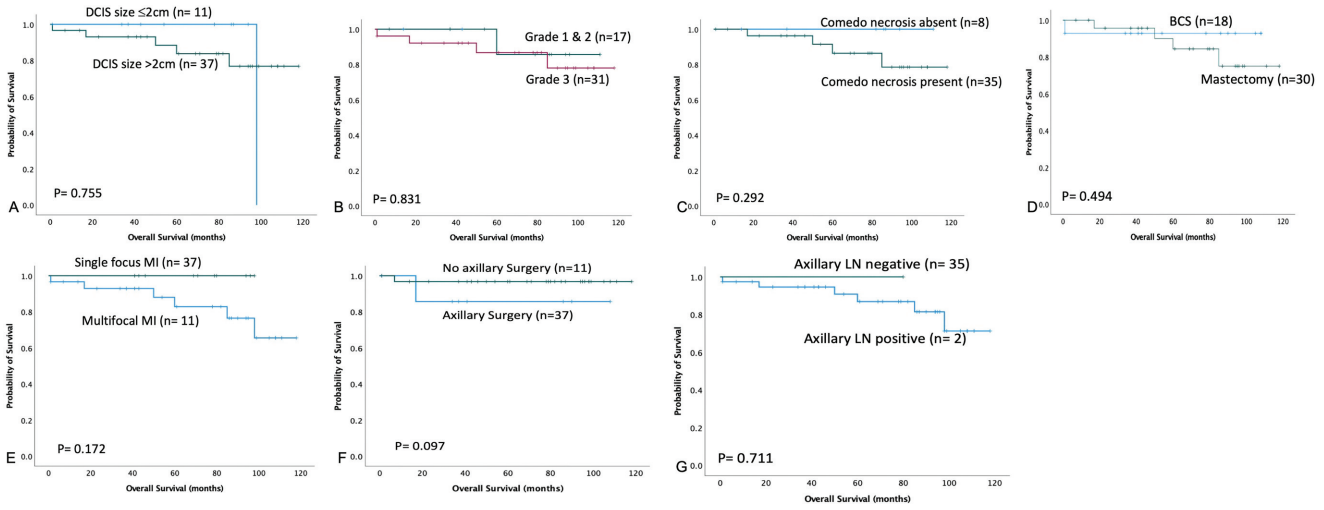
DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; MI, microinvasion; PR, progesterone receptor; WLE, wide local excision.

Table 5 Association between the lymph node status and the different clinicopathological variables in all patients who underwent axillary surgery (*N*=37)

Variables	*n* (%)	LN status		χ^2 (*P* value)
		Negative [*n* (%)]	Positive [*n* (%)]	
Age (years)				
≤50	6 (14.6)	6 (100.0)	0	0.409 (0.522)
>50	31 (85.4)	29 (93.5)	2 (6.5)	
DCIS grade				
Low	2 (5.4)	2 (100.0)	0	1.287 (0.525)
Intermediate	12 (32.4)	12 (100.0)	0	
High	23 (62.2)	21 (91.3)	2 (8.7)	
DCIS size				
≤2 cm	8 (21.6)	8 (100.0)	0	0.583 (0.445)
>2 cm	29 (78.4)	27 (93.1)	2 (6.9)	
Comedo necrosis				
Absent	6 (18.2)	6 (100.0)	0	0.473 (0.492)
Present	27 (81.8)	25 (92.6)	2 (7.4)	
ER/PR				
Negative	10 (37.0)	8 (80.0)	2 (20.0)	3.672 (0.055)
Positive	17 (61.3)	17 (100.0)	0	
HER2				
Negative	17 (68.0)	17 (100.0)	0	4.620 (0.032)
Positive	8 (32.0)	6 (75.0)	2 (25.0)	
Number of MI foci				
Single	27 (73.0)	26 (96.3)	1 (3.7)	0.566 (0.452)
Multiple	10 (27.0)	9 (90.0)	1 (10.0)	
Surgical procedure				
WLE	7 (29.7)	7 (100.0)	0	0.895 (0.344)
Mastectomy	30 (70.3)	28 (93.3)	2 (6.7)	

DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LN, lymph node; MI, microinvasion; PR, progesterone receptor; WLE, wide local excision.

Figure 2



Kaplan–Meier curves show the association between different clinicopathological parameters and patient outcome. There was no significant association between DCIS size, tumor grade, comedo necrosis, type of surgical modality, number of microinvasive foci, axillary lymph node surgery, or presence of positive LN (all $P>0.05$). DCIS, ductal carcinoma *in situ*; LN, lymph node.

surgery in the form of SLNB, axillary sample, or ALND depending on the preoperative clinicopathological findings and the surgeon's experience, where cases of DCISM with large size, comedo necrosis, and high grade mostly had undergone ALND. We identified only two (5.4%) cases with LN micro-metastasis. These results are similar to previous studies [33,34] which also recommended avoiding axillary staging in DCISM as a routine management.

Many studies have reported different records for the survival of DCISM in comparison with pure DCIS; some have stated an unfavorable prognosis, whereas others have shown similar outcome [5,7,25,32,35]. We have not identified any significant factor that contributed to poor survival outcome in cases with DCISM. Similarly, Wang *et al.* [10], suggested that the presence of a single focus of microinvasion was not associated with adverse outcomes, and patients have had the same natural behavior as those with pure DCIS.

Limitations of our study include being a retrospective study, small sample size, incomplete pathological data in some cases, and non-standardized management of the axilla following breast surgery, which has been influenced by physicians' experience and patient preferences. Further large-scale studies are recommended to consolidate our results.

Conclusion

Factors significantly related to the increased incidence of axillary lymph node metastasis in DCISM are not well established, except the HER2 status. Moreover, DCISM did not show any compromised survival rate in relation to the studied clinicopathological parameters. We conclude that performing axillary staging for DCISM based on the core biopsy should not be done as a routine management for all cases, and only selected cases with high risk of clinicopathological parameters may be tailored for axillary surgery individually after discussion in the MDT.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Fu F, Gilmore RC, Jacobs LK. Ductal carcinoma in situ. Surg Clin North Am 2018: 98:725–745.

2 Steinman S, Wang J, Bourne P, Yang Q, Tang P. Expression of cytokeratin markers, ER-alpha, PR, HER-2/neu, and EGFR in pure ductal carcinoma in situ (DCIS) and DCIS with co-existing invasive ductal carcinoma (IDC) of the breast. Ann Clin Lab Sci 2007; 37:127–134.

3 Muggerud AA, Hallett M, Johnsen H, Kleivi K, Zhou W, Amini RM, *et al.* Molecular diversity in ductal carcinoma in situ (DCIS) and early invasive breast cancer. Mol Oncol 2010; 4:357–368.

4 Bianchi S, Vezzosi V. Microinvasive carcinoma of the breast. Pathol Oncol Res 2008: 14:105–111.

5 Fang Y, Wu J, Wang W, Fei X, Zong Y, Chen X, *et al.* Biologic behavior and long-term outcomes of breast ductal carcinoma in situ with microinvasion. Oncotarget 2016; 7:64182–64190.

6 Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010; 17:1471–1474.

7 Vieira CC, Mercado CL, Cangiarella JF, Moy L, Toth HK, Guth AA. Microinvasive ductal carcinoma in situ: clinical presentation, imaging features, pathologic findings, and outcome. Eur J Radiol 2010; 73:102–107.

8 Guth AA, Mercado C, Roses DF, Darvishian F, Singh B, Cangiarella JF. Microinvasive breast cancer and the role of sentinel node biopsy: an

institutional experience and review of the literature. Breast J 2008; 14:335–339.

9 Flanagan MR, Stempel M, Brogi E, Morrow M, Cody HS III. Is sentinel lymph node biopsy required for a core biopsy diagnosis of ductal carcinoma in situ with microinvasion? Ann Surg Oncol 2019; 26:2738–2746.

10 Wang L, Zhang W, Lyu S, Liu X, Zhang T, Liu S, *et al.* Clinicopathologic characteristics and molecular subtypes of microinvasive carcinoma of the breast. Tumour Biol 2015; 36:2241–2248.

11 Wang W, Zhu W, Du F, Luo Y, Xu B. The demographic features, clinicopathological characteristics and cancer-specific outcomes for patients with microinvasive breast cancer: a SEER database analysis. Sci Rep 2017; 7:42045.

12 Lyman GH, Somerfield MR, Bosserman LD, Perkins CL, Weaver DL, Giuliano AE. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017; 35:561–564.

13 Lyons JM III., Stempel M, Van Zee KJ, Cody HS III. Axillary node staging for microinvasive breast cancer: is it justified? Ann Surg Oncol 2012; 19:3416–3421.

14 van la Parra RF, Ernst MF, Barneveld PC, Broekman JM, Rutten MJ, Bosscha K. The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol 2008; 34:631–635.

15 Lee SK, Cho EY, Kim WW, Kim SH, Hur SM, Kim S, *et al.* The prediction of lymph node metastasis in ductal carcinoma in situ with microinvasion by assessing lymphangiogenesis. J Surg Oncol 2010; 102:225–229.

16 Kapoor NS, Shamonki J, Sim MS, Chung CT, Giuliano AE. Impact of multifocality and lymph node metastasis on the prognosis and management of microinvasive breast cancer. Ann Surg Oncol 2013; 20:2576–2581.

17 Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, *et al.* Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2014; 32:1365–1383.

18 Zheng J, Yu J, Zhou T. Clinical characteristics of breast ductal carcinoma in situ with microinvasion: a narrative review. J Int Med Res 2020; 48:300060520969304.

19 Hammond ME, Hayes DF, Wolff AC, Mangu PB, Temin S. American society of clinical oncology/college of american pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Oncol Pract 2010; 6:195–197.

20 Rakha EA, Pinder SE, Bartlett JM, Ibrahim M, Starczynski J, Carder PJ, *et al.* Updated UK Recommendations for HER2 assessment in breast cancer. J Clin Pathol 2015; 68:93–99.

21 Kim M, Kim HJ, Chung YR, Kang E, Kim EK, Kim SH, *et al.* Microinvasive carcinoma versus ductal carcinoma in situ: a comparison of clinicopathological features and clinical outcomes. J Breast Cancer 2018; 21:197–205.

22 Pu T, Zhong X, Deng L, Li S, Qiu Y, Liu Y, *et al.* Long term prognosis of ductal carcinoma in situ with microinvasion: a retrospective cohort study. Int J Clin Exp Pathol 2018; 11:2665–2674.

23 Liu B-T., Ding J-N., Wang J-L., Li Z-S., Ding Y-L., Ma R. Differences in pathologic characteristics between ductal carcinoma in situ (DCIS), DCIS with microinvasion and DCIS with invasive ductal carcinoma. Int J Clin Exp Pathol 2020; 13:1066–1072.

24 Zhang G, Li C, Tian G, Cheng X, Li Y, Ma L. Comparison of breast ductal carcinoma in situ and ductal carcinoma in situ with microinvasion, and analysis of axillary lymph node metastasis. Medicine (Baltimore) 2020; 99: e23593–e23593.

25 Margalit DN, Sreedhara M, Chen YH, Catalano PJ, Nguyen PL, Golshan M, *et al.* Microinvasive breast cancer: ER, PR, and HER-2/neu status and clinical outcomes after breast-conserving therapy or mastectomy. Ann Surg Oncol 2013; 20:811–818.

26 Champion CD, Ren Y, Thomas SM, Fayanju OM, Rosenberger LH, Greenup RA, *et al.* DCIS with microinvasion: is it in situ or invasive disease? Ann Surg Oncol 2019; 26:3124–3132.

27 Bello MA, Bergmann A, Dias R, Thuler LCS, Tonellotto F, Pinto RR, *et al.* Incidence complications following sentinel lymph node biopsy or axillary lymph node dissection after breast cancer surgery. J Clin Oncol 2012; 30:97.

28 Hanna MG, Jaffer S, Bleiweiss IJ, Nayak A. Re-evaluating the role of sentinel lymph node biopsy in microinvasive breast carcinoma. Mod Pathol 2014; 27:1489–1498.

29 Magnoni F, Massari G, Santomauro G, Bagnardi V, Pagan E, Peruzzotti G, *et al.* Sentinel lymph node biopsy in microinvasive ductal carcinoma in situ. Br J Surg 2019; 106:375–383.

30 Andea AA, Bouwman D, Wallis T, Visscher DW. Correlation of tumor volume and surface area with lymph node status in patients with multifocal/multicentric breast carcinoma. Cancer 2004; 100:20–27.

31 Coombs NJ, Boyages J. Multifocal and multicentric breast cancer: does each focus matter? J Clin Oncol 2005; 23:7497–7502.

32 Matsen CB, Hirsch A, Eaton A, Stempel M, Heerdt A, Van Zee KJ, *et al.* Extent of microinvasion in ductal carcinoma in situ is not associated with sentinel lymph node metastases. Ann Surg Oncol 2014; 21:3330–3335.

33 Gojon H, Fawunmi D, Valachis A. Sentinel lymph node biopsy in patients with microinvasive breast cancer: a systematic review and meta-analysis. Eur J Surg Oncol 2014; 40:5–11.

34 Orzalesi L, Casella D, Criscenti V, Gjondedaj U, Bianchi S, Vezzosi V, *et al.* Microinvasive breast cancer: pathological parameters, cancer subtypes distribution, and correlation with axillary lymph nodes invasion. Results of a large single-institution series. Breast Cancer 2016; 23:640–648.

35 Parikh RR, Haffty BG, Lannin D, Moran MS. Ductal carcinoma in situ with microinvasion: prognostic implications, long-term outcomes, and role of axillary evaluation. Int J Radiat Oncol Biol Phys 2012; 82:7–13.