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EPIDEMIOLOGY

Impact of primary local treatment on the development of distant metastases or death through locoregional recurrence in young breast cancer patients

E. J. Bantema-Joppe · E. R. van den Heuvel · L. de Munck · G. H. de Bock · W. G. J. M. Smit · P. R. Timmer · W. V. Dolsma · L. Jansen · C. P. Schröder · S. Siesling · J. A. Langendijk · J. H. Maduro

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Abstract In this study, we tested the hypothesis whether breast conserving therapy (BCT) compared with mastectomy is associated with a negative outcome in terms of distant metastases or death (DMD) and investigated the relation between locoregional recurrence (LRR) and DMD in young breast cancer (BC) patients. This study included a consecutive series of 536 patients ≤40 years of age at diagnosis with pathological T1N0-3M0 BC, treated between 1989 and 2005. A multistate survival model was used to evaluate the influences of local treatment and LRR on DMD, adjusted for potential prognostic factors. Patients were treated with mastectomy ($N = 213$) or BCT ($N = 323$). Median age at diagnosis was 36.3 years, with a median follow-up of 9.0 years. The 10-year actuarial cumulative incidence of DMD was 30.6 % after mastectomy and 26.3 % after BCT ($P = 0.04$). In total, 81 (15 %) LRRs were observed. After BCT, patients had a threefold higher risk of LRR than after mastectomy (HR 2.9; 95 % CI 1.6–5.3). Patients with LRR had a higher risk of DMD compared with patients without LRR (HR 5.5; 95 % CI 2.1–14.5). However, BCT was not negatively associated with DMD-after-LRR (HR 0.47; 95 % CI 0.2–1.1, BCT vs mastectomy). In conclusion, although LRR significantly affected DMD, the increased risk of LRR after BCT compared with mastectomy did not lead to a worse DMD outcome in BC patients ≤40 years of age.

Keywords Breast cancer · Therapy · Young · Locoregional recurrence · Radiotherapy · Breast conserving therapy · Mastectomy

Introduction

In breast cancer (BC), young age is associated with increased locoregional recurrence (LRR) and poorer sur-

E. J. Bantema-Joppe · W. V. Dolsma · J. A. Langendijk · J. H. Maduro (✉)
Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, P.O. Box 30 001, 9700 RB Groningen, The Netherlands
e-mail: j.h.maduro@umcg.nl

E. R. van den Heuvel · G. H. de Bock
Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

L. de Munck · S. Siesling
Department of Registration and Research, Comprehensive Cancer Centre the Netherlands, Utrecht, The Netherlands

W. G. J. M. Smit
Radiotherapeutic Institute Friesland, Leeuwarden, The Netherlands

P. R. Timmer
Department of Radiation Oncology, Isala Clinics, Zwolle, The Netherlands

L. Jansen
Department of Surgical Oncology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

C. P. Schröder
Department of Medical Oncology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

S. Siesling
Department of Health Technology and Services Research, MIRA Institute of Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

vival [1–9]. The primary surgical options in young women diagnosed with invasive BC are essentially the same as in older women. In general, for patients with small tumours with diameters up to 5 cm, breast conserving surgery (BCS) followed by radiotherapy (breast conserving therapy (BCT)) is the treatment of choice. In these young patients, LRR rates are higher after BCT than after mastectomy [10, 11]. Furthermore, higher LRR rates are associated with an increased risk of distant metastases (DM) and LRRs are possibly a source of distant spread by itself, resulting in worse overall survival [12–17]. Based on this assumption, mastectomy is sometimes recommended instead of BCT in young BC patients.

In a series of consecutive young BC patients (≤40 years) with tumours up to 2 cm, we addressed the following research questions: (1) Is BCT compared with mastectomy associated with a negative outcome in terms of distant metastases or death (DMD)? (and 2) What is the relation between LRR and DMD?

Patients and methods

Patients

This study population consisted of a consecutive series of 571 female patients—≤40 years at diagnosis treated between January 1989 and January 2005, with pathological T1N0-3M0 BC—who were treated with either mastectomy or BCT. Patients were identified from the Netherlands Cancer Registry (NCR) [18], restricted to the Northern region of the Netherlands, covering 2.1 million inhabitants. Patients were staged according to the TNM classification (IUCC 2002) [19].

Data collection

Additional clinicopathological data were retrieved retrospectively from the patients' files after approval of the hospital institutional review boards. Data collected included type of surgery, adjuvant therapy, tumour recurrence, DM and death, with the corresponding dates. Pathological data were retrieved directly from the pathological reports. Oestrogen and progesterone receptor status were routinely assessed from 2003. Receptor status and resection margin status were frequently missing and therefore not considered as covariates.

If no follow-up data were available, the general practitioner was contacted for information on follow-up status. Patients with previous diagnosis of invasive cancer, other than non-melanoma skin cancer ($N = 11$; 2 %), and in situ carcinoma of the cervix; patients with synchronous contralateral BC ($N = 3$); and patients treated with neo-adjuvant systemic therapy ($N = 5$) were excluded. For 16 patients, no pathological data could be retrieved. Ultimately, 536 cases were available for inclusion in our study.

Definitions

Primary local treatment (mastectomy or BCT) was classified according to the last surgical procedure performed. In cases where a subsequent mastectomy was performed in addition to lumpectomy because of involved margins, local treatment was defined as a mastectomy.

Local recurrence (LR) was defined as recurrence of invasive carcinoma in the ipsilateral breast, overlying skin, or chest wall. New primaries could not be differentiated from secondary primaries. Regional recurrence (RR) was defined as recurrence in the ipsilateral axillary, supraclavicular or internal mammary lymph nodes without clinical-radiological evidence of DM. LRR was defined as the combination of LR and RR. DM were defined as cancers spreading to sites other than local or regional. Because of the young age of the cohort, we included all deaths irrespective cause, and not only BC-related deaths. In this way, potential treatment-related long-term deaths were taken into account.

Endpoints were calculated as the interval between pathological diagnosis of primary BC and the event of interest or date of last follow-up. The primary endpoint was defined as DMD, i.e. the development of DM or death (D). This endpoint was chosen because all DM inevitably lead to death.

Primary surgery

Surgery was performed in 16 hospitals. Primary local treatment consisted of either BCS followed by radiotherapy (BCT) or mastectomy either or not followed by post-operative radiotherapy when indicated. Initially, axillary staging consisted of axillary lymph node clearance. Since the late 1990s, sentinel node biopsy followed by axillary clearance in case of a positive sentinel node has gained general acceptance and has increasingly been used.

Radiotherapy

Patients were referred to three radiotherapy centres in the Northern region of the Netherlands. In patients who were treated with BCS, whole-breast irradiation consisting of 50 Gy in 5 weeks (fraction dose 2.0 Gy, 5 days per week) was generally followed by a boost dose applied to the tumour bed area. The boost was administered with external beam radiotherapy with a dose ranging from 16 to 20 Gy in 2 Gy fractions or 15 Gy with interstitial iridium implants ($N = 31$).

Post-operative thoracic wall irradiation was given in case of focally positive resection margins after mastectomy

($N = 8$). Regional radiotherapy (direct photon beams) to the draining nodal areas, including the axillary, supraclavicular and internal mammary chain, was indicated if more than three positive axillary lymph node metastases or a positive apical lymph node (≥pN2) were detected. Internal mammary chain irradiation was applied by mixed photon and electron techniques. In case of regional radiotherapy following mastectomy, the thoracic wall was always part of the treatment ($N = 37$).

Systemic therapy

Before the early 1990s, only node-positive patients were treated with adjuvant chemotherapy, generally consisting of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) given simultaneously with radiotherapy. Anthracycline-based chemotherapy has been used increasingly since the mid-1990s and was given sequentially to radiotherapy. In the late 1990s, chemotherapy was also indicated for pre-menopausal high-risk node-negative patients, depending on tumour size, grade and hormonal receptor status. Around 2001, adjuvant systemic treatment was recommended to patients aged ≤35 years, irrespective of tumour characteristics.

At the beginning of the study period, adjuvant hormonal therapy was not routinely given to pre-menopausal women. From 1998 onwards, hormonal status was assessed routinely and, since then, hormonal therapy (5 years of tamoxifen) has been recommended for all hormone-receptor-positive, node-positive patients and unfavourable node-negative patients [20, 21]. Trastuzumab was not used as an adjuvant treatment during the inclusion period of this series.

Statistical modelling and analysis

The clinicopathological characteristics of both treatment groups were described and compared with a Chi square test.

The risk of DMD by treatment type was estimated with the Kaplan–Meier method and compared with the log-rank test. The impact of primary local treatment was tested by a Cox proportional hazards analysis. Since local treatment type was our primary interest, this covariate was forced into the model. Other covariates were included in the model if the probability value was <0.1 in univariate analysis. Age at diagnosis was included based on the literature.

The impact of primary local treatment on LRR and DMD was determined by using an illness–death model. In this specific multistate model, Cox proportional hazards analysis is applied using clinical variables as covariates in addition to a state-dependent covariate, as described by Putter et al. [22, 23]. Three states or outcomes can be distinguished at any time during follow-up; state 1: disease-free, and alive after primary local treatment; state 2: alive, and salvaged after LRR; state 3: patients with DMD (Fig. 1). Each transition from one state to the other could be affected by treatment and other variables. If LRR and DMD were detected simultaneously during follow-up, then we assumed that the patient was in the LRR state first and then transitioned to DMD the following day. We used this model to assess the transitions during the course of the disease and to study prognostic factors for each transition [12, 22, 23].

To compare the transition from primary local treatment to DMD with and without a LRR, we introduced a state-dependent covariate in the model. This enhanced model was used to assess the impact of primary local treatment on the development of DMD. The state-dependent covariate itself indicates the risk ratio of DMD between transition 2 and 3 (Fig. 1), and therefore the prognostic risk of DMD-after-LRR. To estimate the risk of development of LRR on DMD at a certain time, we introduced a second state-dependent covariate with two categories: LRR occurrence within 3 years post-diagnosis and after 3 years [12].

The number of events (subdivided into LR and RR) from one state to the other were provided for both treatments separately. These transitions and several follow-up/event times were tested using Chi square tests or the Wilcoxon rank sum test.

All tests were two sided, and probability values of <0.05 were considered to be statistically significant. The analyses were performed using the SPPS software package, version 16.0 (SPSS, Chicago, IL, USA) and SAS/STAT Software, version 9.2 (SAS Institute Inc, Cary, NC, USA).

Results

Patient characteristics

Of the total population, 213 patients (40 %) were treated with mastectomy and 323 with BCT. Overall, 38 % of the

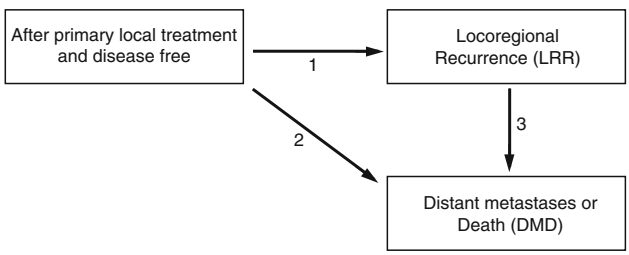

Fig. 1 Breast cancer progression in a multistate model. A patient can be in three different states at any time during follow-up. After primary local treatment without any recurrence; disease-free after locoregional recurrence (LRR); or with distant metastases or death (DMD). Three different paths can be followed: *1* transition from local treatment to LRR; *2* transition from local treatment to DMD; and *3* transition from LRR to DMD

women were aged 35 years or less at diagnosis. The median follow-up time was 9.0 years (interquartile range (IQR) 5.5–12.8).

In Table 1, patient and tumour characteristics are listed according to primary local treatment. The patients treated with mastectomy had more unfavourable prognostic factors such as younger age and more positive lymph nodes. Consequently, more mastectomy patients were treated with regional radiotherapy and chemotherapy. Median follow-up was equal in both groups

Table 1 Patient and tumour characteristics according to primary local treatment ($N = 536$)

Characteristic	M ($N = 213$) N (%)	BCT ($N = 323$) N (%)	Total N (%)	P value[a]
Age at diagnosis (year)				
≤35	94 (44.1)	107 (33.1)	201 (37.5)	**0.01**
36–40	119 (55.9)	216 (66.9)	335 (62.5)	
BCRA mutation				
Absent	18 (8.5)	25 (7.7)	43 (8.0)	0.83
Present	11 (5.2)	17 (5.3)	28 (4.2)	
Unknown	154 (86.4)	281 (87.0)	465 (86.8)	
Pathological T-stage				
p1ab	50 (23.5)	75 (23.2)	125 (23.3)	0.95
p1c	163 (76.5)	248 (76.8)	411 (76.7)	
Pathological N-stage				
pN0	124 (58.2)	224 (69.4)	348 (64.9)	**0.008**
pN1	62 (27.2)	78 (24.1)	136 (25.4)	
pN2	21 (9.9)	17 (5.3)	38 (7.1)	
pN3	10 (4.7)	4 (1.2)	14 (2.6)	
Histology				
Invasive ductal	176 (82.6)	286 (88.5)	462 (86.2)	**0.002**
Invasive lobular	22 (10.3)	12 (3.7)	34 (6.3)	
Other	15 (7.0)	25 (7.7)	40 (7.5)	
Multifocality				
No	139 (65.3)	309 (95.7)	448 (83.6)	**<0.001**
Yes	74 (34.7)	14 (4.3)	88 (16.4)	
Extensive DCIS				
Absent	166 (77.9)	298 (92.3)	464 (86.6)	**<0.001**
Present	47 (22.1)	25 (7.7)	72 (13.4)	
Lymphovascular invasion				
Absent	179 (84.0)	298 (92.3)	477 (89.0)	**0.003**
Present	34 (16.0)	25 (7.7)	59 (11.0)	
Adjuvant chemotherapy				
No	110 (51.6)	198 (61.3)	308 (57.5)	**0.03**
Yes	103 (48.4)	125 (38.7)	228 (42.5)	
Adjuvant hormonal therapy				
No	167 (78.4)	261 (80.8)	428 (79.9)	0.5
Yes	46 (21.6)	62 (19.2)	108 (20.1)	
Regional radiotherapy				
No	165 (77.5)	283 (87.6)	448 (83.6)	**0.002**
Yes	48 (22.5)	40 (12.4)	88 (16.4)	
Second cancer				
Contralateral BC	13 (6.1)	19 (5.9)	32 (6.0)	0.38
Ovarian	1 (0.5)	4 (1.2)	5 (0.9)	
Other	3 (1.4)	10 (3.1)	13 (2.4)	

Bold print signifies $P < 0.05$

M mastectomy, *BCT* breast conserving therapy, *DCIS* ductal carcinoma in situ, *BC* breast cancer

[a] χ^2 test with feature divided in 2 categories

[mastectomy 8.8 (IQR 5.4–12.1), BCT 9.1 (IQR 5.7–13.9) years].

Development of distant metastases or death univariate and multivariate analysis

The 10-year actuarial cumulative incidence of DMD was 30.6 % (95 % confidence interval (CI) 23.5–37.7) after mastectomy and 26.3 % (95 % CI 20.6–32.0) after BCT ($P = 0.04$). This is shown in Fig. 2. Controlled for unfavourable prognostic factors, primary local treatment had no significant impact on DMD (HR 0.80, 95 % CI 0.6–1.2, $P = 0.24$, mastectomy is the reference) (Table 2). No other statistically significant prognostic factors for DMD were identified (Table 2).

Patterns of distant metastases or death

The number of events according to primary local treatment is shown in Fig. 3. In total, DMD occurred in 132 (25 %) patients, and 13 patients (2 %) died without DM. In the mastectomy group, 48 patients (23 %) had DMD without a LRR compared with 47 (15 %) in the BCT group ($P = 0.02$) (Fig. 3). DMD was preceded by a LRR in 37 patients, consisting of 16 patients with LRs (43 %), 17 with RRs (46 %) and 4 with simultaneous LR and RR (11 %). Out of the 21 patients who developed a LRR in the mastectomy group, 13 (62 %) had DMD, compared with 24 out of 60 (40 %) in the BCT group ($P = 0.08$). In all patients, the proportions of patients developing DMD after LR or RR were 30 and 75 % ($P = 0.001$), respectively.

Median time-to-LRR was shorter [2.7 years (IQR 1.8–5.3)] for patients who subsequently developed DMD than for those who did not [median 6.9 years (IQR 3.5–9.3); $P < 0.001$].

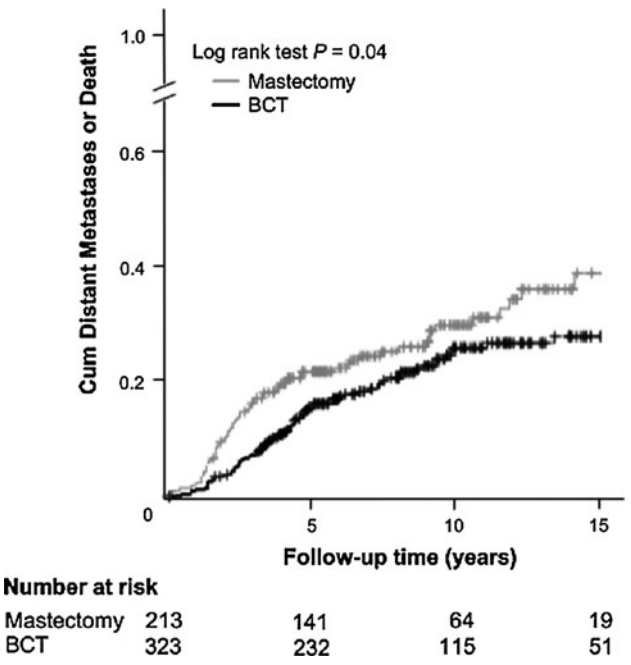

Fig. 2 Actuarial cumulative incidence curves of distant metastases or death (DMD) by primary local treatment [mastectomy or breast conserving therapy (BCT)], including the number at risk, compared with the log-rank test

Patterns of locoregional failure

In the total population, 81 patients developed LRR (15 %), with 21 LRRs (10 %) in the mastectomy group and 60 LRRs (19 %) in the BCT group. LR as first event occurred in 53 patients (65 %), 23 patients (28 %) developed RR, while 5 patients (7 %) had LR and RR simultaneously. Of the RRs, 9 (39 %) were localized in the axilla, 11 (48 %) in the supraclavicular region, and 1 (4 %) in both sites simultaneously. Of the patients with RR, two developed an internal mammary chain recurrence, combined with recurrences located in the axillary, infra, and supraclavicular nodes. Median time-to-LRR was 4.7 years (IQR 2.1–8.2); 3.9 years in the mastectomy group (IQR 1.5–6.9) and in the BCT group 5.1 years (IQR 2.5–8.5, not significant).

Multi-state analysis

The results of the multistate analysis of the transition LRR to DMD (transition 3) are shown in Table 3, right column. The occurrence of DMD-after-LRR was not associated with primary local treatment (HR 0.47; 95 % CI 0.2–1.1, BCT vs mastectomy). The hazard ratio of developing

Table 2 Cox proportional hazard model for distant metastases or death

Characteristic	HR	95 % CI	*P* value
Primary local treatment			
BCT vs Mastectomy[a]	0.80	0.6–1.2	0.24
Age at diagnosis (year)			
36–40 vs ≤35[a]	0.83	0.6–1.2	0.29
Pathological N-stage			
pN+ vs pN0[a]	1.1	0.7–1.7	0.63
Multifocality			
Yes vs No[a]	1.2	0.8–2.0	0.35
Lymphovascular invasion			
Present vs Absent[a]	1.4	0.8–2.3	0.21
Regional radiotherapy			
Yes vs No[a]	1.2	0.7–2.0	0.49

HR hazard ratio, *CI* confidence interval, *BCT* breast conserving therapy

[a] Latter category is the reference

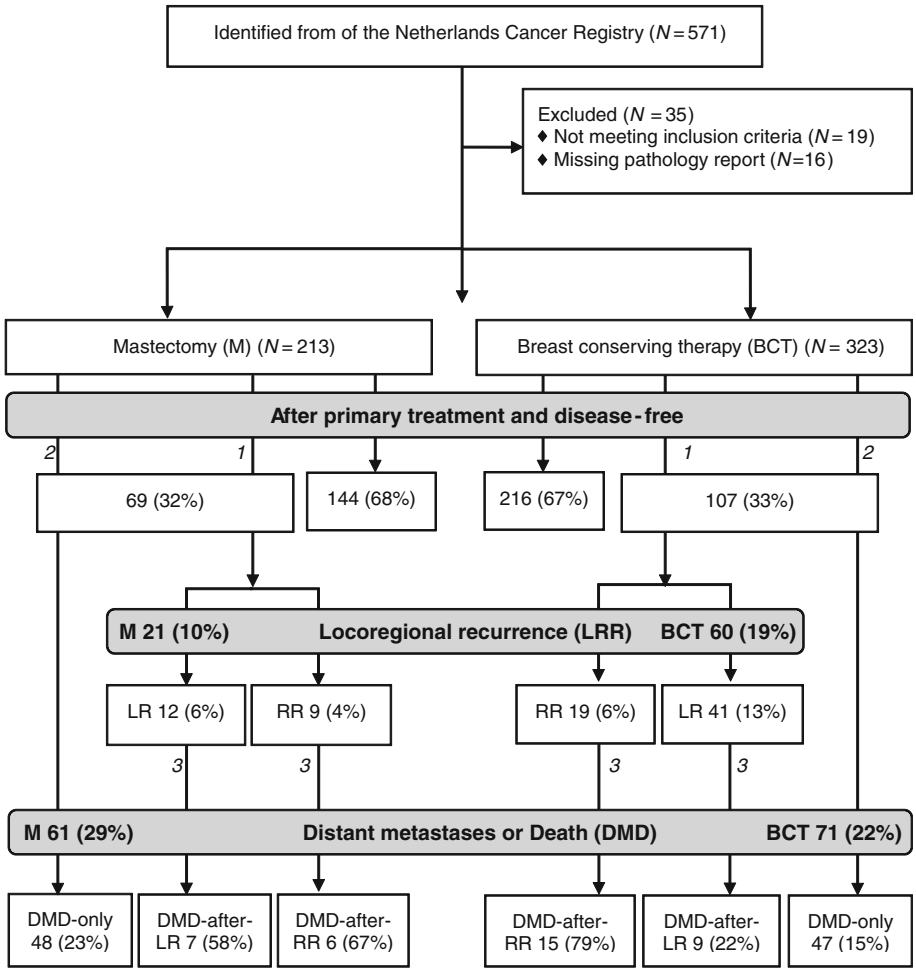

Fig. 3 Flow diagram of the three transitions (1, 2 or 3) of the multistate model and the number of events according to primary local treatment. In total, five patients developed a LR and RR simultaneously, reported as RR in this table: One patient in the mastectomy group, and four in the BCT group

DMD-after-LRR was 5.5 (95 % CI 2.1–14.5). Consequently, the occurrence of a LRR increased the risk of DMD more than fivefold. Furthermore, the occurrence of a LRR within 3 years after diagnosis significantly increased the risk of DMD compared to the occurrence of a LRR later than 3 years (HR 2.5; 95 % CI 1.1–5.6).

In modelling primary local treatment to LRR (transition 1) (Table 3, left column), it was observed that after BCT, patients had a threefold higher risk of LRR than after mastectomy (HR 2.9; 95 % CI 1.6–5.3). A higher rate of LRR was also observed amongst patients with multifocal tumours (HR 4.0; 95 % CI 2.2–7.3).

Discussion

The current study showed an actuarial 10-year cumulative incidence of DMD 30.6 % after mastectomy versus 26.3 % after BCT ($P = 0.04$). The mastectomy patients who had a LRR developed DMD in 62 % of the cases. In the BCT group, the occurrence of DMD-after-LRR was 40 %. Corrected for potential confounding, LRR was a significant risk factor for DMD (HR 5.5; 95 % CI 2.1–14.5). Patients who developed a LRR in the first 3 years after diagnosis were most at risk of DMD compared to those with a recurrence after 3 years (HR 2.5; 95 % CI 1.1–5.6). In the multistate model, young patients treated with BCT had a threefold higher risk of developing LRR compared with post-mastectomy patients. This has been reported previously and is consistent with our initial assumption that BCT results in more LRRs than mastectomy [1, 10, 11]. However, although LRR significantly affected DMD, the increased risk of LRR after BCT did not lead to a worse DMD outcome in this population of young BC patients. This was seen in both the Cox proportional hazards analysis and transition 3 of the multistate model.

Other BC studies have suggested that LRR is associated with a higher (HR 2.5–5.3) risk of DMD in all age groups [12, 17, 24]. The current analysis demonstrates this specifically for BC patients aged 40 or younger.

Botteri et al. [17] showed a linear decrease of the risk of DMD with increasing time to relapse. In the first 2 years after surgery, they estimated the risk of DMD for patients who had a LRR to be 3.2 times higher than for patients who

Table 3 Multi-state Cox proportional hazard models with associations for each transition

Characteristic	Transition 1			Transition 2			Transition 3		
	From primary treatment only to LRR			From primary treatment to DMD			From LRR to DMD		
	HR	95 % CI	*P* value	HR	95 % CI	*P* value	HR	95 % CI	*P* value
Primary local treatment									
BCT vs Mastectomy[a]	**2.9**	**1.6–5.3**	**<0.001**	0.66	0.4–1.0	0.07	0.47	0.2–1.1	0.10
Age at diagnosis (year)									
36–40 vs ≤35[a]	0.71	0.5–1.1	0.13	0.85	0.6–1.3	0.45	1.1	0.5–2.4	0.84
Pathological N-stage									
N+ vs N0[a]	0.55	0.2–1.5	0.24	1.9	0.8–4.6	0.14	2.0	0.2–19.8	0.60
Multifocality									
Yes vs No[a]	**4.0**	**2.2–7.3**	**<0.001**	1.0	0.6–1.8	0.95	0.53	0.2–1.5	0.22
Extensive DCIS									
Present vs Absent[a]	1.2	0.6–2.4	0.66	0.9	0.5–1.7	0.77	0.78	0.3–2.4	0.67
Lymphovascular invasion									
Present vs Absent[a]	1.3	0.6–2.9	0.58	1.4	0.8–2.5	0.27	2.7	0.8–8.7	0.10
Adjuvant chemotherapy									
Yes vs No[a]	1.5	0.6–3.6	0.41	0.60	0.3–1.4	0.25	0.54	0.1–4.5	0.57
Adjuvant hormonal therapy									
Yes vs No[a]	0.49	0.2–1.2	0.10	0.94	0.5–1.6	0.83	0.33	0.1–1.6	0.17
Regional radiotherapy									
Yes vs No[a]	0.64	0.3–1.6	0.34	1.4	0.8–2.6	0.25	2.6	0.5–14.7	0.27
LRR									
Present vs Absent[a]	–			–			**5.5**	**2.1–14.5**	**<0.001**
≤3 vs >3 year after diagnosis[a]	–			–			**2.5**	**1.1–5.6**	**0.03**

Adjusted for all covariates in the model

LRR locoregional recurrence, *DMD* distant metastases or death, *HR* hazard ratio, *CI* confidence interval, *DCIS* ductal carcinoma in situ, *BCT* breast conserving therapy

Bold print signifies $P < 0.05$

[a] Latter category is the reference

developed a recurrence later on. We introduced time-to-occurrence of LRR as covariate in the analysis. Although previous research has clearly shown that there is no plateau phase for in-breast recurrences, most true LRs develop in the first 3–4 years after treatment [25]. We dichotomized time-to-LRR as follows: LRR within 3 years after primary treatment and LRR more than 3 years after treatment. This analysis showed a 2.5-fold increase in the risk of DMD if LRR developed within 3 years, compared with more than 3 years. Furthermore, median time-to-LRR in the group without DMD was 6.9 years compared with 2.7 years in the group transitioning to DMD. This demonstrates the different biological behaviour of early and late recurrences.

Given the relatively low number of events, LR ($N = 53$) and RR ($N = 28$), we considered LRR as a combined endpoint. Therefore, it was not possible to analyse the impact of the type of recurrence on DMD separately. This limits the interpretation of our results, as a RR is a more advanced stage of disease than an in-breast recurrence, which might be salvaged by a mastectomy [26], thus implying a different prognosis. However, in the raw data (Fig. 3), a RR compared to a LR was associated with a higher risk of DMD. This was especially the case in the BCT group (22 % after LR vs 79 % after RR). Botteri et al. [17] also observed a difference between local and regional recurrences in the 5-year cumulative incidence of DMD-after-LRR: 22 % (LR) versus 51 % (RR), respectively.

In the mastectomy group, the proportion of patients with LRRs that developed DMD was larger than in the BCT group. This could be explained by the higher proportion of LR, compared with RR in the BCT-treated patients. Furthermore, 58 % of the mastectomy patients developed DMD-after-LR compared with 22 % in the BCT group. This suggests that LRR after BCT has a more favourable prognosis than LRR after a mastectomy. In addition, the time-to-LRR differed between patients treated with mastectomy (3.9 years) and those treated with BCT (5.1 years), although this difference is not statistically

significant. As stated above, the early recurrences could help us explain the differences found in prognostic implication between LRR after mastectomy compared with BCT. This supports the previous finding [27] that early onset chest-wall recurrences after mastectomy, rather than LRR after BCT, represent the highest risk of DM and BC-associated death, also in a population of young patients. These data suggest that not all LRRs have the same biological behaviour. This could explain the similar DMD outcome of BCT patients relative to post-mastectomy patients, despite the higher rates of LRR after BCT.

One of the strengths of the current study is the large homogeneous cohort of young (≤40 years) BC patients included. Only patients with small tumours were included, and hence, all patients could potentially be treated with BCT, and possible selection bias of the surgeon based on unfavourable tumour characteristics should be limited. The statistical analysis is robust and was specifically designed to introduce a conditional covariate. This conditional covariate indicates the risk of DMD-after-LRR. Another important advantage of our analysis is that all three transitions were estimated in one statistical model, and so no repeated tests were performed.

The findings of the present study are limited by the inherent weakness of any retrospective study. As shown in Table 1, clear differences are apparent in the two treatment arms. We used multivariate analysis to account for these differences. However, a number of important prognostic factors, such as oestrogen, progesterone and HER2-receptor status, could not be accounted for in the analysis because they were not routinely assessed during the inclusion period of our series. However, as these factors were not known pre-operatively, they did not affect the choice of primary surgical treatment, and are expected to be equally distributed. This was the case for the patients with available data (results not shown).

In our series, a relatively small number of BC patients were treated with adjuvant systemic therapy after primary surgery. Only 17.7 % of these young patients were treated with a combination of chemotherapy and hormonal treatment (data not shown). Trastuzumab was not administered at all. With current guidelines, the majority of women below 40 years will receive systemic therapy. The short-term results of a recent analysis in young women treated with BCT including a boost to the tumour bed, showed only 14 events in 752 patients with no difference in loco-regional control rates between ≤50 and >50 years at 3 years: 99 % [28]. The promising preliminary data of the Dutch Young Boost Trial show very few locoregional events in both treatment arms, suggesting favourable outcome in young BC patients (<51 years) treated with BCT (including a boost) [29]. Thus, an increasing use of adjuvant systemic therapy combined with a better delivery of radiotherapy might result in a further reduction of LRRs. This could lead to less DMD and improve the outcome of young women with BC.

In our series, although LRR significantly affected DMD, the increased risk of LRR after BCT did not lead to a worse DMD outcome in BC patients ≤40 years of age, compared with patients treated with mastectomy. Therefore, young women should not be counselled to undergo a mastectomy based on the erroneous assumption of improved likelihood of survival.

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Disclosures None.

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