



Original article

Risk factors of sentinel and non-sentinel lymph node metastases in patients with ductal carcinoma in situ of the breast: A nationwide study



Emil Villiam Holm-Rasmussen^{a,*}, Maj-Britt Jensen^b, Eva Balslev^c, Niels Kroman^a, Tove Filtenborg Tvedskov^a

^a Department of Breast Surgery, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, DK-2100, Copenhagen, Denmark

^b Danish Breast Cancer Group, Copenhagen University Hospital, Blegdamsvej 9, DK-2100, Copenhagen, Denmark

^c Department of Pathology, Herlev Hospital, Copenhagen University Hospital, Herlev Ringvej 75, DK-2730, Herlev, Denmark

ARTICLE INFO

Article history:

Received 31 July 2018

Received in revised form

12 September 2018

Accepted 15 September 2018

Available online 18 September 2018

ABSTRACT

Objectives: Unexplained axillary metastases have been detected in some patients with ductal carcinoma *in situ* (DCIS), possibly because of occult invasion or iatrogenic tumor cell displacement. The significance of these metastases is unknown and brings into questions the need for upstaging and axillary surgery. What are the risk factors for sentinel lymph node (SN) and non-SN metastases, including the risk of iatrogenic displacement of tumor cells in relation to an excisional biopsy, in patients diagnosed with DCIS?

Methods: Nationwide data on 1787 women diagnosed with DCIS between 2001 and 2015 were retrieved from the Danish Breast Cancer Group database. The association of clinicopathological variables with a positive SN (isolated tumor cells (ITCs), micro- or macrometastases) was evaluated using univariate and multivariate analyses.

Results: Of the 1787 patients, 71 (4.0%) had a positive SN: 15 (0.8%) had macrometastases, 42 (2.4%) had micrometastases, and 14 (0.8%) had ITCs. Five patients with a positive SN also had a positive non-SN. In adjusted analysis, a positive SN was associated with younger age ($P = 0.036$), increased size ($P = 0.002$), palpability ($P = 0.0004$) and surgical excisional biopsy ($P < 0.001$).

Conclusions: The overall risk of a positive SN in patients with DCIS on final pathology is low and less than 9% of these patients had positive non-SNs. This argues against using axillary lymph node dissection in this group. The odds of positive SN after surgical excisional biopsies showed more than a four-fold increase, indicating iatrogenic tumor cell displacement. It is questioned whether these patients should be upstaged and classified as having invasive carcinoma.

© 2018 Elsevier Ltd. All rights reserved.

1. Introduction

During the last four decades the incidence of ductal carcinoma *in situ* (DCIS) of the breast has increased almost a five-fold in high-income countries. Since the late 1990s, the increase has been dramatic because of widespread mammographic screening [1,2]. It is estimated that 13–25% of all breast neoplasms found by mammographic screening, and 20–25% of all breast neoplasms overall are

represented by DCIS, with some variation between countries [2–4].

By definition, DCIS has no metastatic potential and is not able to spread to the axillary lymph nodes. However, researchers have found metastases in the sentinel lymph node (SN) in 1–22% of patients with only DCIS of the breast [5]. These patients are generally upstaged to invasive carcinomas despite no sign of invasion into the breast. Evidence of further metastatic spread to non-SN in DCIS patients with a positive SN is basically unknown [3]. The underlying mechanism of metastatic spread in patients with DCIS is not fully understood. It is suggested that the presence of an undetected occult cancer or iatrogenic displacement of tumor cells in relation to recent surgical excisional biopsy could be the origin of the positive SN in patients with only DCIS of the breast [5,6].

The rate of positive SNs as a result of iatrogenic displacement of

* Corresponding author.

E-mail addresses: emil.villiam.holm-rasmussen@regionh.dk (E.V. Holm-Rasmussen), mj@dbcg.dk (M.-B. Jensen), eva.balslev@regionh.dk (E. Balslev), niels.kroman@regionh.dk (N. Kroman), tove.holst.filtenborg.tvedskov@regionh.dk (T.F. Tvedskov).

tumor cells in DCIS patients has only briefly been described in previous studies [5]. However, it is better described in patients with invasive carcinoma [7]. The mechanisms of iatrogenic displacement in patients with invasive carcinomas might also apply to patients with only DCIS of the breast.

Axillary lymph node status is the most important prognostic factor in breast cancer patients. Currently, sentinel lymph node biopsy (SLNB) is the standard procedure for staging invasive carcinomas. However, the use of axillary staging of DCIS patients has been increasingly debated [2,5,6,8,9]. According to the Danish guidelines, SLNB is only indicated when there is a risk of invasive carcinoma on final pathology i.e. when the DCIS lesion is larger than 50 mm (ultrasound or mammographic), has Van Nuys Classification group III, is palpable and in the case of mastectomy or surgery in the upper lateral quadrant with the risk of damaging lymph vessels, thereby making subsequent SLNB impossible [10]. On average, 23% of patients pre-operatively diagnosed with DCIS are upstaged to invasive carcinoma on final histopathological examination [8]. Although SLNB is considered to cause a minimal morbidity compared to the far more extensive axillary lymph node dissection (ALND) the procedure is not without side effects [11,12].

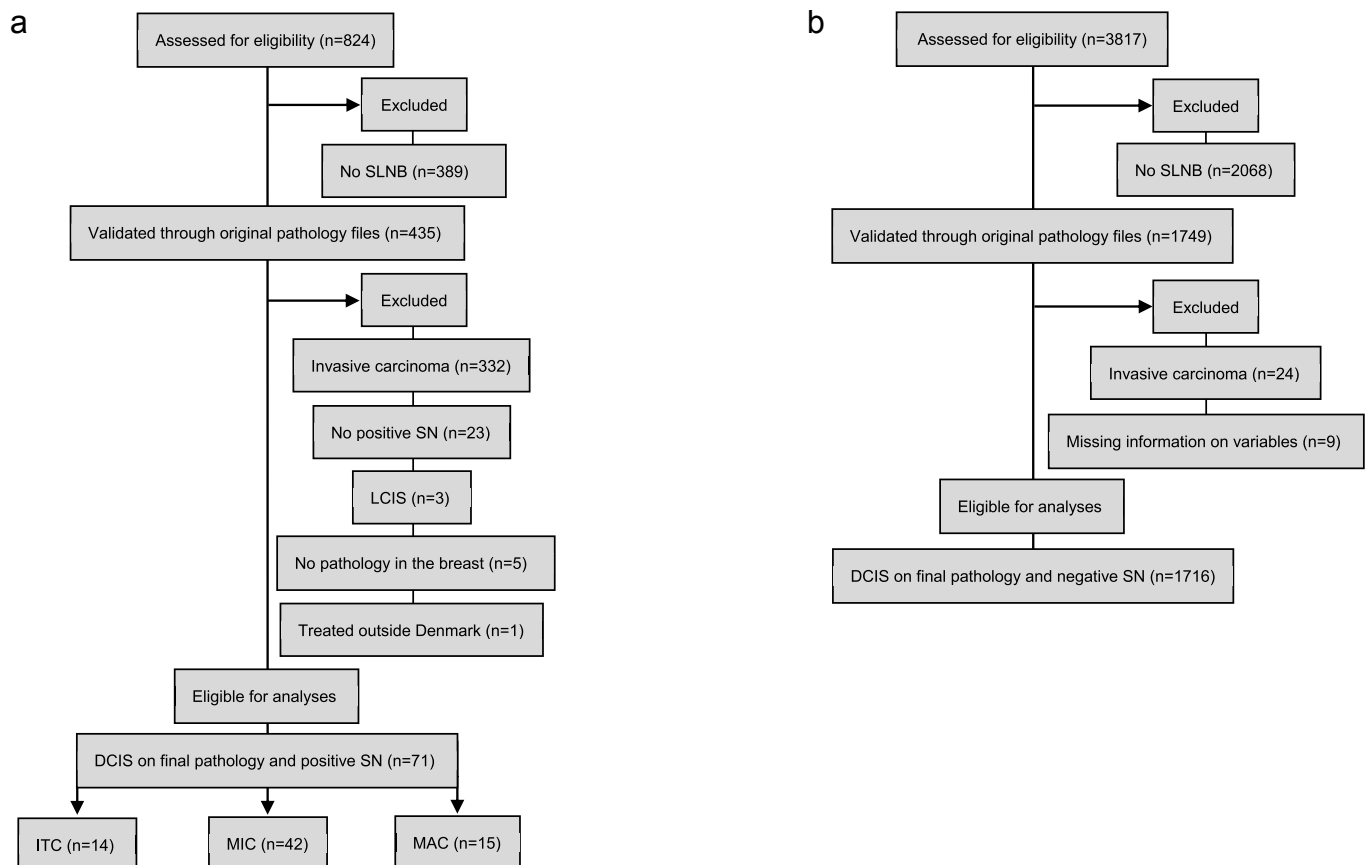
The aim of this study was to identify risk factors for metastases to the SN and the risk of further spread to non-SN in patients diagnosed with DCIS of the breast, to identify subgroups of patients where axillary surgery can safely be omitted. Additionally, the aim was to examine whether positive SN in DCIS patients can be caused

by iatrogenic tumor cell displacement after recent surgical excision and clarify whether an ALND is indicated in this group of patients.

2. Methods

2.1. Study population

The Danish breast cancer database administered by the Danish Breast Cancer Group (DBCG) was used to identify patients in this nationwide register-based study. Information on clinical and histopathological data in the Danish breast cancer database has prospectively been collected since 1977 [13]. Since 1982, data on DCIS patients has been registered in the database [14]. Patients with metastases in the SN, but only DCIS in the breast are registered in the database as having invasive carcinoma. For these patients, tumor size is registered as “unknown”, “missing”, or “0”. Between 2001 and 2015, 824 breast cancer patients with tumor size “unknown”, “missing” or “0” were registered in the database. In 389 patients no SLNB was performed and these were excluded. Information on the remaining 435 patients was validated using original pathology files. After validation a total number of 71 patients had a final diagnosis of DCIS together with a positive SN and were eligible for final analysis. Criteria for inclusion/exclusion are shown in Fig. 1a. A positive SN was defined according to the American Joint Committee on Cancer as isolated tumor cells (ITCs) if metastases were ≤ 0.2 mm, micrometastases with size >0.2 –2 mm, or



Abbreviations: DBCG, Danish Breast Cancer Group; SLNB, sentinel lymph node biopsy; SN, sentinel node; LCIS, lobular carcinoma *in situ*; DCIS, ductal carcinoma *in situ*; ITC, isolated tumor cells; MIC, micrometastases; MAC, macrometastases.

Fig. 1. a) Flowchart for inclusion of patients from the DBCG database. Patients with a final diagnosis of DCIS together with a positive SN (ITC, MIC or MAC). b) Flowchart for inclusion of patients from the DBCG database. Patients with DCIS on final pathology together with a negative SN.

Download English Version:

<https://daneshyari.com/en/article/11033610>

Download Persian Version:

<https://daneshyari.com/article/11033610>

[Daneshyari.com](https://daneshyari.com)