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Original article

Breast-conserving therapy for primary Ductal Carcinoma in Situ in The Netherlands: A multi-center study and population-based analysis

Jan J. Jobsen [a, b, c, *], Luc J.E.E. Scheijmans [d], Wilma G.J.M. Smit [e], Marika C. Stenfert Kroese [f], Henk Struikmans [g], Job van der Palen [a, h]

[a] Department of Epidemiology, Medisch Spectrum Twente, Enschede, The Netherlands
[b] Department of Radiation Oncology, Medisch Spectrum Twente, Enschede, The Netherlands
[c] Breast Clinic Oost-Nederland, Ziekenhuis Groep Twente, Hengelo, The Netherlands
[d] Institute Verbeeten, Tilburg, The Netherlands
[e] Radiotherapy Institute Friesland, Leeuwarden, The Netherlands
[f] Radiotherapy Institute Steden en Omstreken, Deventer, The Netherlands
[g] Department of Radiation Oncology, Haaglanden Medical Centre, Leidschendam, The Netherlands
[h] Departement of Research Methodology, Measurement, and Data Analysis, Faculty of Behavioural Science, University of Twente, The Netherlands

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ABSTRACT

Objective: The aim of this study was to analyse the efficacy of breast-conserving therapy (BCT) for women with primary DCIS in a population-based setting.
Methods: Data were used from five Radiotherapy centres in The Netherlands from 2000 to 2010, all treated with BCT. Of all the cases, 59.2% received a boost of radiotherapy after their whole breast irradiation (WBI), irrespective of margin status.
Results: A total of 1248 cases with primary DCIS were analysed. The 10-years LRFS was 92.9%. Age $\leq$50 years and a positive margin were significantly related to local relapse free survival (LRFS). Having a boost had no impact on LRFS, showing a nearly equal recurrence pattern in patients with and without a boost. Separate analyses were done on patients who had received and not received a boost of radiotherapy after WBI. We noted 9.1% contra-lateral breast tumours. The 10-years disease specific survival (DSS) rate was 99.0%.
Conclusions: DCIS of the breast and treated with BCT results in excellent LRFS and DSS. Primary surgical lumpectomy with negative margins followed by WBI seems to be the treatment of choice in DCIS treated with BCS with respect to IBTR.

1. Introduction

Ductal Carcinoma in Situ (DCIS) is not considered to be an invasive carcinoma (IC), but a premalignant lesion. It displays a broad spectrum of tumour biology. Traditionally, DCIS has been treated through breast conserving surgery (BCS) or ablative surgery. Nationwide screening mammography was initiated in The Netherlands in 1990. From 1990 until 2016,we noted an increase of DCIS in The Netherlands from 375 to 2675 cases per year. Furthermore, a sharp increase in the incidence of DCIS was noted after 2005 [1,2].

In the 1980s and 1990s, four randomized controlled trials were performed to evaluate the efficacy of whole breast irradiation (WBI) following BCS in women with DCIS [3–7]. In a recent review, Shah et al. concluded from these results that surgery and WBI should remain the standard care treatment in the management of DCIS [8].

However, over the past decade, doubt has emerged as to whether current treatment paradigms for DCIS may represent overtreatment. In 2015, Narod et al. presented the results of an observational study of more than 100.000 women diagnosed with DCIS, finding the 20-year rate of breast cancer mortality to be 3.3% [9]. Invasive cancer recurrences represent about 50% of all recurrences and are associated with a low rate of breast cancer mortality [4,6,7].

The addition of WBI is associated with long-term side effects. In 2012, the long-term cosmetic changes after breast-conserving

* Corresponding author. Department of Epidemiology, Medisch Spectrum Twente, Haaksbergerstraat 55, 7513, ER Enschede, The Netherlands.
E-mail address: jjjobsen@hetnet.nl (J.J. Jobsen).

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therapy (BCT) of 348 breast cancer participants of the EORTC 'boost versus no boost' trial showed that a boost dose worsened the breast appearance the during the initial years and that the development of fibrosis associated with WBI is an ongoing process [10]. Considering cardiovascular morbidity and mortality, a recent study noted no increased risk, with 10-year median follow-up, after radiotherapy for DCIS when compared with surgery alone [11].

In The Netherlands, since the first results of the EORTC 10853 trial, BCT has been the standard treatment for localized DCIS [6]. This trial, together with two other trials, resulted in roughly a 35%–45% reduction in local recurrence with WBI. However, in contrast to invasive breast cancer the survival benefit for adjuvant WBI has not been established with DCIS. However, in a recent large longitudinal cohort study reported by Sagara et al. (n = 32.144, SEER-data) the prognostic score of DCIS (Smith et al.) identifies subgroups of patients for whom the breast cancer mortality and overall mortality will decrease by applying WBI. In another analysis of SEER data (Qian 2015, n = 56.968) WBI had showed a survival benefit for patients ≤ 50 years and negative ER-status [12–14]. Further studies will be needed to confirm these findings. Internationally there is a growing interest in omitting WBI for low risk patients or administrating partial breast radiotherapy. Therefore, it is important to also assess the efficacy of DCIS treatment (including WBI) in a population-based setting.

This study aims to assess the efficacy of BCT for women with primary DCIS in a population-based setting.

2. Patients and methods

Clinical data from 1328 patients with DCIS and all treated between 2000 and 2011 through BCT, were collected from five radiotherapy departments in The Netherlands. In the Netherlands,

Table 1
Patients and tumour characteristics of 1248 patients with ductal carcinoma in situ (DCIS) and treated through breast-conserving therapy.

Characteristics	All Patients n = 1248 (%)	No-boost group n = 509 (%)	Boost group n = 739 (%)	P value
Age				
≤51 years	244 (19.5)	102 (20.0)	142 (19.2)	
>50 years	1004 (80.4)	407 (80.0)	597 (80.8)	ns
Family history on first degree relative				
None	884 (70.8)	366 (71.9)	518 (70.1)	
One first degree relative	233 (18.7)	90 (17.7)	143 (19.3)	ns
≥2 first degree relatives	53 (4.2)	24 (4.7)	29 (3.9)	
Unknown	78 (6.2)	29 (5.7)	49 (6.6)	
Localisation primary				
Lateral upper quadrant	644 (51.6)	266 (52.3)	378 (51.1)	
Lateral lower quadrant	107 (8.6)	53 (10.4)	54 (7.3)	
Medial upper quadrant	196 (15.7)	83 (16.3)	113 (15.3)	ns
Medial lower quadrant	87 (7.0)	31 (6.1)	56 (7.6)	
Central	192 (1534)	65 (12.8)	127 (17.2)	
Unknown	22 (1.8)	11 (2.2)	11 (1.5)	
Primary surgery				
Lumpectomy	586 (47.0)	276 (54.2)	310 (41.9)	
Lumpectomy + re-excision	235 (18.8)	109 (21.4)	126 (17.1)	<0.001
Lumpectomy + re-excision + SN	51 (4.1)	3 (0.6)	48 (6.5)	
Lumpectomy + SN (axilla)	374 (30.0)	120 (23.6)	254 (34.4)	
Unknown	2 (0.2)	1 (0.2)	1 (0.1)	
Histology				
Ductal carcinoma in situ	1219 (97.7)	495 (97.2)	724 (98.0)	
Intracyst. papillary carcinoma	22 (1.8)	9 (1.8)	13 (1.8)	ns
Morbus Paget	7 (0.6)	5 (1.0)	2 (0.3)	
Malignancy grading				
Grade 1	190 (15.2)	134 (26.3)	56 (7.6)	
Grade 2	445 (35.7)	187 (36.7)	258 (34.9)	<0.001
Grade 3	559 (44.8)	157 (30.8)	402 (54.4)	
Unknown	54 (4.3)	31 (6.1)	23 (3.1)	
Margin Status				
Negative	970 (77.7)	443 (87.0)	527 (71.3)	
Positive	73 (5.8)	13 (2.5)	60 (8.1)	<0.001
Marginal ≤1 mm	193 (15.5)	47 (9.2)	146 (19.8)	
Unknown	12 (1.0)	6 (1.2)	6 (0.8)	
Tumour size				
<11 mm	385 (30.8)	165 (32.4)	220 (29.8)	
11–20 mm	417 (33.4)	174 (34.2)	243 (32.9)	ns
>20 mm	164 (13.1)	65 (12.8)	99 (13.4)	
Unknown	282 (22.6)	105 (20.6)	177 (23.9)	
Low Risk DCIS				
None	1149 (92.1)	433 (85.1)	716 (96.9)	<0.001
Yes	99 (7.9)	76 (14.9)	23 (3.1)	
Timing radiotherapy after lumpectomy				
<36 days	453 (36.3)	132 (25.9)	321 (43.4)	
36–56 days	509 (40.8)	213 (41.8)	296 (40.1)	<0.001
>56 days	286 (22.9)	164 (32.2)	122 (16.5)	
Histology contra lateral tumour				
None	1135 (90.9)	461 (90.6)	674 (91.2)	
DCIS	34 (2.7)	13 (2.5)	21 (2.8)	ns
Invasive carcinoma	79 (6.3)	35 (6.9)	44 (5.9)	

P-value has been calculated on the known components of the variables.