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## Original Paper

# Family History of Breast Cancer and Local Recurrence after Breast-conserving Therapy

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**The impact of a family history of breast cancer on the local recurrence (LR) risk after breast-conserving therapy (BCT) was performed within the framework of a large, multicentre matched case–control study of risk factors for LR after BCT (BORST study). Family history was assessed for 218 breast cancer patients with LR (cases) and 480 patients without LR (controls). Detailed histological tumour features were determined by review of the primary tumour. The risk of LR for patients with a positive family history was similar to or less than that of non-familial patients (unadjusted odds ratio ($OR_{unadj}$) 0.66 (95% confidence interval (CI) 0.40–1.08)). Familial patients were older than non-familial patients ($P = 0.07$) and their tumours had a lower histological grade ($P = 0.07$). A second primary tumour occurred significantly more often in familial patients ($P = 0.02$). Adjustment for these factors did not essentially alter the results ($OR_{adj}$ 0.71 (0.38–1.32)). Separate analyses according to age at onset (younger and older than 50 years) and time to LR/site of LR produced similar results. The sole presence of a positive family history of breast cancer does not appear to be a risk factor for local recurrence after BCT. Whilst this might be different for genetically predisposed patients, a positive family history does not appear to be a contra-indication for BCT.** © **1999 Elsevier Science Ltd. All rights reserved.**

**Key words: breast cancer, ipsilateral breast tumour recurrence, breast-conserving surgery, family history, risk factors, case–control study**
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## INTRODUCTION

SEVERAL RANDOMISED trials have shown that breast-conserving therapy (BCT) is as effective as mastectomy with respect to overall and distant disease-free survival in patients with early-stage breast cancer [1–5]. However, the long-term risk of local recurrence after BCT is higher due to the continued development of cancer foci in the preserved breast. Early recurrences most likely represent outgrowth of residual disease, whereas late recurrences are more suggestive of a new primary tumour and have a tendency to occur outside the originally involved area [6]. Rates of recurrence in the preserved breast vary between 2 and 10% after 5 years and between 5 and 15% after 10 years. Apart from the possible impact on survival, local recurrence has considerable psychological distress and anxiety for the patient and the prospect of undergoing further surgery. It is, therefore, of interest to define risk factors for local recurrence after BCT in order to improve patient selection for BCT and to reduce the risk of recurrence.

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Reported risk factors include the presence of an extensive intraductal component (EIC), vascular invasion, a large tumour diameter, incomplete tumour excision and a young age (under 35 years) of the patient [7–9]. The biological meaning of this last finding remains so far unexplained and might be associated with a high proliferation index and oestrogen receptor (ER)-negativity, factors that are also associated with a positive family history of breast cancer. On average, 15–20% of breast cancer patients report the occurrence of this disease in one or more close relatives whilst a quarter of these familial cases represent truly inherited forms of breast cancer due to a germline mutation [10]. These percentages are higher in younger breast cancer patients. Whilst the high risk of contralateral breast cancer is repeatedly demonstrated for familial and hereditary breast cancer patients [11, 12], there is less information on the local recurrence rate after BCT in the presence of a family history of breast cancer or in patients with a proven *BRCA* germline mutation. Reports of small numbers of patients with a positive family history suggest no increased risk of local recurrence in general [13, 14].

Until now, no studies have compared time and exact location of the recurrence between patients with and without a family history of breast cancer. This might be important for the adequate local treatment of familial breast cancer. Therefore, we investigated the impact of a positive family history of breast cancer on local recurrence risk. This was done within the framework of a large, multicentre case–control study of risk factors for local recurrence. In this study, detailed histological tumour characteristics were assembled and pathologically reviewed so that risk estimates for a positive family history could be assessed whilst adjusting for a range of other risk factors of local recurrence. As numbers of recurrences were large it was possible to investigate differences in risk according to time of occurrence and localisation of the recurrence.

## PATIENTS AND METHODS

*BORST study*

The current investigation was performed within the framework of a nested case–control study on risk factors for local recurrence after breast-conserving therapy (BCT) [15]. That study (BORST) included primary breast cancer patients with pathological stage I and II treated with BCT between 1980 and 1992 in ten surgical departments and radiotherapeutic institutes in The Netherlands; 360 patients with local recurrence were identified (cases). For each case, two or three controls without local recurrence were sought, matched for axillary lymph node status and menopausal status. Further, controls should have survived at least as long as the time between BCT and diagnosis of the local recurrence of the matching case. Data were assembled on several patient and treatment characteristics. All patients received total breast irradiation and all but 3 were delivered a booster dose to the primary tumour. Adjuvant systemic therapy was given to axillary node-positive patients only. All slides of the primary tumour were reviewed by three pathologists, with respect to histological grade, microscopic margin involvement, and the presence of vascular invasion and extensive intraductal component. Patients with a diagnosis of ductal carcinoma *in situ* (DCIS) instead of invasive cancer after pathological revision were excluded from the study.

*Family history*

Six institutes where family history was checked routinely took part in the current study, so that current analyses were based on 218 cases and 480 controls (Table 1). Family history was assessed from medical files as noted at the time of diagnosis of the primary tumour. Additional information noted after this date was ignored, as this might introduce a bias, as cases could have been questioned more often and/or thoroughly than controls, especially after the diagnosis of local recurrence. Information was assembled on the occurrence of breast cancer in first- (mother or sister) and second-degree relatives (grandmother or aunt). If available, age at onset and number of sisters with and without breast cancer were also noted.

As a young age at diagnosis in combination with a family history is more suggestive of truly hereditary disease, we performed separate analyses for patients under and over the age of 50 years.

*Outcome variables and follow-up*

Cases for this study were patients with local recurrence, defined as any recurrence of tumour within the treated breast or overlying skin, before or synchronously (within 3 months) with the occurrence of distant metastases. 18 cases (and their matched controls) with local recurrences appearing more than 3 months after distant metastases were excluded from the study. As there was a special interest in different types of local recurrence with respect to time and location we made a further distinction between early (less than 5 years after primary diagnosis) and late recurrences (more than 5 years after primary diagnosis). Separate analyses were performed for location of recurrence (at or near the site of the primary tumour, elsewhere in the breast or diffuse/in skin). For all cases, the follow-up after the diagnosis of local recurrence was registered (postrelapse-survival); death (of breast cancer or intercurrent) was the endpoint of interest for this analysis.

*Statistical analysis*

The frequency–distribution of tumour characteristics was assessed separately for patients with and without a family history of breast cancer. Differences in distribution were

*Table* 1. *Number of cases and controls available for the analyses*

| Institute | Cases | Controls | Total |
|---|---|---|---|
| Comprehensive Cancer Center South, Eindhoven | 44 | 135 | 179 |
| Dr Daniel den Hoed Cancer Center, Rotterdam | 56 | 112 | 168 |
| Dr Bernard Verbeeten Institute, Tilburg | 52 | 107 | 159 |
| Netherlands Cancer Institute, Amsterdam | 39 | 77 | 116 |
| Radiotherapy Institute Friesland, Leeuwarden | 21 | 38 | 59 |
| Academic Medical Center, Amsterdam | 6 | 11 | 17 |
| Total | 218 | 480 | 698 |

tested by chi-square and *t*-tests in controls to investigate the confounding role of these characteristics [16]. Conditional logistic regression techniques were used to investigate the relative risk of local recurrence associated with a family history of breast cancer, adjusted for confounders. Separate odds ratios were computed for early and late recurrence and exact localisation of the recurrence (at or near the site of the primary tumour, elsewhere in the breast or diffuse/in skin). Subjects with unknown values for the variables determined at pathology review were excluded from the univariate and multivariate analyses except for outline of the tumour margin and microscopic margin involvement.

Overall survival after local recurrence was assessed by Kaplan–Meier survival analysis. Differences were tested with the logrank test. All analyses were performed with SPSS-PC and STATA software (release 5).

## RESULTS

114 of 698 patients (16.3%) reported a positive family history; this percentage varied from 14 to 19% between the six different institutions that took part in this study. In 80 patients (11.5%) information on family history was missing, due either to the unavailability of the medical record or the absence of any information on family history. When excluding these 80 patients, the frequency of a positive family history was 18.5%. In Table 2 the distribution of a number of known risk factors for local recurrence is described for patients with and without a first-degree family history of breast cancer. Patients with unknown family history or a family history based on a second-degree relative only were excluded from these and further analyses, except for the analyses presented in Table 3. The only significant difference was for a second primary tumour (both contralateral breast cancer and other cancer types), which occurred significantly more often in familial patients ($P = 0.02$) (Table 2).

In Table 3, absolute numbers and percentages of cases and controls with a positive first- and second-degree family history are shown, together with crude and adjusted odds ratios. Overall, the risk of local recurrence was non-significantly decreased for familial patients; the crude odds ratio (OR) for any first-degree relative affected (mother and/or sister(s)) was 0.66 (95% confidence interval (CI) 0.40–1.08). Adjustment for age and histological grade did not essentially alter the results (adjusted OR 0.71 (0.38–1.32)). We looked at sub-

*Table 2. Distribution of patient and tumour characteristics in* 402 *control patients with and without a positive family history of breast cancer*

| Variable | Family history* ($n = 87$) | No family history ($n = 315$) | *P* value |
|---|---|---|---|
| Age at primary diagnosis (mean (SEM)) | 52.7 (1.25) years | 50.2 (0.61) years | 0.07 |
| Primary tumour size (mean (SEM)) | 16.7 (0.80) mm | 17.7 (0.37) mm | 0.18 |
| Histological tumour type | $n = 76$ | $n = 290$ | 0.19† |
| Ductal | 50 (65.8) | 213 (73.4) | |
| Lobular | 6 (7.9) | 32 (11.0) | |
| Mixed | 10 (13.2) | 20 (6.9) | |
| Tubular | 6 (7.9) | 9 (3.1) | |
| Medullary | 0 | 8 (2.8) | |
| Colloid | 3 (3.9) | 3 (1.0) | |
| Other | 1 (1.3) | 5 (1.7) | |
| Outline of tumour margin | $n = 87$ | $n = 315$ | 0.23 |
| Clearly outlined | 50 (57.5) | 172 (54.6) | |
| Poorly outlined | 6 (6.9) | 36 (11.4) | |
| Unknown | 31 (35.6) | 107 (33.9) | |
| Microscopic margin | $n = 87$ | $n = 315$ | 0.96 |
| Free | 41 (47.1) | 158 (50.0) | |
| Involved | 13 (14.9) | 46 (14.6) | |
| Doubtful | 7 (8.0) | 28 (8.9) | |
| Unknown | 26 (29.9) | 83 (26.3) | |
| Intraductal component | $n = 71$ | $n = 276$ | 0.44 |
| No/minimal | 23 (32.4) | 111 (40.2) | |
| Moderate | 40 (56.3) | 133 (48.2) | |
| Extensive | 8 (11.3) | 32 (11.6) | |
| Histological tumour grade | $n = 66$ | $n = 246$ | 0.07 |
| I | 18 (27.3) | 37 (15.0) | |
| II | 23 (34.8) | 101 (41.1) | |
| III | 25 (37.9) | 108 (43.9) | |
| Vascular invasion | $n = 72$ | $n = 266$ | 0.76 |
| No | 50 (69.4) | 174 (65.4) | |
| Yes/doubtful | 22 (30.6) | 92 (34.6) | |
| Second primary tumour | $n = 87$ | $n = 315$ | 0.02 |
| No | 71 (81.6) | 290 (92.1) | |
| Yes, contralateral breast | 9 (10.3) | 15 (4.8) | |
| Yes, other | 7 (8.0) | 10 (3.2) | |

Total numbers in categories can differ due to missing data. *At least one first-degree family member affected with breast cancer. †Ductal invasive tumour type was tested against all other histological types. SEM, standard error of the mean.

*Table 3. Crude and adjusted odds ratios (OR) of local recurrence of breast cancer family history*

| Family history | No. of cases (%) ($n = 218$) | No. of controls (%) ($n = 480$) | $OR_{unadj}$ (95% CI) | $OR_{adj}$‡ (95% CI) |
|---|---|---|---|---|
| No first- or second-degree relative with breast cancer | 145 (66.5) | 315 (65.6) | 1.00 | 1.00 |
| First degree affected* (mother and/or sister(s)) | 27 (12.4) | 87 (18.1) | 0.66 (0.40–1.08) | 0.71 (0.38–1.32) |
| only mother | 14 (6.4) | 34 (7.1) | 0.90 (0.48–1.71) | 0.83 (0.36–1.90) |
| only sister(s) | 11 (5.0) | 50 (10.4) | 0.54 (0.29–1.04) | 0.60 (0.27–1.36) |
| both | 2 (0.9) | 3 (0.6) | 1.21 (0.20–7.43) | 1.09 (0.18–6.61) |
| Only second-degree affected (grandmother or aunt)† | 16 (7.4) | 28 (5.8) | 1.26 (0.64–2.46) | 1.59 (0.67–3.79) |
| Unknown | 30 (13.8) | 50 (10.4) | 1.24 (0.80–1.94) | 1.27 (0.71–2.23) |

*Might include those with a second-degree relative also affected; †Those with a first-degree relative affected excluded; ‡Adjusted for age and histological grade. CI, confidence interval.

groups of a first-degree positive family history in which only the mother, sister(s) or mother and sister(s) were affected, as well as the subgroup of only second-degree affected relatives. None of the crude or adjusted ORs differed significantly from one.

In Table 4 the distribution of patient and tumour characteristics in controls was assessed separately for patients under and over the age of 50 years. In the younger subgroup, as with the overall analysis, the only significant difference was for a second primary tumour (contralateral breast cancer and other types combined), occurring more frequent in young familial patients ($P = 0.003$). For the older subgroup, no clear differences were found between patients with and without a family history of breast cancer.

In Table 5, the risk of local recurrence for family history was assessed separately in patients under and over the age of 50 years. In both groups, a slightly decreased risk in patients with a family history was seen that was most clear in the older subgroup (OR 0.79 (0.39–1.59) and 0.54 (0.24–1.22), respectively, for patients younger and older than 50 years).

*Table 4. Distribution of patient and tumour characteristics in control patients with and without a family history of breast cancer, separately for age at diagnosis < and > 50 years*

| | Age at diagnosis < 50 years | | | Age at diagnosis > 50 years | | |
|---|---|---|---|---|---|---|
| Variable | Family history* ($n = 36$) | No family history ($n = 166$) | $P$ value | Family history* ($n = 51$) | No family history ($n = 149$) | $P$ value |
| Age at primary diagnosis (mean (SEM)) | 41.4 (0.80) years | 41.8 (0.39) years | 0.69 | 60.6 (1.11) years | 59.7 (0.60) years | 0.44 |
| Primary tumour size (mean (SEM)) | 15.7 (1.07) mm | 17.3 (0.43) mm | 0.15 | 17.4 (1.13) mm | 18.1 (0.59) mm | 0.53 |
| Histological tumour type | | | 0.09 | | | 0.70 |
| ductal | 17 (56.7) | 110 (72.4) | | 33 (71.7) | 103 (74.6) | |
| other | 13 (43.3) | 42 (27.6) | | 13 (28.3) | 35 (25.4) | |
| Outline of tumour margin | | | 0.92 | | | 0.39 |
| clearly outlined | 17 (47.2) | 80 (48.2) | | 33 (64.7) | 92 (61.8) | |
| poorly outlined | 4 (11.1) | 20 (12.0) | | 2 (3.9) | 16 (10.7) | |
| unknown | 15 (41.7) | 66 (39.8) | | 16 (31.4) | 41 (27.5) | |
| Microscopic margin | | | 0.45 | | | 0.82 |
| free | 14 (38.9) | 78 (47.0) | | 27 (52.9) | 80 (53.7) | |
| involved | 5 (13.9) | 28 (16.9) | | 8 (15.7) | 18 (12.1) | |
| doubtful | 3 (8.3) | 15 (9.0) | | 4 (7.8) | 13 (8.7) | |
| unknown | 14 (38.9) | 45 (27.1) | | 12 (23.5) | 38 (25.5) | |
| Intraductal component | | | 0.76 | | | 0.43 |
| no/minimal | 8 (28.6) | 52 (35.6) | | 15 (34.9) | 59 (45.4) | |
| moderate | 15 (53.6) | 72 (49.3) | | 25 (58.1) | 61 (46.9) | |
| extensive | 5 (17.9) | 22 (15.1) | | 3 (7.0) | 10 (7.7) | |
| Histological tumour grade | | | 0.14 | | | 0.39 |
| I | 7 (30.4) | 18 (14.0) | | 11 (25.6) | 19 (16.2) | |
| II | 6 (26.1) | 47 (36.4) | | 17 (39.5) | 54 (46.2) | |
| III | 10 (43.5) | 64 (49.6) | | 15 (34.9) | 44 (37.6) | |
| Vascular invasion | | | 0.76 | | | 0.77 |
| no | 19 (65.5) | 92 (64.8) | | 31 (72.1) | 82 (66.1) | |
| yes/doubtful | 10 (34.5) | 50 (35.2) | | 12 (27.9) | 42 (33.9) | |
| Second primary tumour | | | 0.003 | | | 0.029 |
| no | 29 (80.6) | 157 (94.6) | | 42 (82.4) | 133 (89.3) | |
| yes, contralateral breast or other | 7 (19.4) | 9 (5.4) | | 9 (17.6) | 16 (10.7) | |

Total numbers in categories can differ due to missing data. *At least one first-degree family member affected with breast cancer. SEM, standard error of the mean.

*Table 5. Odds ratios (OR) for familial versus sporadic breast cancer patients, separately for age at diagnosis < and ≥ 50 years*

| | Age at diagnosis < 50 years | | | | Age at diagnosis > 50 years | | | |
|---|---|---|---|---|---|---|---|---|
| | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) |
| Family history | | | | | | | | |
| Negative | 92 (83.6) | 166 (82.2) | 1.00* | 1.00* | 53 (85.5) | 149 (74.5) | 1.00* | 1.00* |
| Positive | 18 (16.4) | 36 (17.8) | 0.79 (0.39–1.59) | 0.99 (0.39–2.55) | 9 (14.5) | 51 (25.5) | 0.54 (0.24–1.22) | 0.99 (0.37–2.66) |

*Reference group; †Adjusted for tumour histology and histological grade.

*Table 6. Odds ratios (OR) of early and late recurrence for familial versus sporadic breast cancer patients*

| | Early recurrence (< 5 years after primary tumour) | | | | Late recurrence (≥ 5 years after primary tumour) | | | |
|---|---|---|---|---|---|---|---|---|
| | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) |
| Family history | | | | | | | | |
| Negative | 111 (84.1) | 259 (78.0) | 1.00* | 1.00* | 34 (85.0) | 56 (80.0) | 1.00* | 1.00* |
| Positive | 21 (15.9) | 73 (22.0) | 0.64 (0.36–1.13) | 0.83 (0.40–1.70) | 6 (15.0) | 14 (20.0) | 0.72 (0.27–1.91) | 0.53 (0.13–2.11) |

*Reference group; †Adjusted for age and histological grade.

After correction for tumour histology and grade, the ORs were 0.99 (0.39–2.55) and 0.99 (0.37–2.66), respectively, for patients younger and older than 50 years.

The risk of early (less than 5 years after diagnosis of primary tumour) and late recurrence (more than 5 years after diagnosis of primary tumour) was investigated separately. No clear differences with respect to unadjusted or adjusted odds ratios of early and late recurrence were seen (Table 6). Separate analyses were performed according to location of recurrence. Again, no clear differences were seen (Table 7).

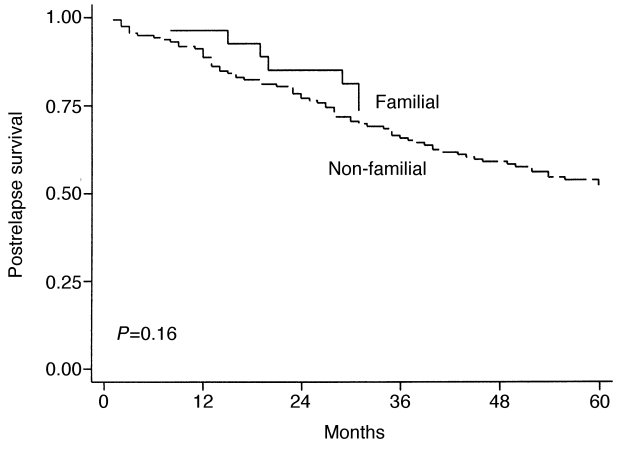


**Figure 1. Post relapse survival for familial ($n = 27$) and non-familial cases ($n = 145$) with local recurrence**

Figure 1 shows the overall post-relapse-survival after local recurrence for cases with and without a family history of breast cancer. There was a tendency towards a better post-relapse-survival for cases with a positive family history: post-relapse-survival at 2 and 5 years was 85% (95% CI 65–94) and 73% (52–86) for familial patients, and 79% (71–84) and 54% (45–61) for sporadic patients ($P = 0.16$).

## DISCUSSION

We found that the local recurrence risk after breast-conserving therapy (BCT) for patients with a positive family history was similar to or less than that of patients without a family history of breast cancer. To our knowledge, this is the first case–control study that investigates the relation between a family history of breast cancer and local recurrence risk. Our results are in line with those of follow-up studies that found an identical or (non-significantly) decreased risk of local recurrence in familial as compared with non-familial breast cancer patients. Solin and colleagues [13] prospectively investigated the local recurrence rate after BCT in 171 patients under 40 years with respect to 'family history' (which is not further defined in their study) [13]. The 8-year local failure rate in patients with a positive family history was 13% as compared with 19% in patients with a negative family history ($P = 0.16$). Israeli and colleagues [14] found no differences in local, distant or disease-free survival between 179 patients with and 569 patients without a family history of breast cancer. The local recurrence rate for women with a family history was 16 and 23% for women without a family

*Table 7. Odds ratios (OR) of different locations of recurrence for familial versus sporadic breast cancer patients family history*

| Location of recurrence | At or near original site | | | | Elsewhere in breast | | | |
|---|---|---|---|---|---|---|---|---|
| | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) | Cases (%) | Controls (%) | $OR_{unadj}$ (95% CI) | $OR_{adj}$† (95% CI) |
| Family history | | | | | | | | |
| Negative | 90 (88.2) | 205 (80.4) | 1.00* | 1.00* | 18 (75.0) | 30 (63.8) | 1.00* | 1.00* |
| Positive | 12 (11.8) | 50 (19.6) | 0.58 (0.29–1.14) | 0.57 (0.24–1.34) | 6 (25.0) | 17 (36.2) | 0.46 (0.14–1.54) | 0.53 (0.12–2.43) |

$OR_{adj}$ for diffuse location or in skin was 1.26 (0.36–4.45). *Reference group; †Adjusted for age and histological grade.

history (*P* value not given). Smitt and associates [17] reported a 5-year freedom from local recurrence of 94% among patients with a first-degree family history, which was not different from patients without a family history of breast cancer (92%). For patients younger than 50 years no differences were found. Ravaioli and associates [18] compared prognostic factors and relapse rate in 68 hereditary breast cancer patients (according to a modified version of the 'Amsterdam criteria' for hereditary non-polyposis colorectal cancer) and 510 non-hereditary patients. A higher overall relapse rate was found, that included local and distant relapse as well as contralateral breast cancer (26.5% in hereditary patients, compared with 12.9% in non-hereditary patients; $P = 0.03$). No statistical difference in the type of relapse was found ($P = 0.59$).

In our study we further investigated the distribution of a number of established clinical risk factors for local recurrence. Patients with a positive family history were older than patients without a family history ($P = 0.07$). The most likely explanation for this finding is that familial breast cancer can occur, apart from hereditary causes (with an age at onset that is younger than average), by chance clustering. As the risk of breast cancer rises with age, so does the probability of this chance clustering of breast cancer in the family with older age. We further found a tendency towards more tumours of grade I histology and a smaller tumour diameter in familial patients. This finding was also reported by Fukutomi and colleagues [19] and suggests, apart from possible biological differences between patients with and without a family history of breast cancer, earlier detection as a result of a higher awareness because of breast cancer family history. All of these factors have been demonstrated to decrease the risk of a local recurrence [9, 20]. Correction for the abovementioned factors could only partly explain the risk difference between patients with and without a family history of breast cancer. In addition, a significantly increased risk of a second primary tumour (contralateral breast cancer as well as other types) in familial patients, a finding that has been reported by others in patients with either familial breast cancer or a proven germline mutation in *BRCA1* [11, 12].

As age at diagnosis was an important confounder and there was a special interest in younger familial patients (to better delineate the subgroup of likely hereditary patients) we performed separate analyses for patients under and over the age of 50 years. In both groups, the risk of local recurrence was not increased by family history.

We further performed separate analyses according to time to recurrence and location of recurrence. As we found an increased risk of contralateral breast tumours in familial breast cancer patients, we expected family history to be primarily related to late recurrences and recurrences elsewhere in the breast, as these are most likely to represent second primary tumours [21]. No indication of a different distribution of family history according to time or location of recurrence was seen. As CIs were wide it might be that our numbers were insufficient to warrant these subgroup analyses. Due to these small numbers it was not possible to stratify for time interval and age to investigate possible risk differences for the younger subgroup only. As a crude indication, we found that the proportion of recurrences elsewhere in the breast was not increased in familial as compared with sporadic cases younger than 50 years (data not shown).

Our results of a (non-significantly) decreased risk of local recurrence in familial patients might be explained by an increased sensitivity to radiotherapy. This is suggested by Fourquet and colleagues [22] as a possible explanation for their observation of a similar 5-year disease-free survival in *BRCA1*-positive patients as compared with sporadic patients, notwithstanding the more adverse prognostic features among the *BRCA1*-positive group.

Our study was performed within the framework of a matched case–control study set up to investigate risk factors for local recurrence. Total numbers of this multicentre study were large, but separation in subgroups, such as time and location of recurrence, made estimates imprecise. Further, the mean duration of follow-up after the primary diagnosis was limited to 3.5 years. In particular, the numbers of late recurrences and recurrences located elsewhere in the breast were small so that an existing risk difference might have been missed. The presence of a positive family history was assessed retrospectively through medical files, at the time of diagnosis of the primary tumour. Of nearly 12% of our study group no information on family history could be retrieved. If this incompleteness of information is non-random it might lead to biased estimates in either direction. As 16% of patients (18% including only patients with known family history) reported at least one affected first-degree relative, the underreporting of a positive family history is unlikely. However, data on the age of onset in affected relatives was mostly missing, information that is important for the delineation of possible hereditary cancer. On average, 20% of breast cancer patients report at least one affected relative, whereas only 5–8% of all breast cancers is expected to be hereditary. Other reasons such as the sharing of environmental breast cancer risk factors might explain the clustering of breast cancer in some families. In our study, information was too limited to delineate these likely hereditary cases; this requires a more extensive family history based among others on numbers and age at diagnosis of affected family members. A definite diagnosis can only be made after detection of a deleterious germline mutation in the family. It might be that (subgroups of) truly hereditary cases perform differently with respect to local recurrence rate and other outcome variables. A large historical cohort study is being prepared at the Dr Daniel den Hoed Cancer Center that specifically addresses these issues.

In the meantime our results and those of others suggest that a positive family history in general does not increase the risk of a local recurrence. While this might be different for more severely affected families or families with a proven germline mutation, the sole presence of a positive family history is no contra-indication for breast-conserving therapy.

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