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Ductal Carcinoma In Situ with Microinvasion on Core Biopsy: Evaluating Tumor Upstaging Rate, Lymph Node Metastasis Rate, and Associated Predictive Variables

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ABSTRACT

Introduction. The role of sentinel lymph node biopsy (SLNB) when ductal carcinoma in situ with microinvasion (DCISM) is identified on core biopsy is unclear.

Objective. Our aim was to assess the upstage rate to invasive cancer and axillary lymph node metastasis in patients diagnosed with DCISM, and whether predictive variables could be identified that may help inform who would most likely benefit from a surgical axillary evaluation.

Methods. We performed a retrospective review of 70 patients diagnosed with DCISM on core biopsy. Patients with concomitant or prior invasive cancer were excluded. Demographic, clinical, radiographic, histologic, and treatment data were collected. Fisher's exact test and univariable and multivariable logistic regression were performed to identify variables that may be associated with tumor upstaging and nodal metastasis. Time-to-event distributions were summarized using the Kaplan–Meier method.

Results. On final surgical pathology, 49 patients (70%) had a final diagnosis of DCISM or T1mi cancer, whereas 21 patients (30%) were upstaged to measurable invasive cancer (> 1 mm). One of 49 patients (2%) with DCISM on final pathology and 4 of 21 patients (19%) with measurable invasive cancer showed sentinel lymph node metastases.

Conclusion. Although the upstage rate to measurable invasive cancer in our cohort of patients with DCISM on core biopsy was 30%, findings of a positive SLNB remain low at 7%. No predictive variables were identified to inform whether the routine practice of SLNB may be omitted in some patients with DCISM.

Ductal carcinoma in situ with microinvasion (DCISM) is a subtype of ductal carcinoma in situ (DCIS). The American Joint Committee on Cancer (AJCC) defines microinvasion as the extension of cancer cells beyond the basement membrane into the adjacent tissue with foci of $\leq$ 1 mm.[1] Based on the AJCC staging system, DCISM is considered a T1mi tumor.[1] The management of DCISM has been unclear since the term microinvasion was introduced by Lagios and colleagues in the 1980s.[2] For patients with a diagnosis of pure DCIS on core biopsy treated with breast-conserving surgery, sentinel lymph node biopsy (SLNB) is not recommended;[3] however, an SLNB is considered in select patients identified as having a higher likelihood of occult invasive cancer. This includes patients with high-grade DCIS, a large area of mammographic calcifications, or an associated radiographic or clinical mass.[4–10] An SLNB is also considered in patients who undergo mastectomy and are diagnosed with DCIS, which could later interfere with the ability to perform a successful

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SLNB if an invasive cancer is found on final surgical specimen. The reported rate of nodal metastasis in microinvasive breast cancer ranges from 2.1 to 20%.[11–22]

Patients diagnosed with DCISM are considered for axillary surgery when invasive cancer > 1 mm (i.e. measurable invasive cancer) is identified after operation. Multiples studies have identified predictors of upstage from pure DCIS to measurable invasive disease, including tumor size, palpable mass, radiographic features, high-grade DCIS, core biopsy needle size, and number of core samples.[4–8,10,23–25] However, few studies have reported the rate of upstaging to measurable invasive carcinoma when DCISM is found on core biopsy. Namm et al. and Cox et al. reported upgrade rates to invasive carcinoma of 42% and 44%, respectively.[12,15]

Few studies have evaluated the rates of nodal metastasis when DCISM is diagnosed on core biopsy, questioning the utility of an SLNB when DCISM is found on core biopsy. The primary aim of this study was to review our experience with patients diagnosed with DCISM on core biopsy and to determine the rate of nodal metastasis. Our secondary aim was to assess whether predictive variables exist that might inform clinical decision making regarding the performance of SLNB in patients with DCISM. We hypothesized that the rate of nodal metastasis in this patient group would be low and that performing an SLNB may not be necessary on all patients with a preoperative diagnosis of DCISM.

METHODS

Following approval by the local Institutional Review Board, a single-institution review at Carolinas Medical Center from January 2006 through December 2017 identified patients diagnosed with DCISM on core biopsy and underwent surgical excision. Patients were included if core biopsy yielded DCISM. Microinvasion was defined as a ≤ 1 mm extension of cancer cells beyond the basement membrane into adjacent tissue, consistent with the AJCC staging system.[1] Invasive cancer measuring > 1 mm (≥ T1a cancer) was defined as measurable invasive cancer. Patients were excluded if they had a prior personal history of breast cancer, had concomitant findings of invasive carcinoma on core biopsy, or were treated at an outside facility after their core biopsies. Data on patient demographics, clinical findings, type of surgery, histologic findings, and radiographic findings were collected. For ultrasound (US)-guided core biopsies, a 14-gauge needle was utilized to obtain between 3 and 5 core specimens. For stereotactic-guided core biopsies, a 9-gauge needle was utilized to obtain between 3 and 12 core specimens. Histopathologic variables included histologic pattern, nuclear grade, number of foci of microinvasion, presence of necrosis, presence of microcalcifications, and prognostic markers (estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 [HER2]). Radiographic variables included microcalcifications, mass, architectural distortion, and size of microcalcifications.

The size of the metastasis was based on findings cited in the final pathological report. We defined lymph node metastasis as a cluster of tumor cells > 0.2 m. Specifically, micrometastasis was defined as > 0.2 to ≤ 2 mm, while macrometastasis was defined as > 2 mm. Locoregional recurrences (LRRs) were defined as in-breast recurrence after breast-conservation surgery, chest wall recurrence after mastectomy, or recurrence within the ipsilateral axilla. Distant recurrences were defined as all other recurrences.

Statistical Analysis

Patient characteristics were summarized using frequency and percentage for categorical variables, and descriptive statistics, including median and range, for continuous variables. Fisher's exact tests for categorical variables were performed to identify characteristics associated with upstaging and lymph node metastasis on final pathological report. Univariable logistic models were used to evaluate individual associations between factors related to DCISM diagnosed on core biopsy and invasive cancer identified at surgical excision, and the outcomes of interest (including incidence of lymph node metastasis and upstaging to invasive cancer). Multivariable logistic regression was performed to identify variables that were independently associated with those. Backward elimination followed by forward selection was performed using an entry/elimination criteria of $p = 0.05$. Analyzed variables included patient characteristics, hormone receptor status, histologic pattern, number of foci of microinvasion, nuclear grade, presence of necrosis, presence of microcalcification, mammographic mass, and architectural distortion. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Of 137 patients diagnosed with DCISM on core biopsy from January 2006 through December 2017, 70 met the inclusion criteria (Fig. 1). Sixty-seven patients were excluded due to a prior history of breast cancer, concurrent findings of invasive disease on core biopsy, or treatment at an outside facility. Patient characteristics and clinical findings are listed in Table 1. Median age was 57 years (range 35–85). All 70 patients underwent breast

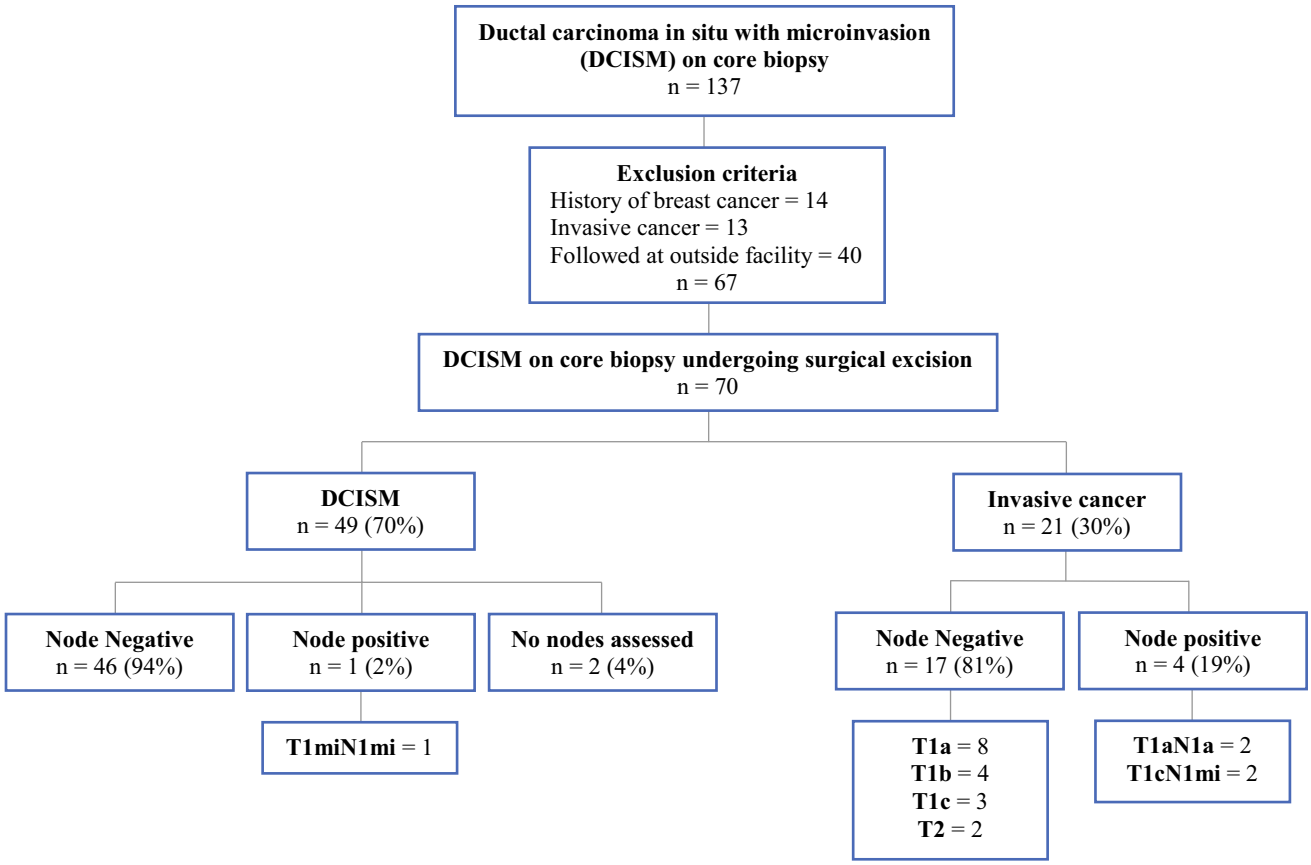

FIG. 1 CONSORT flow diagram for patients included in the study

conservation or mastectomy, and all except two patients underwent an SLNB. Architectural distortion was identified in 38% of patients upstaged to measurable invasive cancer versus 8.3% with T1mi cancer ($p = 0.01$).

Based on the pathological findings of the surgical specimen, 21 patients (30%) were upstaged to measurable invasive cancer at surgical excision, of whom four (19%) had sentinel lymph node (SLN) metastases (two with macrometastasis, two with micrometastasis). Of the 49 patients with a final diagnosis of T1mi cancer, one (2%) had an SLN micrometastasis (Fig. 1).

Twenty percent of patients with measurable invasive cancer had a palpable mass. The median size of measurable invasive cancer was 6 mm (range 2–24). The median size of DCIS on final surgical specimen was 34 mm (range 10–140) for patients with a final diagnosis of measurable invasive cancer and 18 mm (range 0–180) for patients with T1mi cancer ($p = 0.2$). The median size of DCIS was 21 mm (range 0–180) in patients who had no SLN metastasis, and 50 mm (range 16–100) in patients who had lymph node metastasis ($p = 0.65$).

Clinical and radiographic findings of the upstaged patients are listed in Table 2. The median size by US measurement was 6 mm (range 0–23). Of the upstaged patients, one had a breast MRI before surgery that demonstrated a non-mass enhancement measuring 50 mm. One patient with T2 cancer on final surgical pathology had preoperative core biopsies of both the mass and microcalcifications. The pathology of the microcalcifications demonstrated high-grade DCIS, and the pathology of the mass demonstrated DCISM. Five of 49 patients with a final diagnosis of T1mi cancer had a mammographic mass or architectural distortion. The median size by US measurement was 17 mm (range 5–31).

Twenty-six of 49 patients with a final diagnosis of T1mi cancer were ER-positive; of these 26 patients, 21 (81%) received endocrine therapy. Of the patients who underwent breast conservation with a final diagnosis of T1mi cancer, 36 (86%) received adjuvant radiation therapy.

Fisher's exact test and univariable and multivariable logistic regression analyses showed no significant association between any of the variables evaluated and lymph

TABLE 1 Characteristics of patients with a diagnosis of DCISM on core biopsy and who subsequently had a surgical excision

	Microinvasive (n = 49)	Invasive (n = 21)	Overall (n = 70)	p value
Patient characteristics				
Race				0.91
Caucasian	37 (75.5)	15 (71.4)	52 (74.3)	
Black	8 (16.3)	4 (19.1)	12 (17.1)	
Other	4 (8.2)	2 (9.5)	6 (8.6)	
Age at diagnosis, years [median (range)]	57 (40–85)	58 (35–78)	57 (35–85)	0.79
Tobacco use				0.17
Yes	18 (36.7)	4 (19.1)	22 (31.4)	
No	31 (63.3)	17 (81.0)	48 (68.6)	
Family history				0.61
Yes	19 (40.4)	10 (47.6)	29 (42.7)	
No	28 (59.6)	11 (52.4)	39 (57.4)	
Unknown	2 (4.1)	0 (0)	2 (2.9)	
Modality				0.69
Stereotactic	44 (89.8)	18 (85.7)	62 (88.6)	
Ultrasound	5 (10.2)	3 (14.3)	8 (11.4)	
Palpable				0.25
Yes	4 (8.3)	4 (19.1)	8 (11.6)	
No	44 (91.7)	17 (81.0)	61 (88.4)	
Unknown	1 (2.0)	0 (0)	1 (1.4)	
Surgery type				0.01
Partial mastectomy	2 (4.1)	0 (0)	2 (2.9)	
Partial mastectomy and SLNB	40 (81.6)	11 (52.4)	51 (72.9)	
Mastectomy and SLNB	7 (14.3)	10 (47.6)	17 (24.3)	
Histopathologic findings				
Number of foci				> 0.99
1	45 (91.8)	20 (95.2)	65 (92.9)	
2+	4 (8.2)	1 (4.8)	5 (7.1)	
Nuclear grade				0.71
1	1 (2.0)	0 (0)	1 (1.4)	
2	15 (30.6)	8 (38.1)	23 (32.9)	
3	33 (67.4)	13 (61.9)	46 (65.7)	
ER[a]				0.37
Positive	27 (61.4)	13 (76.5)	40 (65.6)	
Negative	17 (38.6)	4 (23.5)	21 (34.4)	
Not performed/unknown	5 (10.2)	4 (19.1)	9 (12.9)	
PR[a]				> 0.99
Positive	12 (41.4)	13 (76.5)	15 (38.5)	
Negative	17 (58.6)	4 (23.5)	24 (61.5)	
Not performed/unknown	20 (40.8)	4 (19.1)	31 (44.3)	
HER2[a]				> 0.99
Positive	7 (29.2)	3 (30.0)	10 (29.4)	
Negative	14 (58.3)	6 (60.0)	20 (58.8)	
Equivocal	3 (12.5)	1 (10.0)	4 (11.8)	
Not performed/unknown	25 (51.0)	11 (52.4)	36 (51.4)	

TABLE 1 continued

	Microinvasive (n = 49)	Invasive (n = 21)	Overall (n = 70)	p value
Comedo necrosis				0.72
Yes	42 (85.7)	17 (81.0)	59 (84.3)	
No	7 (14.3)	4 (19.1)	11 (15.7)	
Mammographic findings				
Microcalcifications				0.64
Yes	45 (91.8)	19 (90.5)	64 (92.8)	
Unknown	1 (2.0)	0 (0)	1 (1.4)	
Mass				0.69
Yes	5 (10.4)	3 (14.3)	8 (11.6)	
Unknown	1 (2.0)	0 (0)	1 (1.4)	
Architectural distortion				0.01
Yes	4 (8.3)	8 (38.0)	12 (17.4)	
Unknown	1 (2.0)	0 (0)	1 (1.4)	
Size of calcifications, range in mm				0.98
0–10.9	11 (26.2)	7 (36.8)	18 (29.5)	
11–19.9	11 (26.2)	3 (15.8)	14 (23.0)	
20–29	8 (19.1)	2 (10.5)	10 (16.3)	
> 29	12 (28.6)	7 (36.8)	19 (31.1)	
Unknown	7 (14.3)	2 (9.5)	9 (12.9)	

Data are expressed as n (%) unless otherwise specified

SLNB sentinel lymph node biopsy, *ER* estrogen receptor, *PR* progesterone receptor, *HER2* human epidermal growth factor receptor 2

[a]ER, PR, and HER2 status obtained from the invasive focus

node metastasis or upstaging to invasive cancer (Table 3). The odds ratio (OR) for palpability was high in those with nodal metastasis but this was not statistically significant (OR 6.22, 95% confidence interval [CI] 0.86–44.95, p = 0.07). Similarly, the OR for architectural distortion was high in those upstaged to measurable invasive cancer but again this was not statistically significant (OR 6.77, 95% CI .75–26.12, p = 0.07).

Of the entire cohort, four (6%) developed LRR and distant metastases. Of those with a final diagnosis of T1mi cancer, two (4%) developed LRR within 5 years. Both patients had ipsilateral breast recurrence. One patient who developed LRR had concurrent contralateral axillary lymph node metastases and brain metastases. This patient died within 5 years of her initial diagnosis. Of the 21 patients with a final diagnosis of measurable invasive carcinoma, two (10%) developed LRR within 5 years. The 5-year breast cancer-specific survival for patients with a final diagnosis of T1mi cancer was 100%, and the 5-year overall survival for patients with a final diagnosis of measurable invasive cancer was also 100%. Median follow-up was 2.32 years (range 0.02–10.28).

DISCUSSION

The incidence of DCIS has increased with the widespread adoption of mammography for breast cancer screening. In the United States, DCIS accounts for approximately 25% of all newly diagnosed breast cancers.[11,13,18] Currently there is no consensus regarding the utility of SLNB in patients with DCISM. The reported rate of pure DCIS upstaging to invasive cancer on surgical excision ranges from 19 to 20%.[8,18] A meta-analysis of patients with pure DCIS at core needle biopsy reports nearly one in four represented understaged invasive breast cancer.[23] Tuttle et al.[17] report incidences of both macrometastasis and micrometastasis by SLNB in pure DCIS of approximately 1%.

Conversely, few studies exist describing patients with lymph node metastases when DCISM is found on core biopsy. Namm et al. observed 104 patients with DCISM or DCIS with suspicion of microinvasion on core biopsy. Of these patients, 80% had SLNB and 7% had lymph node metastases.[15] The risk factor associated with lymph node metastasis in patients with DCIS with suspicious microinvasion was the size of DCIS $\geq$ 1.4 cm. In our study, the rate of SLN metastasis in patients diagnosed with DCISM on core biopsy was 7%. For patients with a final diagnosis of T1mi cancer, only 1 of 49 (2%) had SLN

TABLE 2 Clinical and radiographic findings of 21 patients with a final diagnosis of measurable invasive cancer

Pathologic stage	Palpable	Mammographic findings	Mammographic size of calcifications (mm)	Size of mass on ultrasound (mm)	Magnetic resonance imaging
T1aN0	No	Calcs	6	0	No
T1aN0	No	Calcs	6	0	No
T1aN0	No	Calcs	10	0	No
T1aN0	No	Calcs	13	0	No
T1aN0	No	Calcs/AD	25	3	No
T1aN0	No	Calcs	40	0	No
T1aN0	Yes	Calcs	60	0	Yes
T1aN0	No	Calcs	NR	0	No
T1aN1a	No	Calcs	11	0	No
T1aN1a	No	Calcs/AD	19	0	No
T1bN0	No	Calcs/AD	20	0	No
T1bN0	No	Calcs/AD	50	0	No
T1bN0	No	Calcs	115	4	No
T1bN0	No	Calcs/AD	NR	0	No
T1cN0	No	Calcs/AD	5	5	No
T1cN0	No	Calcs/AD	10	6	No
T1cN0	No	Calcs/AD	55	6	No
T1cN1mi	Yes	Mass	0	18	No
T1cN1mi	No	Calcs	80	0	No
T2N0	Yes	Mass	0	22	No
T2N0	Yes	Calcs/mass	60	23	No

calcs calcifications, *AD* architectural distortion, *NR* not reported

micrometastases, but no significant predictive factors were identified. Although the OR for palpability was 6.22, the 95% CI ranged from 0.86 to 45, which was perhaps due to the small sample size.

Multiple studies report a low incidence of axillary metastasis in patients with T1mi cancer. Kim et al.[28] report lymph node metastases in 4 of 110 patients (4%) with T1mi cancer, while other authors also report similarly low rates, i.e. macrometastasis of 1% and micrometastasis of 4–6%. The presence of lymphovascular invasion and ER-positive disease were found to be predictive factors for lymph node metastases.[29,30]

Relatively few studies report the rate of upstaging on final surgical pathology with the diagnosis of DCISM on core biopsy, with rates ranging from 10 to 44%.[12,15,16] In a retrospective study of 30 patients with DCISM diagnosed by core biopsy, Pimiento et al.[16] reported a 10% upstaging rate to measurable invasive cancer, whereas another recent study reported a rate of upstaging to measurable invasive cancer of 42%.[15] Predictive factors included lesion size $\geq$ 1.4 cm on imaging, and smaller needle size (11- to 14-gauge needle vs. 9- to 10-gauge needle). In our study, the rate of upstaging was 30%, although no significant predictive factors were identified. However, the OR for architectural distortion was 6.77, although the 95% CI ranged from 0.75 to 26.12, perhaps due to our small sample size.

Multiple studies have identified predictive factors associated with the upstaging rate of pure DCIS diagnosed on core biopsy. Some of these studies included a small number of DCISMs. Kurniawan et al.[7] evaluated 390 patients diagnosed with pure DCIS or DCISM on core biopsy; $<$ 1% of patients had DCISM, with an upstaging rate of 73%. Predictive factors associated with upstaging included the presence of any mammographic mass, a mammographic lesion $>$ 2 cm, or a palpable mass.[7] A few studies report that increasing the number of core samples reduces the underestimation of final diagnosis of invasive cancer. Obtaining more than 9–10 samples when using US-guided 11- or 14-gauge core biopsy may reduce underestimation of pure DCIS, although this finding has not been replicated.[24–26] Similarly, having less than five core samples using a 14-gauge needle biopsy has been associated with higher underestimation.[27] In our study, the larger needle size used in a stereotactic biopsy versus the smaller needle size used in an US-guided core biopsy was not

TABLE 3 Univariable logistic regression analysis of predictors of invasive breast cancer and nodal metastasis in patients with ductal carcinoma in situ with microinvasion on core biopsy

Univariable associations	Upstage to invasive cancer			Nodal metastasis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Demographic and clinical variables						
Race			0.94			0.99
Caucasian versus other	0.81	0.13–4.91		NE	NE	
Black or other	1.00	0.13–8.00		NE	NE	
Age at diagnosis, categorized			0.45			0.53
$\geq$ 50 versus < 50 years	0.65	0.21–19.81		0.55	0.09–3.61	
Tobacco use			0.15			0.71
Yes versus no	0.41	0.12–1.39		1.43	0.22–9.27	
Family history			0.58			0.13
Yes versus no	1.34	0.48–3.77		5.76	0.61–54.65	
Palpable			0.21			0.07
Yes versus no	2.59	0.58–11.54		6.22	0.86–44.95	
Modality						
Stereotactic versus US	0.68	0.14–3.16	0.62	0.5	0.05–5.13	0.56
Histopathologic variables						
Number of foci			0.62			0.98
2 + versus 1	0.56	0.06–5.36		NE	NE	
ER[a]			0.27			0.74
Yes versus no	2.05	0.57–7.32		0.73	0.11–4.76	
PR[a]			0.94			0.75
Yes versus no	0.94	0.22–4.09		0.67	0.06–8.06	
HER2[a]			0.87			0.62
Yes versus no	0.92	0.31–2.68		0.59	0.08–4.53	
Grade			0.86			0.97
1 versus 3	NE	NE		NE	NE	
2 versus 3	1.35	0.46–3.95		1.30	0.20–8.40	
Solid			0.21			0.96
Yes versus no	2.40	0.61–9.45		NE	NE	
Cribriform			0.07			0.95
Yes versus no	0.29	0.07–1.11		NE	NE	
Papillary			0.55			0.97
Yes versus no	0.65	0.16–2.65		NE	NE	
Necrosis			0.62			0.81
Yes versus no	0.71	0.18–2.74		0.75	0.08–7.47	
Radiographic variables						
Microcalcification			0.63			0.30
Yes versus no	0.63	0.10–4.10		0.28	0.03–3.08	
Mass			0.65			0.57
Yes versus no	1.43	0.31–6.64		1.96	0.19–20.15	
Architectural distortion			0.07			0.85
Yes versus no	6.77	0.75–26.12		1.25	0.13–12.28	
Size category			0.72			0.56
$\geq$ 2 versus 2 cm	1.22	0.41–3.62		1.74	0.27–11.26	

OR odds ratio, *CI* confidence interval, *ER* estrogen receptor, *PR* progesterone receptor, *HER* human epidermal growth factor receptor, *NE* not evaluated, *US* ultrasound

[a]ER, PR, and HER2 status obtained from the invasive focus

predictive of upstaging. Of note, one of the limitations in our study is the lack of a specific number of obtained specimens, which may have impacted our upstaging rate.

Little data exist on recurrence and distant metastasis in patients with T1mi cancer. Parikh et al.[31] reported an LRR rate of 7% and a distant metastasis rate of 1%. These authors did not find DCISM to be an independent predictor of overall survival or recurrence. For patients with T1mi cancer who had a negative SLN metastasis, Matsen et al.[29] reported a distant recurrence rate of $< 1\%$. In our study, one patient with a final diagnosis of T1mi cancer developed LRR and distant metastases, whereas another patient developed distant metastases within 5 years. Neither of these patients had SLN metastases at initial surgery.

Our study does have some limitations. We utilized a single-institution cohort, a retrospective design, and a small sample size. Four of the eight patients in our cohort presenting with a palpable mass were upstaged to measurable invasive cancer, suggesting these patients were incorrectly diagnosed on core biopsy due to sampling error. We recognize that if a definitive diagnosis of measurable invasive cancer had been made at the time of core biopsy, then the outcome for the rate of upstaging in our patient cohort would have been lower. Our study also did not identify any significant predictive factors for upstaging to invasive cancer on final surgical specimen or SLN metastasis, perhaps reflecting the small sample size and few observed events. A large, prospective study with strict selection criteria may yield more definitive associations.

Despite these limitations, clinicians should be aware of the risks of nodal involvement and upstaging to measurable invasive cancer. The benefits of performing SLNB and its complications should be considered. An SLNB is generally considered a relatively safe procedure but is not risk-free. Complications include an anaphylactic reaction to the dye, wound infections, pain, and lymphedema. In patients with breast cancer, reported rates of lymphedema following SLNB range from 5 to 6%;[32,33] however, in our study we found a 7% rate of SLN metastasis when DCISM was found on core biopsy. Therefore, we propose that patients diagnosed with DCISM may be managed with a partial mastectomy initially, followed by SLNB only if measurable invasive cancer is identified, similar to patients with DCIS.

CONCLUSIONS

Thirty percent of patients diagnosed with DCISM on core biopsy were upstaged to measurable invasive cancer on surgical excision; findings of a positive SLNB were low (7%). No predictive variables were identified to inform whether the routine practice of performing an SLNB may safely be omitted in some patients with DCISM.

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REFERENCES

1. Amin MB, American joint committee on cancer: AJCC Cancer staging manual. Basel: Springer; 2017.
2. Lagios MD, Westdahl PR, Margolin FR, Rose MR. Duct carcinoma in situ. Relationship of extent of noninvasive disease to the frequency of occult invasion, multicentricity, lymph node metastases, and short-term treatment failures. *Cancer.* 1982;50:1309–14.
3. National Comprehensive Cancer Network. Breast Cancer (Version 3.2018). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed 7 Oct 2018.
4. Dillon MF, McDermott EW, Quinn CM, et al. Predictors of invasive disease in breast cancer when core biopsy demonstrates DCIS only. *J Surg Oncol.* 2006;93:559–63.
5. Goyal A, Douglas-Jones A, Monypenny I, et al. Is there a role of sentinel lymph node biopsy in ductal carcinoma in situ? Analysis of 587 cases. *Breast Cancer Res Treat.* 2006;98:311–4.
6. Hoorntje LE, Schipper ME, Peeters PH, et al. The finding of invasive cancer after a preoperative diagnosis of ductal carcinoma-in situ: causes of ductal carcinoma-in situ underestimates with stereotactic 14-gauge needle biopsy. *Ann Surg Oncol.* 2003;10:748–53.
7. Kurniawan ED, Rose A, Mou A, et al. Risk factors for invasive breast cancer when core needle biopsy shows ductal carcinoma in situ. *Arch Surg.* 2010;145:1098–104.
8. Moran CJ, Kell MR, Flanagan FL, et al. Role of sentinel lymph node biopsy in high-risk ductal carcinoma in situ patients. *Am J Surg.* 2007;194:172–175.
9. Vieira CC, Mercado CL, Cangiarella JF, et al. Microinvasive ductal carcinoma in situ: clinical presentation, imaging features, pathologic findings, and outcome. *Eur J Radiol.* 2010;73:102–7.
10. Yen TW, Hunt KK, Ross MI, et al. Predictors of invasive breast cancer in patients with an initial diagnosis of ductal carcinoma in situ: a guide to selective use of sentinel lymph node biopsy in management of ductal carcinoma in situ. *J Am Coll Surg.* 2005;200:516–26.
11. American Cancer Society: Breast Cancer Facts & Figures 2017–2018. 2017. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf. Accessed 20 Apr 2018.
12. Cox CE, Nguyen K, Gray RJ, et al. Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): why map DCIS? *Am Surg.* 2001;67:513–9; discussion 519–521.
13. Kerlikowske K. Epidemiology of ductal carcinoma in situ. *JNCI Monogr.* 2010;2010:139–41.

14. Klauber-DeMore N, Tan LK, Liberman L, et al. Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in situ and ductal carcinoma-in situ with microinvasion? *Ann Surg Oncol*. 2000;7:636–42.
15. Namm JP, Mueller J, Kocherginsky M, Kulkarni S. The utility of sentinel lymph node biopsy in patients with ductal carcinoma in situ suspicious for microinvasion on core biopsy. *Ann Surg Oncol*. 2015;22:59–65.
16. Pimiento JM, Lee MC, Esposito NN, et al. Role of axillary staging in women diagnosed with ductal carcinoma in situ with microinvasion. *J Oncol Pract.* 2011;7:309–13.
17. Tuttle TM, Shamliyan T, Virnig BA, Kane RL. The impact of sentinel lymph node biopsy and magnetic resonance imaging on important outcomes among patients with ductal carcinoma in situ. *J Natl Cancer Inst Monogr*. 2010;2010:117–20.
18. Virnig BA, Tuttle TM, Shamliyan T, Kane RL. Ductal carcinoma in situ of the breast: a systematic review of incidence, treatment, and outcomes. *J Natl Cancer Inst.* 2010;102:170–8.
19. Lyons JM, Stempel M, Van Zee KJ, Cody HS. Axillary node staging for microinvasive breast cancer: is it justified? *Ann Surg Oncol.* 2012;19(11):3416–21.
20. 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(8):2576–81.
21. de Mascarel I, MacGrogan G, Mathoulin-Pélissier S, et al. Breast ductal carcinoma in situ with microinvasion. *Cancer.* 2002;94:2134–42.
22. Guth AA, Mercado C, Roses DF, et al. Microinvasive breast cancer and the role of sentinel node biopsy: an institutional experience and review of the literature. *Breast J.* 2008;14:335–9.
23. Brennan ME, Turner RM, Ciatto S, Marinovich ML, French JR, Macaskill P, et al. Ductal carcinoma in situ at core-needle biopsy: meta-analysis of underestimation and predictors of invasive breast cancer. *Radiology.* 2011;260(1):119–28.
24. Jackman RJ, Burbank F, Parker SH et al. Stereotactic breast biopsy of nonpalpable lesions: determinants of ductal carcinoma in situ underestimation rates. *Radiology*. 2001;218(2):497–502.
25. Lee JW, Han W, KO E, et al. Sonographic lesion size of ductal carcinoma in situ as a preoperative predictor for the presence of an invasive focus. *J Surg Oncol.* 2008;98(1):15–20.
26. Kim M, Kim, HJ, Chung YR, et al. Microinvasive carcinoma versus ductal carcinoma in situ: a comparison of clinicopathological features and clinical outcomes. *J Breast Cancer.* 2018;21(2):197–205.
27. Matsen CB, Hirsch A, Eaton A, et al. Extent of microinvasion in ductal carcinoma in situ is not associated with sentinel lymph node metastases. *Ann Surg Oncol.* 2014;21:3330–5.
28. Ko BS, Lim WS, Kim HJ, et al. Risk factor for axillary lymph node metastases in microinvasive breast cancer. *Ann Surg Oncol.* 2012;19:212–6.
29. Houssami N, Ambrogetti D, Marinovich ML et al. Accuracy of a preoperative model for predicting invasive breast cancer in women with ductal carcinoma-in situ on vacuum-assisted core needle biopsy. *Ann Surg Oncol*. 2011;18:1364–71.
30. Park AY, Gweon HM, Son EJ, Yoo M, Kim JA, Youk JH. Ductal carcinoma in situ diagnosed at US-guided 14-gauge core-needle biopsy for breast mass: preoperative predictors of invasive breast cancer. *Eur J Radiol.* 2014; 83(4):654–9.
31. 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.
32. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol.* 2013;14:500–15.
33. Shaitelman SF, Cromwell KD, Rasmussen JC, et al. Recent progress in cancer-related lymphedema treatment and prevention. *CA Cancer J Clin.* 2015;65:55-81.