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ORIGINAL ARTICLE

Clinical presentation and surgical quality in treatment of ductal carcinoma in situ of the breast

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Abstract

To assess quality of surgical treatment of ductal carcinoma in situ (DCIS) and to compare teaching and non-teaching hospitals that constitute the Comprehensive Cancer Centres of the Middle Netherlands (IKMN), we retrospectively reviewed 499 patients with 502 DCIS lesions treated in the period 1989–2002. In teaching hospitals fewer patients presented with clinical symptoms compared to non-teaching hospitals (15% versus 24.0%, $p = 0.01$). Finally, 65% of patients underwent breast-conserving surgery and 35% of patients a mastectomy (no significant differences between the two types of hospitals). In teaching hospitals 19% of the patients had a disease-involved or unknown surgical margins versus 13% in non-teaching hospitals ($p = 0.04$). Twenty patients (4%) received radiation therapy postoperatively with no differences between teaching and non-teaching hospitals ($p = 0.98$).Quality of surgical treatment is the most important prognostic factor in treatment of DCIS. The quality of excisions should be improved and the exact status of margins should be recorded in pathology reports.

Ductal carcinoma in situ (DCIS) of the breast constitutes a spectrum of non-invasive malignant lesions of the breast [1–3]. Since the introduction of mammographic screening for breast cancer there has been a marked increase in the frequency of DCIS detection and in current practice DCIS accounts for approximately 20% to 30% of all screening detected breast lesions [4]. Due to the non-invasive nature of DCIS there is a potential cure rate of almost 100% if treated with a mastectomy [5,6]. Breast-conserving therapy has proven to be a safe alternative treatment option compared to mastectomy for patients with invasive breast cancer [7]. Breast-conserving treatment of DCIS is also assumed to be effective and is used widely [3–5,8,9].

However, treatment with breast-conserving therapy carries the risk of local recurrence. In the case of DCIS, half of these recurrences are invasive carcinomas with the risk of distant disease and subsequent death [10–12]. Although, the risk of dying due to breast cancer in DCIS patients is low (2% after 10 years of follow-up), local recurrence is still of major concern [13]. Several tumour- and treatment-related risk factors are identified for an increased risk of recurrence after breast-conserving treatment of DCIS [14]. Radiation therapy after breast-conserving surgery for DCIS has been shown to decrease the incidence of local recurrences [15–19]. However, the cornerstone in prevention of recurrent disease is the quality of the primary surgical procedure. Residual tumour within the treated breast probably will give rise to a tumour recurrence [20–23].

Breast-conserving treatment of DCIS has been widely advocated, however, significant variability in treatment of DCIS by geographic region has been

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shown with different rates of breast-conserving surgery [8].

The aim of the present population-based study was to assess both clinical presentation and quality of surgical treatment of DCIS. Indicators for quality of surgical treatment are the number of surgical procedures and results on margin status. We also compared these variables between teaching and non-teaching hospitals.

Materials and methods

The Comprehensive Cancer Centre of the Middle Netherlands "Integraal Kanker Centrum Midden Nederland" (IKMN) is constituted of four regional hospitals, two teaching hospitals and one university hospital. Together, these seven hospitals treat all patients diagnosed with DCIS living in the central part of the Netherlands.

The Cancer Registry from the Comprehensive Cancer Centre of the Middle Netherlands identified patients with DCIS treated in the seven hospitals between January 1989 and December 2002. The IKMN guidelines for treatment of DCIS recommended a microscopically complete excision of the lesion with either breast-conserving surgery or with a mastectomy for lesions of greater size or multifocal lesions. During the study period, the routine use of adjuvant therapy was not recommended.

Patients with a history of breast cancer or with simultaneous invasive breast cancer and/or other malignancies (except for non-melanoma skin cancer) were excluded. 604 patients were identified and their medical records were reviewed. For 36 patients no medical record was available. After reviewing medical records, 69 patients were excluded, because of a micro-invasive component of the initial DCIS lesion (12 patients), DCIS with lobular carcinoma in situ (eight patients), invasive breast carcinoma as initial diagnosis (nine patients), simultaneously contralateral invasive breast carcinoma (three patients), previous history of breast cancer (six patients), no further information or follow-up data (20 patients), or other criteria (no diagnosis of DCIS or an unknown malignancy elsewhere, 11 patients).

From the remaining 499 patients with 502 DCIS lesions all available clinical and pathology data were collected. The items noted were: detection method (clinical diagnosis or mammographic detection), mammographic appearance (calcifications, architecture distortion or both), age at diagnosis, family history of breast cancer (both first and second degree), location of primary DCIS (inner quadrant, outer quadrant or central), size of DCIS lesion (according to mammographic or pathology reports, if specified), and surgical treatment (including the performance of re-excision and the total number of surgical procedures).

Histopathological classification of the DCIS lesion and margin status was determined by routine pathologists in the different hospitals and no special protocols were used. According to the treatment guidelines, specification of an exact margin width of excision was not required. It stated that if normal breast tissue was present between the DCIS lesion and the specimen margin a complete excision could be assumed.

Patient and tumour characteristics were compared between teaching hospitals ($n=3$) and non-teaching ($n=4$) and significance of differences were calculated with the χ^2 test or Fisher's exact test, when appropriate. For continuous variables Student's t test was used. For all statistical analysis a p-value <0.05 was considered statistically significant.

Hospitals were randomly referred as A (55 patients, 11%), B (90 patients, 18%), C (42 patients, 8%), D (44 patients, 9%), E (68 patients, 14%), F (121 patients, 24%) and G (82 patients, 16%) of which A, B and G are teaching-hospitals.

Results

Table I lists patient and tumour characteristics of the study population. The number of patients treated in both type of hospitals was comparable during the study period (data not shown). Median age at diagnosis was 56 years (range: 27–90 years) with no differences between teaching and non-teaching hospitals ($p=0.85$).

During time, the number of DCIS increased: 102 tumours were diagnosed before 1993 compared to 214 lesions after 1998. The majority of tumours were detected by mammography (399 patients, 80%) and the predominant mammographic findings were microcalcifications (375 patients, 94%). Ninety nine patients (20%) were diagnosed by clinical symptoms of whom 71 presented with a palpable tumour, 28 with nipple discharge, and four with other symptoms not further specified. During time, the percentage of DCIS detected by clinical symptoms decreased (29% before 1993 and 15% after 1998, $p=0.01$).

In teaching hospitals, DCIS was diagnosed by clinical symptoms less frequently compared to non-teaching hospitals (15% versus 24%, $p=0.01$).

A histopathological classification could be obtained from pathology reports from 214 DCIS lesions (43%). Among hospitals, different classification systems were used: 29 lesions (19%) were classified as grade I or well differentiated, 45 lesions (29%) as grade II or moderately differentiated and 79 lesions (52%) as grade III or poorly differentiated. 52 DCIS tumours were classified as comedo type whereas nine

Table I. Patient and tumour characteristics compared between teaching and non-teaching hospitals.

Characteristic	All hospitals % (n = 502)	Teaching hospitals % (n = 227)	Non-teaching hospitals % (n = 275)	p-value 0.85
Mean age at diagnosis (years)	57.2	57.2	57.4	
Age at diagnosis				
≤50 years	22.7 (114)	22.0 (50)	23.3 (64)	0.74
>50 years	77.3 (388)	78.0 (177)	76.7 (211)	
Menopausal status				
Premenopausal	14.8 (74)	16.3 (37)	13.5 (37)	0.86a
Postmenopausal	23.3 (117)	26.4 (60)	20.8 (57)	
Unknown	61.9 (311)	57.3 (130)	65.7 (181)	
Family history of breast cancer				
Positive	19.9 (100)	23.3 (53)	17.1 (47)	0.97a
Negative	46.4 (233)	54.6 (124)	39.6 (109)	
Unknown	33.7 (169)	22.1 (50)	43.3 (119)	
DCIS diagnosis				
Mammographic findings	79.5 (399)	84.1 (191)	75.6 (208)	**0.01a**
Clinical symptoms	19.7 (99)	14.5 (33)	24.0 (66)	
Unknown	0.8 (4)	1.4 (3)	0.4 (1)	
Mammographic findings				
Microcalcifications	83.7 (334)	82.2 (157)	85.1 (177)	0.71
Architecture distorsion	6.0 (24)	6.3 (12)	5.8 (12)	
Microcalcifications within distorsion	10.3 (41)	11.5 (22)	9.1 (19)	
Location of DCIS				
Inner quadrant	18.5 (93)	19.8 (45)	17.4 (48)	0.49a
Outer quadrant	56.2 (282)	56.4 (128)	56.0 (154)	
Central	24.1 (121)	21.6 (49)	26.2 (72)	
Unknown	1.2 (6)	2.2 (5)	0.4 (1)	
Mean size of DCIS (millimetres)	16.9	16.6	17.2	0.80a

[a] Excluding unknown values.

were classified as non-comedo type DCIS. Pathology reports noted merely 'ductal carcinoma in situ' in 288 patients (57%) and this was comparable for both types of hospitals ($p = 0.56$).

An exact size of DCIS lesions was documented in radiology or pathology reports for 133 tumours (27%) with no difference between teaching and non-teaching hospitals ($p = 0.82$). DCIS tumours detected by clinical symptoms were of significantly greater size compared to lesions detected by mammography (mean size 23 mm and 14 mm, respectively, $p = 0.001$).

Table II presents the treatment characteristics. Initially, attempts were made to treat with breast-conserving surgery in the majority of patients (479 patients, 95%). 23 patients (5%) underwent mastectomy as first procedure and these patients were of older age compared to patients initially treated with breast-conserving surgery (mean age 64 years versus 57 years, $p = 0.04$) Patients treated with mastectomy initially on average had DCIS tumours of greater size (mean 36 mm versus 15 mm in women treated with breast-conserving surgery, $p < 0.01$). In teaching hospitals initial mastectomy rates were lower (range: 1%–6% versus 3%–11% in non-teaching hospitals, $p = 0.06$).

Of those patients treated with breast-conserving surgery, a complete excision was achieved in 233 (46%), leaving a rather high percentage of patients (44%, 222 patients) with surgical margins not free of disease after the first operation. For 47 patients (9%) no information about the margin status was available. Results of margin status after first excision were comparable for the two types of hospitals.

Subsequently, a second or third surgical procedure was performed in 248 patients (49%) and 150 of these patients underwent mastectomy. Mastectomy as a re-operation was performed in teaching hospitals less frequently (54% versus 67%, $p = 0.03$).

After re-excision, residual DCIS was found in 103 patients (42%) whereas in 115 patients (47%) no residual DCIS was found. Eighteen patients (7%) had residual DCIS which was not completely excised. Of 12 patients (4%) no information about the re-excised specimen was available.

The mean number of surgical procedures was 1.5 (median 1, range: 1–3) and this was comparable for teaching and non-teaching hospitals (1.58 and 1.51 respectively, $p = 0.22$). Finally, 329 patients (65%) were treated by breast-conserving surgery and 173 patients (35%) were treated by mastectomy. Final mastectomy rates showed a slight statistically non-significant difference between teaching and non-teaching hospitals: 31% versus 37%, respectively ($p = 0.17$). The proportion of patients finally treated with mastectomy decreased during the study period, (37% before 1993 versus 29% after 1998, $p = 0.05$). Patients finally treated with mastectomy were of

Table II. Treatment characteristics of all DCIS patients compared between teaching and non-teaching hospitals.

Characteristic	All hospitals % (n = 502)	Teaching hospitals % (n = 227)	Non-teaching hospitals % (n = 275)	p-value
Initial treatment				
Lumpectomy	95.4 (479)	97.4 (221)	93.8 (258)	0.06
Mastectomy	4.7 (23)	2.6 (6)	6.2 (17)	
Margin status after first procedure				
Positive	44.2 (222)	48.9 (111)	40.4 (111)	0.14
Negative	46.4 (233)	41.9 (95)	50.2 (138)	
Unknown	9.4 (47)	9.2 (21)	9.4 (26)	
Re-excision				
No	50.6 (254)	46.7 (106)	53.8 (148)	0.11
Yes	49.4 (248)	53.3 (121)	46.2 (127)	
Re-excision performed				
lumpectomy	39.5 (98)	46.3 (56)	33.1 (42)	**0.03**
mastectomy	60.5 (150)	53.7 (65)	66.9 (85)	
Final treatment				
Lumpectomy	65.5 (329)	68.7 (156)	62.9 (173)	0.17
Mastectomy	34.5 (173)	31.3 (71)	37.1 (102)	
Final margin status				
Positive	7.6 (38)	10.1 (23)	5.5 (15)	0.09
Negative	84.3 (423)	80.6 (183)	87.3 (240)	
Unknown	8.2 (41)	9.3 (21)	7.3 (20)	
Adjuvant therapy				
Radiation therapy	20 (4)	9 (4)	11 (4)	0.98
No adjuvant therapy	282 (96)	218 (96)	264 (96)	

[a] Excluding unknown values.

younger age compared to patients treated with breast-conserving surgery (56 years versus 58 years, p = 0.09).

After performance of one or more surgical procedures, 38 patients (8%) had tumour-positive surgical margins whereas for 41 patients (8%) final margin status was not specified (Table III). In teaching hospitals 44 patients (19%) had disease-involved or unknown margins versus 35 patients (13%) in non-teaching hospitals (p = 0.04).

An exact margin width was specified for 141 patients only, of whom the majority (123 patients, 87%) had a margin width of 1 millimetre or less (no differences between teaching and non-teaching hospitals, p = 0.27).

Discussion

This retrospective, population-based review showed an increase in numbers of DCIS detected, with more tumours diagnosed by mammography during time. This is mainly due to the introduction of the breast cancer screening program. Similar to other countries, the incidence of DCIS has increased since then [4,24].

Cornerstone in treatment of DCIS is a radical, microscopically complete excision of the lesion, the only factor a surgeon is able to control [5]. This is crucial, because most recurrences after breast-conserving surgery occur at the same site of and are clonally related to their primary lesions [22,23,25]. Though, radiation therapy has proven to decrease the risk of local recurrence after breast-conserving surgery, radiation therapy cannot compensate for surgical margins not free of disease [15–19,21,26,27].

A complete excision of DCIS can be difficult to achieve: in the presented population DCIS was completely excised after the first procedure in 46% only, and, in the end, 35% of patients were treated by mastectomy, mainly because of tumour-involved margins after the first excision. This difficulty can be explained by the growth pattern of DCIS. It has been shown that most tumours involve a single

Table III. Final margin status for different hospitals.

Final margin status	All hospitals % (n =)	A[1] % (n = 55)	B[1] % (n = 90)	C % (n = 42)	D % (n = 44)	E % (n = 68)	F % (n = 121)	G[1] % (n = 82)
Negative	84 (423)	82 (45)	86 (77)	93 (39)	98 (43)	82 (56)	84 (102)	74 (61)
Positive	8 (38)	13 (7)	3 (3)	7 (3)	0 (0)	9 (6)	5 (6)	16 (13)
Unknown	8 (41)	5 (3)	11 (10)	0 (0)	2 (1)	9 (6)	11 (13)	10 (8)

[1] Teaching hospital.

ductal unit only with multiple foci of DCIS within that duct system [28–30]. Gaps between these foci rarely exceeded 10 millimetres [29]. This is supported by the finding that growth of DCIS occurs predominantly along an axis toward and away from the nipple, i.e. along a duct system [31]. Therefore, complete eradication could be achieved in approximately 90% of patients if DCIS is excised with a rim of at least one centimetre of normal breast tissue [21,29]. However, a microscopically complete excision of a screening-detected DCIS lesion has to be performed with the use of a localisation procedure without the guidance of a palpable mass and mammographic estimates of DCIS size frequently do not correlate with the histological DCIS size [28].On the other hand, with regard to a margin width of 1 centimetre or more, cosmetic outcome is another important factor in breast-conserving surgery. Though, the volume of the excised tissue is inversely related to cosmetic outcome, it is similar related to presence of residual DCIS [32–35].

The percentage of final mastectomies in the presented population (35%) is comparable to results published recently from a population-based study performed in the United States (34% mastectomy rate) [8]. We found that in teaching hospitals, mastectomy rates initially (3% versus 6%, $p = 0.06$) and finally (31% versus 37%, $p = 0.17$) were lower when compared to non-teaching hospitals. However, patients in teaching hospitals were diagnosed by clinical symptoms less often (15% versus 24%, $p = 0.01$) and are thus likely to had DCIS tumours of smaller size. Therefore, it could be assumed that these patients were better candidates for breast-conserving surgery.

In contrast to invasive breast cancer, no randomised clinical trials have compared mastectomy with breast-conserving surgery for DCIS. Treatment of DCIS with mastectomy offers excellent results with cure rates near 100% [5,6,32]. Therefore, based on medical criteria (e.g. tumour size, breast size) or patients' preference, mastectomy could be an appropriate treatment option, especially if patients are offered immediate breast reconstruction. Otherwise, a high percentage of mastectomies could also represent over-treatment. According to our data, it seems likely that tumour characteristics (size) influenced the decision to perform a mastectomy. At least a proportion of patients who underwent mastectomy were offered immediate breast reconstruction, but we did not have data on this treatment option.

Considering the importance of complete excision, final results in our population are somehow disappointing: 38 patients (8%) had involved surgical margins and for 41 patients (8%) margin status could not be specified. These results are comparable to findings from two randomised trials, which reported the beneficial effects of radiation therapy after breast-conserving treatment of DCIS [15–19]. A retrospective analysis of 77% of patients from the National Surgical Adjuvant Breast Project (NSABP) cohort showed 16% of patients had uncertain or involved margins. A similar analysis of 85% of patients from the European Organisation for Research and Treatment of Cancer (EORTC) study cohort revealed that 9% of the patients had close or involved margins whereas no information on margin status was available in 12% [15–19].

Another issue to address is the quality of histopathological reports. Among hospitals, different classification systems were used and the majority of lesions were classified as 'ductal carcinoma in situ' only. Similar, tumour size could be obtained from 27% only. As both histopathological grade and size of DCIS are risk factors for recurrences, reporting these factors is of great importance to guide treatment strategy [1,14,20,22].

In conclusion, this report shows an increase in numbers of DCIS detected and a shift towards more non-symptomatic, non-palpable lesions over a period of 10 years. Rates of breast-conserving surgery increased during time, but, still a relative large number of patients (35%) are treated with mastectomy, which could represent over-treatment. Furthermore, we found a rather high percentage of patients (16%) with unknown or tumour-involved margins. This clearly demonstrates that surgical treatment of DCIS is still a challenge. Improvements of surgical care could be made by obtaining a microscopically complete resection. Therefore, reports on histopathological examination should emphasize on histopathological grade, tumour size, and margin status thereby providing further insight into excision quality and guide treatment strategy.

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