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Original article

Re-resection rates and risk characteristics following breast conserving surgery for breast cancer and carcinoma in situ: A single-centre study of 1575 consecutive cases

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ABSTRACT

Objectives: To examine the frequency of re-resections and describe risk characteristics: invasive carcinoma or carcinoma in situ (CIS), palpability of the lesion, and neoadjuvant chemotherapy.
Results: 1703 breast conserving surgeries were performed: 1575 primary breast conserving surgeries (BCS), and 128 diagnostic excisions (DE). 176 BCS (11.2% [9.6; 12.7]) and 100 DE had inadequate margins indicating re-resection. The overall re-resection rate was 16.2% [14.5; 18.0]. 10.3% of invasive carcinoma BCS patients, and 28.6% CIS patients underwent re-resection (relative risk (RR) 2.8 [1.9; 4.1]). Invasive lobular carcinoma (ilc) had an RR of re-resection of 2.5 [1.7; 3.8], compared with invasive ductal carcinoma (idc).
Conclusion: Overall 11.2% of the BCS patients needed a re-resection. For isolated CIS (28.6%), RR of re-resection was almost three times as high compared to invasive carcinoma (10.3%). Ilc had an RR of re-resection of 2.5 compared to idc. Palpability and neoadjuvant chemotherapy did not significantly influence the risk of re-resection.

Introduction

The surgical treatment of breast cancer should aim at local control of the disease and at the same time obtaining the best possible cosmetic and functional result with as few sequelae as possible. Therefore, breast-conserving surgery (BCS) defined as lumpectomy followed by adjuvant radiotherapy, has become a well-established treatment for breast cancer worldwide [1,2].

However, the trade-off between cosmesis and cure may lead to inadequate or positive resection margins, particularly with uncertain preoperative diagnosis, carcinoma in situ component, lobular pathology, large tumours and smaller breast size [3–10]. The rates of re-resection after BCS have been reported to range from 15.5% to 48.5% [3,5,7,8,11–14], and 63% for ductal carcinoma in situ (DCIS) alone [15].

In Denmark, adequate surgical margins in BCS are defined in national guidelines constituted by the Danish Breast Cancer Cooperative Group (DBCG). The guidelines were changed in October 2009 and adequate microscopic margins were changed from ≥5 mm for both DCIS and invasive cancer to ≥2 mm [16,17].

Little is known about re-resection rates in Denmark and Europe, and in particular, it is not known whether the change in guidelines has had any bearing on the re-resection rate.

The aim of the present study was to examine the rate of re-resection after BCS in a large breast cancer centre in Denmark with particular focus on risk factors for re-resection and the possible influence of changes in national guidelines according to margin recommendations.

Materials and methods

Study population

The study included all patients undergoing surgery at the department of breast surgery, Vejle Hospital, Denmark, from May 2005 to May 2012. We included all surgeries on the breast, with a postoperative diagnosis of carcinoma in situ or invasive carcinoma, in total 2360 surgeries (Fig. 1). A patient was counted twice if both breasts were operated on. We excluded 6 patients with one breast surgery each, because they received their primary surgery at other

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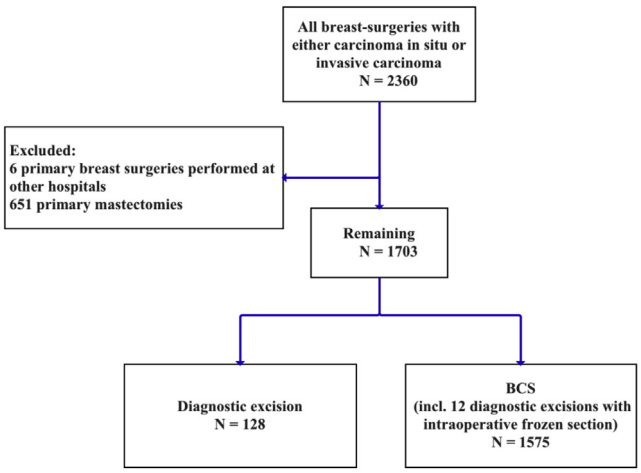

Fig. 1. Study population.

hospitals. 651 primary mastectomies were excluded, as they had no risk of being re-resected. This left 1703 breast surgeries, comprising 1575 BCS and 128 diagnostic excisions, for inclusion.

All BCS had a preoperative diagnosis of malignancy based on a triple test. In 12 cases a diagnostic excision was performed with intraoperative frozen section, making the surgeon able to convert the diagnostic excision to a proper BCS during a single surgery, and these 12 cases are therefore included in the BCS group.

A re-resection was indicated to achieve radical surgery when adequate surgical margins were not obtained in the primary surgery. 276 re-resections were performed due to inadequate surgical margins, 176 of these in the BCS group. Re-operations in the axillary bed and re-operations caused by postoperative complications were not defined as re-resections.

Breast surgeries at Vejle Hospital

A diagnostic excision was performed when the triple test or core needle biopsy failed to provide certainty of either malignant or benign diagnosis [18]. As a diagnostic excision can turn out to be benign, it is preferable to remove as little breast tissue as possible, i.e. adequate surgical margins are not mandatory, since the goal is to obtain a definitive diagnosis.

In this study all lesions categorised as carcinoma in situ were isolated carcinoma in situ without foci of invasive carcinoma, whereas the idc were not stratified for containing in situ components or not. A non-palpable lesion was defined as a lesion removed at an operation requiring a wire for localisation.

All breast cancer surgeons in Denmark are specialists in surgery before they can subspecialise in breast cancer surgery.

A pathologist is present in the operating theatre to handle the specimen at all BCS at Vejle Hospital. Both the pathologist and the surgeon examine the specimen in theatre to ensure macroscopically adequate margins. More tissue can thus be removed immediately if deemed necessary. This was not regarded as a re-resection in the present study, only re-resections performed at a second operation were counted as such in this study.

Statistical analysis

We calculated the re-resection rates for each year from 2005 to 2012, overall, and before and after the guideline change in 2009. We used the χ^2-test to examine the association between groups defined by final pathological diagnosis, palpability, and neoadjuvant therapy respectively. We calculated re-resection rates and the RR for re-resection with regard to these groups along with 95% confidence intervals (95%CI) and *p*-values. The slopes of the curves (Fig. 2), expressing the average yearly decrease and increase in rates of re-resection before and after change of guidelines, were calculated using simple linear regression. Reresection rates before and after the guideline change were also compared using the χ^2-test. All tests were two-sided and *p*-values lower than 0.05 were considered statistically significant.

All calculations were performed using SPSS version 20.

Results

Re-resection rates

Between May 2005 and May 2012, 1703 BCS and diagnostic excisions were performed, 1427 required only one operation and 276 needed at least one re-resection to obtain adequate surgical margins.

When looking at the BCS group ($N = 1575$), 1399 required only one surgery to achieve adequate surgical margins. 176 needed at least one re-resection, i.e. a re-resection rate of 11.2% (95%CI [9.6; 12.7]) (Fig. 2, Table 1). The re-resection rate from 2005 to 2009 before implementing the new 2 mm guideline was 14.1% 95%CI [11.7; 16.5] and after 2009 it was 8.0% 95%CI [6.1; 10.0] ($p < 0.001$). The annual average decrease in re-resection rates 2005–2009 was 2.2% (95%CI [-1.0; 5.3], $p = 0.094$). After implementing the new guidelines the re-resection rates in 2009–2012 increased with an annual average of 0.7 (95%CI [−27.2; 25.8], $p = 0.802$).

The overall re-resection rate for BCS and all diagnostic excisions was 16.2% (95%CI [14.5; 18.0]). The overall re-resection rate decreased from 23.0% (95%CI [17.3; 28.7]) in 2005 to 12.1% (95%CI [8.0; 16.1]) in 2012 (Fig. 2, Table 1). The average annual decrease in re-resection rates 2005–2009 was 2.8% (95%CI [-1.1; 6.7], $p = 0.091$). From 2009 to 2012 the re-resection rates increased with an annual average of 0.2 (95%CI [−3.4; 3.0], $p = 0.620$).

Risk characteristics

The RR of re-resection for the BCS group ($N = 1575$) was 2.8 (95% CI [1.9; 4.1], $p < 0.001$) for carcinoma in situ compared to invasive carcinoma (Table 2). When looking at invasive carcinoma alone, the RR of re-resection was 2.5 (95%CI [1.7; 3.8], $p < 0.001$) for invasive lobular carcinoma (ilc) compared to invasive ductal carcinoma (idc). Other pathology compared to idc showed no significant difference in RR of re-resection (RR = 0.7, 95%CI [0.3; 1.7], and $p = 0.479$).

For the BCS group ($N = 1575$) no significant RR was found when comparing palpable and non-palpable lesions (RR = 1.0, 95%CI [0.7; 1.2], and $p = 0.857$) (Table 2). For the BCS and all the diagnostic excisions the RR of re-resection was 2.0 (95%CI [1.6; 2.5], $p < 0.001$) for non-palpable lesions compared to palpable lesions.

Neoadjuvant therapy did not significantly lower the RR of re-resection (RR = 0.9, 95%CI [0.4; 1.7], and $p = 0.642$) for the BCS with invasive carcinoma (Table 3). Also, when stratifying for palpability of the lesion no difference in RR was found with regard to receiving neoadjuvant therapy.

Re-resections

When the breast was too small to achieve adequate surgical margins with an acceptable cosmetic outcome, it was necessary to perform a re-resectional mastectomy instead of a breast conserving re-resection. In our study, this was deemed necessary in 59 (33.5%) of the re-resections in the BCS group ($N = 176$) (Fig. 3). These 59 mastectomies correspond to 3.75% of all the BCS ($N = 1575$). Thus