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ORIGINAL ARTICLE

Predicting invasion in patients with DCIS in the preoperative percutaneous biopsy

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Abstract

When ductal carcinoma in situ (DCIS) is suspected in mammography, core needle biopsy or vacuum assisted biopsy is recommended. However, invasion remains undetected with percutaneous biopsy techniques in 10–20% of the patients. Our aim was to evaluate the prevalence of and predictive factors for invasion in the surgical specimen in patients with DCIS in the preoperative biopsy. Sixty-seven consecutive participants of the Helsinki City Mammography Screening program with DCIS in the preoperative percutaneous biopsy were included. The palpability, the mammographical size and appearance and the visibility of the lesion in breast ultrasound were evaluate as factors predictive for invasion, as well as the histopathological features of DCIS in the preoperative biopsy. Twenty patients had invasion in the surgical specimen. The only predictive factor for invasion was the visibility of the lesion in ultrasound, but even this finding failed to reach statistical significance. Thirteen of the 26 patients with lesions visible in US had invasion in their surgical specimens, while only seven of the 41 patients without such a lesion had invasive or microinvasive cancer, Pc = 0.0686. In conclusion, the visibility of the lesion in US may predict detecting invasion in the surgical specimen in patients with DCIS in the preoperative biopsy.

Screening mammography has remarkably increased the number of patients with ductal carcinoma in situ (DCIS). When DCIS is suspected in mammography (MGR), core needle biopsy (CNB) or vacuum assisted biopsy is recommended in order to evaluate invasion. However, invasion may remain undetected with such percutaneous biopsy techniques with limited sampling. In fact, some 10–20% of the patients with DCIS in CNB have invasive cancer in the breast resection or mastectomy specimen [1].

Preoperative tumor features such as palpable tumor or mass lesion in MGR, lesion visible in breast ultrasound (US), suspicion of microinvasion or high-grade histology as well as extensive disease have been considered as characteristics associated with elevated risk of invasion [2]. However, in many studies no factors predicting invasion has been identified [3–5].

Unlike in patients with invasive breast cancer, nodal staging has not been warranted in patients with DCIS. Although tumor positive sentinel node (SN) findings have been observed in up to 14% of patients with "high risk" pure DCIS, the role of even SN biopsy in patients with pure DCIS is still under investigation [3,6–10].

In order to avoid unnecessarily extensive axillary surgery and multiple operations, identification of preoperative features predicting invasion is beneficial in patients with DCIS in the preoperative biopsy. For these reasons, our aim was to evaluate the prevalence of and predictive factors for invasion in the surgical specimen in patients with DCIS in the preoperative percutaneous biopsy.

Patients and methods

Between June 2001 and November 2004 about 74 000 women aged 50–59 years were invited to participate the biennial, population based mammography screening using two-view (medio-lateral-oblique and cranio-caudal) at the Mammography Screening Center of Helsinki. The compliance rate was 82%. About

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2% (1 200 women) of those screened were recalled for further work-up (additional views, cone down magnification views, breast ultrasound, fine needle aspiration biopsy (FNAB), CNB and vacuum assisted biopsy. CNB (14G) or vacuum assisted biopsy were preferred when the image on mammograms was that of microcalcifications or architectural distortion. FNAB was performed in patients with palpable lesions if the image was radiologically malignant.

The data of women participating Helsinki City Mammography Screening program were registered prospectively in a database. In this database, altogether 67 women had DCIS in their percutaneous biopsies during the study period and were included in the study. The project plan was approved by the Ethical Committee of Helsinki University Central Hospital.Vacuum assisted biopsy was performed in 30 (45%) of the 67 patients, CNB in 35 (52%) patients and FNAB in two (3%) patients. The biopsy specimens were obtained under stereotactical guidance except in one patient with ultrasonographically guided vacuum assisted biopsy. The preoperative tumor characteristics of the study patients are presented in Table I.

Surgery

The patients were referred for surgery to the Breast Surgery Unit of Helsinki University Central Hospital. Forty-three (64%) of the 67 patients underwent breast conserving surgery and 24 (36%) mastectomy during the primary operation. A second operation was necessary due to insufficient margins in seven patients. Two patients had a further resection while five underwent mastectomy. The total mastectomy rate was 43% (29 patients). Altogether 16 of the 29 mastectomy patients underwent immediate breast reconstruction.

Table I. Preoperative tumor characteristics of the 67 patients with DCIS in the preoperative percutaneous biopsy specimen.

The size of the lesion in MGR*	20 (5–100) mm
Mass lesion in MGR	19 (28%)
Lesion visible in breast US	26 (39%)
Palpable tumor	12 (18%)
Growth pattern of DCIS	
Comedo	25 (37%)
Cribriform	19 (28%)
Micropapillary	5 (8%)
Flat	6 (9%)
Solid	8 (12%)
Other	2 (3%)
Not assessed	2 (3%)
Nuclear grade	
1	5 (8%)
2	27 (40%)
3	35 (52%)
Large cell DCIS	51 (76%)

*median (range).
MGR = mammography, US = ultrasound.

Altogether 34 (51%) of the 67 patients underwent axillary surgery, that is SN biopsy, AC or both. Twenty-six patients underwent SN biopsy. The indications for SN biopsy in patients with DCIS in the preoperative percutaneous biopsy included palpable tumor, mass lesion in MGR or breast US and an extensive lesion warranting mastectomy, but were individually decided by the surgeon in agreement with the patient. Preoperative lymphatic mapping, a hand-held gamma detector and blue dye were used to identify the SN in the axilla as described in detail earlier [11]. All patients with tumor positive SN findings underwent level I–II axillary clearance (AC).

Six patients underwent partial level I AC in connection with mastectomy and immediate breast reconstruction. In these patients, axillary surgery was performed not only for axillary staging purposes but also in order to facilitate harvesting the latissimus dorsi- flap or performing the microvascular anastomosis in the axilla. Two patients underwent level I–II AC as a second operation due to invasive carcinoma in the surgical specimen.

Histopathological methods

The preoperative percutaneous biopsy specimens. The preoperative percutaneous biopsy specimens were evaluated by a pathologist specialized in breast pathology (PH) at the Department of Pathology of the Helsinki University Central Hospital. The histological classification was based primarily on the nuclear grade, and secondarily on the presence of necrosis, as stated by the Van Nuys Classification [12]. The nuclear grade was considered from one to three as defined by the Consensus Conference on the Classification of Ductal Carcinoma in Situ or WHO classification [13]. The cell size was evaluated either small or large. Seven different architectural patterns were considered; comedo, cribriform, micropapillary, papillary, flat and solid [13]. Necrosis and microcalcifications were also notified.

FNAB was performed in two cases. Both samples showed large atypical cells mainly in loose clusters. Nuclear-cytoplasmic ratio was high. Necrosis was detected as well as calcifications. Based on these features, the diagnosis of DCIS was suggested. Nuclear grade and the presence of necrosis were evaluated from the slides; however, the growth pattern could not be assessed.

The breast resection and mastectomy specimens. The fresh breast resection and mastectomy specimens were oriented by the surgeon. A specimen radiograph was obtained in all resection specimens with impalpable lesions. In the resection specimens, the surfaces of the specimen were marked by different colored inks. The samples were taken from the areas of microcalcifications including also the surrounding tissue and from any other abnormal area. From resection specimens, samples were also taken to include surgical margins to evaluate the resection margins microscopically. In the mastectomy specimens, further samples, in addition to suspect areas, were taken from all quadrants of the breast and from the nipple. The extension of cancer cells beyond the basement membrane into the adjacent tissues, with no single focus larger than 1mm in greatest dimension was considered microinvasion [14].

Lymph nodes. Both the SN and the lymph nodes in the AC specimens were histologically assessed as described in our previous study [8].

Statistical methods

Fisher's exact was used to compare the proportional data. The predictive factors studied included the palpability of the lesion, the size and the appearance of the lesion in the MGR, the visibility of the lesion in breast US, as well as the histopathological features of DCIS in the preoperative biopsy. When evaluating multiple predictive factors, the p-values were corrected for the number of the evaluated factors and were denoted Pc. The means and medians were compared using the Mann-Whitney U-test. Two-tailed p-values or Pc-values < 0.05 were considered statistically significant.

Results

According to the histopathological assessment of the surgical specimens, 47 (70%) patients had pure DCIS, eight (12%) had microinvasive DCIS and 12 (18%) had invasive carcinoma. Among the 12 patients with invasive cancer, the median size of the invasive component was 9 (4–15) mm.

Microinvasive or invasive carcinoma was detected in eight of the 35 patients with preoperative CNB and in 12 of the 30 patients with vacuum assisted biopsy, difference between the groups 17%, 95% CI (-5%, 40%), $p = 0.2213$. The median size of the lesion in MGR was larger, 38(10–100) mm among patients with vacuum assisted biopsy compared with the 12 (5–60) mm in patients with CNB, $p < 0.0001$. Neither of the two patients with preoperative FNAB had invasion detected in their surgical specimens.

Two patients with pure DCIS had tumor positive SN findings, one patient had a micrometastasis and the other had isolated tumor cells. One patient with microinvasive DCIS had isolated tumor cells in a single SN. Two patients with invasive cancer had SN metastases, one had a micrometastasis and the other had a larger metastasis. All these five patients underwent level I–II AC. Only the patient with invasive cancer and SN macrometastasis had further metastases in her AC specimen.

No axillary metastases was detected either in the six patients with partial level I AC in connection with immediate breast reconstruction or in the two patients with level I–II AC due to invasion in the surgical specimen.

The only predictive factor for invasive carcinoma or microinvasive DCIS was the visibility of the lesion in breast US. Even this finding failed to reach statistical significance after the correction of the p-value. Thirteen of the 26 patients with lesions visible in US had invasion in their surgical specimens, while only seven of the 41 patients without such a lesion had invasive or microinvasive cancer, difference between the groups 33% 95%CI (11%, 55%) $Pc = 0.0686$ (Table II).

Twenty-five of the patients had a lesion not visible in US and non-comedo type DCIS in their CNB. Only two (8%) of these 25 patients had invasive cancer or microinvasive DCIS in their surgical specimens. Combining other low risk features to non-visibility in US or with each other was not helpful in identifying a minimal risk of invasion.

Discussion

In the present study, the prevalence of invasive cancer undetected in the preoperative biopsy was rather high, especially when also cases with microinvasive cancer are included. Surprisingly, invasion in the surgical specimen was especially common in patients with vacuum assisted biopsy, most probably because vacuum assisted biopsy was preferred among patients with extensive lesions in MGR. Furthermore, two patients with pure DCIS in the surgical specimen had tumor positive SN findings but were not included among cases with invasion, because the end-point of the present study was invasion in the surgical specimen.

The strongest predictor for invasion was the visibility of the lesion in breast US. This is an issue less addressed in literature in association high risk DCIS. On the other hand, the specimens were obtained under stereotactical guidance except in one patient, regardless the visibility of the lesion in

Table II. The risk of invasive cancer or microinvasive DCIS in the 67 patients with DCIS in the preoperative percutaneous biopsy specimen.

Risk factor	Invasion	95% CI, p, Pc
Size in MGR		
>30mm	9/25 (36%)	10% (−13%, 33%)
<30mm	11/42 (26%)	p =0,5632, Pc =NS
Palpable tumor		
Yes	6/12 (50%)	25% (−6%, 55%)
No	14/55 (25%)	p =0.1869, Pc =NS
Mass lesion in MGR		
Yes	7/19 (37%)	10% (−15%, 35%)
No	13/48 (27%)	p =0.6151, Pc =NS
Growth pattern of DCIS in CNB		
Comedo	12/25 (48%)	28% (5%, 51%)
Non-comedo	8/40 (20%)	p =0.0364, Pc =NS
Large cell DCIS in CNB		
Yes	18/51 (35%)	22% (2%, 44%)
No	2/16 (13%)	p =0.1450, Pc =NS
Nuclear Grade		
3	13/35 (37%)	15% (−6%, 37%)
1–2	7/32 (22%)	p =0.2725, Pc =NS
Lesion visible in breast US		
Yes	13/26 (50%)	33% (11%, 55%)
No	7/41 (17%)	P =0.0098, Pc =0.0686

MGR =mammography, US =ultrasound, NS =not significant.

US. Using ultasonographical guidance in patients with lesions visible in US may have revealed invasion preoperatively at least in some cases. In general, no other imaging modality than MGR has an established role in the diagnostic work-up of DCIS. Nevertheless, our results as well as the findings in previous studies [15,16], indicate that US is beneficial in the evaluation of patients with DCIS, especially as an adjunctive tool to MGR.

However, factors such as comedo type histology, a high nuclear grade, an extensive or a mass lesion in MRG were not strong predictors for invasion, unlike in some previous reports [10,17]. Nevertheless, in many studies no factors predicting invasion has been identified [3–5].

The major limitation of the present study was the small number of the evaluated patients, rendering the conclusions rather uncertain. The patients with either invasive breast cancer or DCIS, who have been referred from the Mammography Screening Center, represented just some 20% of all breast cancer patients treated in the unit. The data of all the breast cancer patients treated at the Breast Surgery Unit have been collected in a database. However, the data regarding the preoperative diagnosis have not been registered. Therefore, it was regrettably impossible to include all the patients with DCIS in the preoperative biopsy in the present study.

In conclusion, in patients with DCIS in the percutaneous preoperative biopsy, the visibility of the lesion in breast US may predict detecting invasion in the surgical specimen.

References

[1] Silverstein MJ. Ductal carcinoma in situ of the breast. Annu Rev Med 2000;51:17–32.

[2] Cody HS,3rd, Klauber-Demore N, Borgen PI, Van Zee KJ. Is it really duct carcinoma in situ? Ann Surg Oncol 2001;8: 617–9.

[3] Mittendorf ME, Arciero CA, Gutchell V, Hooke J, Shriver CD. Core biopsy diagnosis of ductal carcinoma in situ: An indication for sentinel lymph node biopsy. Curr Surg 2005; 62:253–7.

[4] Cox CE, Dupont E, Whitehead GF, Ebert MD, Nguyen K, Peltz ES, et al. Age and body mass index may increase the chance of failure in sentinel lymph node biopsy for women with breast cancer. Breast J 2002;8:88–91.

[5] Lee CH, Carter D, Philpotts LE, Couce ME, Horvath LJ, Lange RC, et al. Ductal carcinoma in situ diagnosed with stereotactic core needle biopsy: Can invasion be predicted? Radiology 2000;217:466–70.

[6] Cox CE, Nguyen K, Gray RJ, Salud C, Ku NN, Dupont E, et al. Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): Why map DCIS? Am Surg 2001;67:513–9; Discussion 519–21.

[7] Klauber-DeMore N, Tan LK, Liberman L, Kaptain S, Fey J, Borgen P, 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.

[8] Leidenius M, Salmenkivi K, von Smitten K, Heikkila P. Tumour positive sentinel node findings in patients with ductal carcinoma in situ. J Surg Oncol 2006;94:380–4.

[9] Pendas S, Dauway E, Giuliano R, Ku N, Cox CE, Reintgen DS. Sentinel node biopsy in ductal carcinoma in situ patients. Ann Surg Oncol 2000;7:15–20.

[10] Yen TW, Hunt KK, Ross MI, Mirza NQ, Babiera GV, Meric-Bernstam F, 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] Leidenius M, Krogerus L, Toivonen T, Leppanen E, von Smitten K. The sensitivity of axillary staging when using sentinel node biopsy in breast cancer. Eur J Surg Oncol 2003;29:849–53.

[12] Silverstein MJ, Poller DN, Waisman JR, Colburn WJ, Barth A, Gierson ED, et al. Prognostic classification of breast ductal carcinoma-in-situ. Lancet 1995;345(8958):1154–7.

[13] Consensus Conference on the classification of ductal carcinoma in situ. The Consensus Conference Committee. Cancer 1997;80:1798–802.

[14] American Joint Committee on Cancer. Cancer Staging Manual. 6th ed. New York: Springer-Verlag; 2002.

[15] Moon WK, Myung JS, Lee YJ, Park IA, Noh DY, Im JG. US of ductal carcinoma in situ. Radiographics 2002;22:269–80; Discussion 280–1.

[16] Yang WT, Tse GM. Sonographic, mammographic, and histopathologic correlation of symptomatic ductal carcinoma in situ. AJR Am J Roentgenol 2004;182:101–10.

[17] Renshaw AA. Predicting invasion in the excision specimen from breast core needle biopsy specimens with only ductal carcinoma in situ. Arch Pathol Lab Med 2002;126:39–41.