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Original article

Prediction of underestimated invasiveness in patients with ductal carcinoma in situ of the breast on percutaneous biopsy as rationale for recommending concurrent sentinel lymph node biopsy

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ABSTRACT

Aim: To develop a model to predict invasion and improve the indication of concurrent sentinel lymph node biopsy (SLNB) for patients with ductal carcinoma in situ (DCIS) on minimally invasive biopsy.
Methods: We evaluated the data of 205 patients with DCIS in minimally invasive biopsy specimens. Clinical, radiological and histological variables were assessed in order to identify predictors of invasive carcinoma in final pathology using logistic regression analyses. We developed and retrospectively tested an algorithm to indicate concurrent SLNB.
Results: Invasiveness was underestimated in 18.0% (37 of 205). Univariate analysis revealed the following significant risk factors: lesion palpability, a mass lesion on ultrasound, the presence of a mammographically detectable mass, architectural distortion or density, a BI-RADS score of 5, a lesion diameter ≥50 mm, and ≥50% of histologically affected ducts. With a palpable mass, which remained the only independent predictor of invasion after multivariate adjustment, and the presence of at least three of the remaining five risk factors, the probability of invasion was 56.0%. If the prediction model had been used to indicate SLNB 9.8% (20 of 205) of patients could have been benefited (i.e. spared unnecessary or correctly recommended concurrent SLNB) compared to the factual performed SLNB procedures. Those patients with pure DCIS treated with breast conserving surgery (BCS) benefited most with a relative risk reduction of nearly 50% for unnecessary SLNB.
Conclusion: The prediction model could rationally guide an informed discussion about risks and benefits of concurrent SLNB in patients with DCIS on minimally invasive biopsy.

Introduction

A biopsy diagnosis of DCIS does not preclude the finding of invasive carcinoma in the resection specimen because minimally invasive biopsy techniques may miss areas of invasive carcinoma. Between 8% and 44%[1–15] of all breast lesions preoperatively diagnosed as DCIS are misclassified and result to harbour microinvasive or invasive foci in the histology of the resected specimen. Due to this diagnostic uncertainty the planning of surgical procedures is challenging, especially with respect to axillary staging.

An SLNB – if necessary – is preferably performed at the same time as the excision of the breast tumour rather than in a second surgery. It spares the patient the psychological distress and risks of additional surgery and anaesthesia and is economically more efficient. Also, while lymphatic mapping usually succeeds if performed before a lumpectomy, it may be less accurate afterwards,[16–18] and technically impossible after a mastectomy.[10,11] For the indicated reasons, the performance of an SLNB concurrently with the breast surgery seems to be the best surgical approach in cases of DCIS which are assumed to be at high risk to harbour invasive carcinoma. However, since this risk is still not clearly defined, many patients experience overtreatment – when SLNB is performed but the final pathology confirms the diagnosis of pure DCIS – or are not optimally treated – when SLNB for invasive carcinoma has to be performed in a second surgery.

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German guidelines recommend SLNB for preoperatively proven DCIS that is to be treated by mastectomy or wide excision close to the axilla because it precludes the possibility of a secondary SLNB.[19,20] In combination with BCS the guidelines offer a "possibility" to perform an SLNB when occult stromal invasion is suspected,[20] or more precisely for lesions ≥5 cm and high grade lesions >2.5 cm (it is a "±" recommendation what means that the surgeon is neither forced nor forbidden to perform an SLNB in these situations).[19] The American Society of Clinical Oncology considers concurrent SLNB acceptable for DCIS treated by mastectomy (with limited evidence) and not recommendable for DCIS treated by BCS except for large DCIS >5 cm on core biopsy or with suspected or proven microinvasion (with insufficient evidence).[21]

It is desirable to define a subgroup of DCIS patients who really are at high risk of invasive carcinoma and could be offered concurrent SLNB. A number of possible predictors for the finding of invasive carcinoma in biopsy-proven DCIS have been described, but there is still little consensus and a lack of clinically applicable risk models. The aim of our study was to further specify and quantify the risk of invasive carcinoma after a core or vacuum biopsy diagnosis of DCIS and to improve the indication to perform (or not perform) a concurrent SLNB in these patients.

Patients and methods

Patient cohort and study design

Female patients who received the preoperative histological diagnosis of pure DCIS between January 2006 and December 2010 and had percutaneous biopsy and consecutive breast cancer surgery performed at the Heidelberg University Breast Unit were included in the study. A total of 205 consecutive patients who were referred from either the screening programme or the symptomatic clinic met the inclusion criteria. Their records were retrospectively reviewed and demographic, clinical, radiological, surgical and histological data were extracted.

Clinical routine work-up

If the suspicious lesion was sonographically detectable, an ultrasound guided core biopsy was carried out with a 14 Gauge needle, yielding a median of 4 (range 2–9) specimens. If the lesion was seen only on mammograms, a stereotactically guided vacuum biopsy was performed with needles ranging in size from 9 to 11 Gauge and a median yield of 12 (range 5–40) specimens. Patients were treated with either BCS or mastectomy according to tumour board recommendation or patient preference. An axillary staging was performed when a mastectomy was planned or the risk of invasion was assumed to be high according to German guidelines.[19,20]

Statistical analysis

The statistical analysis was performed with SPSS Statistics software version 19.0. In our analyses two groups were considered, defined by the result of the final pathologic evaluation as either DCIS only or DCIS with invasion. Baseline comparisons between these two groups were performed using the Chi-square-test for nominal scaled, the Mann–Whitney-*U*-test for ordinal scaled and the two-sample two-sided *t*-test for metric scaled variables. A *p*-value ≤.05 was assumed to indicate a statistically significant difference. Because of the explorative character of the study, we did not adjust for multiplicity. Therefore resulting *p*-values have to be interpreted descriptively. Variables that showed remarkable differences in the baseline comparison between the two groups were tested as potential predictors of occult invasion in univariate and multivariate logistic regression analyses and were included in the development of a prediction model. Procedural data were analysed descriptively.

Ethics approval

The ethics committee of the Heidelberg University Medical Faculty approved the study protocol.

Results

Underestimated invasiveness

Of the 205 patients in the study, the preoperative diagnosis of DCIS was postoperatively confirmed in 168 (82.0%) cases, including 14 (6.8%) patients who had small DCIS on biopsy but no further malignant findings in the resection specimen. Invasive disease was found in the resection specimens of 37 (18.0%) patients, including four (2.0%) patients with microinvasion and 33 (16.1%) patients with invasive carcinoma. Underestimation rates differed significantly between vacuum biopsy and core biopsy diagnoses with underestimation occurring in 9.0% (14 of 155) and 47.9% (23 of 48), respectively ($P < .001$).

Baseline characteristics of patients

Comparing the distribution of the preoperatively collected data (Table 1) we found that a palpable mass ($P < .001$), a mass lesion on ultrasound ($P < .001$), suspicious non-calcified findings on mammography ($P = .002$), a BI-RADS score of 5 ($P = .012$), a larger lesion diameter ($P = .015$) and the histological finding of ≥50% of ducts affected by carcinoma ($P = .003$) correlated significantly with the finding of invasive carcinoma in the final pathology.

Univariate logistic regression analysis

The univariate logistic regression analysis (Table 2) revealed statistically significant associations between the finding of invasion in the final pathology and the presence of a palpable mass (odds ratio [OR] 7.01, 95% confidence interval [95% CI, 3.20; 15.36], $P < .001$), a mass lesion on ultrasound (OR 5.37, 95% CI [2.51; 11.46], $P < .001$), suspicious non-calcified findings on mammography (OR 3.24, 95% CI [1.52; 6.90], $P = .002$), a BI-RADS score of 5 (OR 2.49, 95% CI [1.21; 5.14], $P = .014$) and the histological finding of ≥50% of affected ducts (OR 3.54, 95% CI [1.47; 8.51], $P = .005$). A trend towards statistical significance was seen for the influence of the lesion's size ($P = .053$), measured as the largest diameter at palpation, ultrasound or mammography. Lesions with a diameter ≥ 50 mm were significantly more likely to harbour invasion than lesions ≤20 mm (OR 4.83, 95% CI [1.35; 17.34], $P = .016$).

Based on the univariate logistic regression analysis we calculated the probability to find invasive carcinoma in the final pathology for each of the identified risk factors (please refer to Table 2).

Multivariate logistic regression analyses

After multivariate adjustment the presence of a palpable mass remained the only statistically significant independent predictor of invasive carcinoma (OR 3.71 [1.41; 9.79], $P = .008$).

In order to further characterize the impact of those variables that exclusively showed an influence on the main outcome in the univariate logistic regression analysis, we examined the number of risk factors simultaneously expressed in each patient. These five