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Impact of breast cancer family history on tumor detection and tumor size in women newly-diagnosed with invasive breast cancer

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Abstract This study evaluated the impact of family history (FH) on tumor detection, the patient's age and tumor size at diagnosis in breast cancer (BC). Furthermore, we investigated whether the impact of FH on these features was dependent on degree of relationship, number of relatives with a BC history, or the age of the affected relative at the time that her BC was diagnosed. Out of the entire cohort (n = 1,037), 244 patients (23.5 %) had a positive FH; 159 (15.3 %) had first-degree relatives affected with BC and 85 patients (8.2 %) had second-degree affected relatives. Compared to women who had no BC-affected relatives, the tumors of women who had positive FH were more often found by radiological breast examination (RBE: 31.7 %/27.2 %, $p = 0.008$), and they were smaller (general tumor size: 21.8 mm/26.4 mm, $p = 0.003$; size of tumors found by breast self-examination (BSE): 26.1 mm/30.6 mm, $p = 0.041$). However, this positive effect of increased use of BC screening and smaller tumor sizes was only observed in patients whose first-degree relatives were affected (comparison with second-degree affected relatives: RBE: 43.8 %/24.7 %; odds ratio 2.38, $p = 0.007$; general tumor size: 19.3 mm/26.3 mm; mean difference (MD) -6.9, $p = 0.025$; tumor size found by BSE: 22.5 mm/31.0 mm; MD -8.5, $p = 0.044$). When more second-degree relatives or older relatives were diagnosed with BC, the tumors of these patients were similarly often detected by RBE (relationship: 24.7 %/27.2 %, $p = 0.641$; age: 33.7 %/27.2 %, $p = 0.177$) and had similar tumor sizes (general size: 26.3 mm/26.4 mm, $p = 0.960$; BSE: 31.0 mm/30.6 mm, $p = 0.902$) as those of women without a FH. Women with a positive FH generally use mammography screening more often and perceive changes in the breast earlier than women without such history. The increased awareness of BC risk decreases if the relationship is more distant.

Keywords Breast cancer · Family history · Detection method · Mammography screening · Breast self-examination · Tumor size

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Introduction

It is widely recognized that a woman's risk of developing breast cancer (BC) is increased if she has a family history (FH) of the disease [1, 2]. In Western countries, the life-time excess incidence of BC is 5.5 % for women with one affected first-degree relative and 13.3 % for women with two [1].

This study evaluates to what extent established radiological screening methods for BC detection were utilized in BC patients with a positive FH, compared to women without affected relatives. The increased frequency of radiological examinations in women with a positive FH might demonstrate how personal and familial experiences with BC can influence individuals' behaviors, thus leading to earlier detection of the disease [2–6]. Furthermore, the impact of FH on the patient's age at diagnosis and tumor size at diagnosis was analyzed. As a next step, we investigated whether the impact of FH on tumor detection, patient's age and tumor size was dependent on factors such as degree of relationship (first-degree vs. second-degree), number of relatives with a history of BC (1 vs. $\geq$1), or the age of the affected relative at the time that her BC was diagnosed (<50 vs. $\geq$50 years).

During the last decade, there have only been a few studies which evaluated the impact of FH on BC detection and tumor size in BC patient cohorts [7–9]. To our knowledge, our study is the first comprehensive analysis of the impact of FH on BC detection and tumor size based on a more recent population-based cohort (1990–2009) which does not exclusively consider a subgroup of younger BC patients [8], but rather also analyzes women at an age in which BC mainly occurs (women up to and including 70 years of age).

Patients and methods

Data from the prospective relational Basel Breast Cancer Database (BBCD), which includes all newly diagnosed primary invasive BC cases treated at the University Women's Hospital Basel, Switzerland since 1990 provided the basis for this study. This institution comprises the largest BC center in the canton of Basel and is an adequate representation of the regional population. Within this database, disease-specific clinical and histopathological data, treatment characteristics, personal and family history as well as outcome data was recorded. For this study, data from female patients up to and including 2009, who were $\leq$70 years at diagnosis, was analyzed (n = 1,056). Since the goal of the study was to evaluate the impact of FH on tumor detection method and tumor size, 19 cases with

inflammatory BC were excluded from further analysis. Due to the nature of inflammatory carcinomas, which arise rapidly, affect large parts of the breast, and often have no underlying definable mass, these cases are not suitable for evaluating tumor detection methods and tumor size. In total, our study cohort comprised 1,037 patients.

Family history

The criterion for a positive FH of BC was met when a patient reported:

- one or more first-degree (mother, sister, daughter) affected relatives, n = 159,
- one or more second-degree (aunt, grandmother) affected relatives, n = 107.

In 22 cases, the patients had both first-degree and second-degree affected relatives; we placed these patients in the "first-degree relative"-category, leading to 85 patients being placed in the "second-degree relative"-category.

For patients with a positive FH of BC, the number of BC affected relatives and their age at diagnosis (<50 vs. $\geq$50 years) was evaluated. Thirteen cases (first-degree relatives, n = 10, second-degree relatives, n = 3), in which two or more relatives had been diagnosed in both the younger and older ages, were considered as "<50 years" only.

Clinicopathological data

The following data was available for all patients: age at initial diagnosis, histological subtype, grading, hormonal receptor (HR) status, tumor stage according to the American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) TNM Classification [10, 11]. Because HER-2 status has been routinely assessed for all patients since 2002, we included data from 2002–2009 only in the analysis of this particular characteristic. Carcinomas of the triple negative subtype are characterized by a lack of expression of the estrogen receptor, progesterone receptor, and HER2.

Tumor size

For most of our patients (n = 976, 94.1 %), the size of the primary tumor was measured during pathological examination of the surgically resected lesion. In 40 patients (3.9 %; positive FH: n = 8, negative FH: n = 32), where neoadjuvant therapy was given, the pre-therapeutic clinically assessed tumor sizes were used. The same was the case for 21 patients (2.0 %; positive FH: n = 3; negative FH: n = 19), where no surgery was performed.

Of the entire study cohort, 20 patients presented with synchronous bilateral BC (1.9 %); of these cases, the tumor with the more advanced tumor size ("reference lesion") was considered for analysis.

Tumor detection method

The following two main methods were analyzed:

1. breast self-examination (BSE), n = 600 (57.9 %)
2. radiological breast examination (RBE), n = 253 (24.4 %)

Cases in which the tumor was found by a physician during a clinical breast examination [CBE, n = 151 (14.6 %)] were not considered in the diagnostic method analysis, because, contrary to BSE and the utilization of RBE, CBE does not necessarily reflect the patient's awareness of early BC detection. The following patients were also excluded from this part of analysis: 13 patients (1.2 %), in which other detection modes apart from the ones mentioned above were used, and 20 patients (1.9 %), in which the method of tumor detection was not reported in the clinical files.

Data collection methods and study design were approved by the Ethics Committee of the University of Basel.

Statistical methods

Comparisons between nominal parameters were made using the Fisher exact test. In the case of the dependent variables age and tumor size, univariate linear regression analysis was performed. Results are presented as differences of means (MD) with corresponding 95 % confidence intervals (95 % CI) and p values. In the case of the binary dependent variable (detection method), logistic regressions were performed. Results are presented as odds ratios (OR) with the corresponding 95 % CI and p values. In all statistical tests the level of significance was $p < 0.05$. All evaluations were performed with R Development Core Team software, version 13.1. The study is exploratory; therefore, no adjustments for multiple comparisons were done.

Results

Out of the entire cohort (n = 1,037), 244 patients (23.5 %) had a positive FH for BC. Of these, 159 (15.3 %) had first-degree relatives affected by BC and 85 patients (8.2 %) had second-degree affected relatives only. Table 1 lists the number of relatives with a history of BC and the age group of the affected relative at the time that her BC was diagnosed.

Pathological characteristics (Table 2)

Comparing the incidence of histological subtypes, there were more lobular carcinomas in patients with a positive FH than in those without FH (16.9 vs. 11.7 %, $p = 0.037$). Patients with a positive FH showed less commonly established indicators of tumor aggressiveness such as poorly differentiated carcinomas (G3: 33.9 vs. 46.6 %, $p < 0.001$), a negative HR-negative status (13.5 vs. 19.2 %, $p = 0.052$) and triple-negative subtype (6.5 vs. 13.6 %, $p = 0.007$).

Age at diagnosis (Tables 2 and 3)

There was no significant difference between patients with and without FH with respect to age at diagnosis (53.8 vs. 54.8 years, $p = 0.201$). However, patients with a positive FH, who had only second-degree BC affected relatives, were significantly younger when compared with patients who had no FH (51.2 vs. 54.8 years, MD −3.6 years, 95 % CI −5.9 to −1.3, $p = 0.002$), as well as patients with a positive FH and first-degree BC affected relatives (51.2 vs. 55.2 years, MD −4.0 years, 95 % CI −6.7 to −1.2, $p = 0.004$). There was a similar age distribution in patients with no FH and those who had a positive FH with first-degree BC affected relatives (54.8 vs. 55.2 years, $p = 0.652$).

Patients whose relatives were diagnosed with BC at a younger age (<50 years) were themselves significantly younger at diagnosis than patients with negative FH (51.7 vs. 54.8 years, MD −3.1 years, 95 % CI −5.4 to −0.7, $p = 0.009$) and patients with a positive FH whose relatives were diagnosed with BC at an older age (51.7 vs. 56.1 years, MD −4.4 years, 95 % CI −7.3 to −1.6, $p = 0.002$). Hereby, the number of affected relatives was not found to have a substantial impact upon age at diagnosis ($p = 0.440$).

Tumor detection method: radiological breast examination versus self-examination (Table 2 and 4)

Compared to the tumors of patients without FH, the lesions of patients who had a positive FH were more often found by RBE (37.1 vs. 27.2 %, $p = 0.008$). Within the group of patients with a positive FH the tumors were significantly more often found by RBE in patients with first-degree BC affected relatives than in those with second-degree affected relatives (43.8 vs. 24.7 %; OR 2.38, 95 % CI 1.27–4.54, $p = 0.007$). In patients with a positive FH who had only second-degree BC affected relatives, the tumors were

Table 1 Breast cancer patients (≤70 years) with positive FH of BC (n = 244): Degree of relationship, number of affected relatives, and age of the affected relative at the time that her BC was diagnosed

Characteristic	n (%)
First-degree relatives	159 (65.2)
Second-degree relatives	85 (34.8)
First-degree relatives	159
Relative diagnosed before age 50[1]	70 (44.0)
Relative diagnosed ≥50 years[1]	88 (55.4)
Relative's age unknown	1 (0.6)
One family member affected with BC	141 (88.7)
Two family members affected with BC	17 (10.7)
Three family members affected with BC	1 (0.6)
Mean number	1.1
Second-degree relatives	85
Relative diagnosed before age 50	10 (11.8)
Relative diagnosed ≥ 50 years	38 (44.7)
Relative's age unknown	37 (43.5)
One family member affected with BC	68 (80.0)
Two family members affected with BC	13 (15.3)
Three family members affected with BC	3 (3.5)
Four family members affected with BC	1 (1.2)
Mean number	1.3
Entire group of patients with positive FH (first degree and second-degree relatives)	244
One family member affected with BC	188 (77.1)
Two family members affected with BC	43 (17.6)
Three family members affected with BC	11 (4.5)
Four family members affected with BC	2 (0.8)
Mean number	1.3

BC breast cancer, *FH* family history

[1] In one case, FH showed that the father of the patient had been diagnosed with BC at the age of 80 years; in a second case, one/a brother of the patient was diagnosed at the age of 38 years. According to the age segments, these cases were considered as "<50 years" (brother) and "≥50 years" (father)

found just as often by RBE as in patients without FH (24.7 vs. 27.2 %, $p = 0.641$).

In patients whose relatives were <50 years of age at their BC diagnosis, we found that the tumors tended to be more often found by RBE compared to patients whose relatives were diagnosed with BC at an older age (47.3 vs. 33.7 %; OR 1.79, 95 % CI 1.00–3.23, $p = 0.067$; comparison with patients without FH: 47.3 vs. 27.2 %; OR 2.40, 95 % CI 1.47–3.90, $p < 0.001$). In patients whose relatives were diagnosed with BC at a more advanced age (≥50 years), this observation was not made (33.7 vs. 27.2 %, $p = 0.177$). The number of the affected relatives was not relevant ($p = 0.158$).

Tumor size (Table 2 and 5)

Compared to patients without FH, patients with a positive FH had smaller tumors at diagnosis (21.8 vs. 26.4 mm, $p = 0.003$). Within the group of patients with a positive FH, patients with first-degree BC affected relatives had smaller tumors than those with second-degree affected relatives (19.3 vs. 26.3 mm; MD −6.9, 95 % CI −13.0 to −0.9, $p = 0.025$). The tumor sizes of patients with a positive FH who had only second-degree BC affected relatives were similar to those of patients without a FH (26.3 vs. 26.4 mm, $p = 0.960$). Within the group of patients with positive FH, the age at which the affected relative was diagnosed with BC did not correlate with tumor size (<50 years: 18.4 mm vs. ≥50 years: 21.0 mm, $p = 0.403$).

We found similar results for the subgroup of patients who found their tumors by BSE. Compared to patients without FH, patients with positive FH found smaller lesions (26.1 vs. 30.6 mm, $p = 0.041$). Patients with first-degree BC affected relatives found their tumors at smaller sizes than patients who had only second-degree BC affected relatives (22.5 vs. 31.0 mm; MD −8.5, 95 % CI −17.6 to −0.6, $p = 0.044$) and patients without FH (22.5 vs. 30.6 mm; MD −8.1, 95 % CI −14.4 to −1.7, $p = 0.013$). Patients with positive FH and only second-degree BC affected relatives identified their tumors at a similar size as those with negative FH (31.0 vs. 30.6 mm, $p = 0.902$). Within the group of patients with positive FH, the age at which the affected relative was diagnosed with BC was not significantly correlated with tumor size (<50 years: 23.9 mm vs. ≥50 years: 22.9 mm, $p = 0.841$).

Table 2 Comparison between a cohort of 1,037 BC patients (≤70 years) with and without FH of BC

Variable	Family history (positive) n = 244	Family history (negative) n = 793 (%)	p value
Age (years)			
Mean	53.8	54.8	0.201
Median	54	56	
Tumor detection method			
Breast self-examination	132 (54.1)	468 (59.0)	
Radiologic examination	78 (32.0)	175 (22.1)	**0.008**
Clinical breast examination (by physician)	24 (9.8)	127 (16.0)	
Other method	4 (1.6)	9 (1.1)	
Unknown	6 (2.5)	14 (1.8)	
Tumor size (mm)			
Mean	21.8	26.4	**0.003**
Median (range)	17 (0.5–220)	20 (0–210)	
Tumor category			
T0	0	2 (0.2)	**<0.001**
T1	159 (65.1)	405 (51.1)	
T2	68 (27.9)	296 (37.3)	
T3	10 (4.1)	61 (7.7)	T3/T4: 0.054
Non-inflammatory T4	7 (2.9)	29 (3.7)	
Bilateral synchronous carcinoma	5 (2.1)	15 (1.9)	0.80
AJCC/UICC TNM stage			
I	119 (48.8)	284 (35.8)	**<0.001**
II	82 (33.6)	324 (40.9)	
III	37 (15.2)	142 (17.9)	
IV	6 (2.4)	43 (5.4)	0.059
Histologic subtype			
Ductal invasive	171 (70.7)	609 (77.3)	
Lobular invasive	41 (16.9)	92 (11.7)	**0.037**
Rare types	30 (12.4)	87 (11.0)	
Not available	2	5	
Grading			
G1/2	154 (66.1)	400 (53.4)	
G3	79 (33.9)	349 (46.6)	**<0.001**
Not available	11	44	
Hormonal receptor status			
Positive	205 (86.5)	614 (80.8)	0.052
Negative	32 (13.5)	146 (19.2)	
Not available	7	33	
HER2 status, 2002–2009	n = 124 (%)	n = 339 (%)	
Positive	19 (15.4)	61 (18.1)	0.57
Not available	1	2	
Triple-negative subtype	8 (6.5)	46 (13.6)	**0.007**

AJCC American Joint Committee on Cancer, *UICC* International Union Against Cancer [10, 11]

Statistically significant data (the level of significance $p < 0.05$) are highlighted in bold

Discussion

The Collaborative Group on Hormonal Factors in Breast Cancer reported that 12.9 % of women with BC had first-degree relatives with a history of BC [1]. This review analyzed 52 epidemiological studies in which 58,209 BC patients were analyzed. The results of this large data collection are approximately comparable with our data (15.3 % of the BC patients had first-degree relatives affected by BC).

Table 3 Patient's age according to FH of BC

	MD (95 % CI)	*p* value
Degree of relationship		
0. no FH: 54.8 years		
1. First-degree FH: 55.2 years		
2. Second-degree FH: 51.2 years		
Overall		**0.007**
1 versus 0	0.4 (−1.4, 2.2)	0.652
2 versus 0	−3.6 (−5.9, −1.3)	**0.002**
2 versus 1	−4.0 (−6.7, −1.2)	**0.004**
Number of affected relatives		
Overall		0.322
1 affected relative: 53.5 years		
≥1 affected relative: 54.8 years		
1 versus ≥1	1.2 (−1.9, 4.3)	0.440
Age of the affected relative at the time that her BC was diagnosed		
0. no FH: 54.8 years		
1. FH, <50 years: 51.7 years		
2. FH, ≥50 years: 56.1 years		
Overall		**0.008**
1 versus 0	−3.1 (−5.4, −0.8)	**0.009**
2 versus 0	1.3 (−0.6, 3.3)	0.175
1 versus 2	−4.4 (−7.3, −1.6)	**0.002**

MD mean difference, *CI* confidence interval, *FH* family history, *BC* breast cancer

Statistically significant data (the level of significance *p* < 0.05) are highlighted in bold

Our study confirms previously published data [8], which demonstrated that in a cohort of BC patients, the tumors of women who had a positive FH for BC were more often found by RBE compared to women who had no BC affected relatives. This might result from the fact that women with a family BC history, obviously influenced by personal and familial experiences with BC, generally use BC screening more often than women without such history [2–6]. It is not possible to determine precisely to what extent the higher motivation for mammography can be attributed to the women's own initiative, the direct influence of family members (e.g. mother–daughter communication) or the motivating influence of their doctors who are aware of the positive FH and incorporate this information into their mammography referral practices. However, this positive effect of increased use of and adherence to BC screening is essentially due to a particular subgroup of patients with positive FH, namely those whose first-degree relatives were affected and those whose relatives were diagnosed with BC at an earlier age (<50 years). When more distantly related relatives (second-degree relatives) or older relatives (≥50 years of age) were diagnosed with BC, the motivation to have BC screening could not be positively influenced. The tumors of these patients were similarly often detected by RBE as those of women without FH.

Table 4 Tumor detection method (radiological breast examination vs. self-examination) according to FH of BC

	OR (95 % CI)	*p* value
Degree of relationship		
0. no FH		
RBE: n = 175 (27.2 %); SE: n = 468 (72.8 %)		
1. First-degree FH		
RBE: n = 60 (43.8 %); SE: n = 77 (56.2 %)		
2. Second-degree FH		
RBE: n = 18 (24.7 %); SE: n = 55 (75.3 %)		
Comparison for RBE: Overall		**<0.001**
1 versus 0	2.00 (1.43, 3.05)	**<0.001**
2 versus 0	0.88 (0.50, 1.53)	0.641
1 versus 2	2.38 (1.27–4.54)	**0.007**
Number of affected relatives		
Overall		**0.008**
1 affected relative		
RBE: n = 56 (34.6 %); SE: n = 106 (65.4 %)		
≥1 affected relative		
RBE: n = 22 (45.8 %); SE: n = 26 (54.2 %)		
Comparison for RBE		
≥1 versus 1	1.60 (0.83, 3.10)	0.158
Age of the affected relative at the time that her BC was diagnosed		
0. no FH		
RBE: n = 175 (27.2 %); SE: n = 468 (78.2 %)		
1. FH, <50 years		
RBE: n = 35 (47.3 %); SE: n = 39 (52.7 %)		
2. FH, ≥50 years		
RBE: n = 35 (33.7 %); SE: n = 69 (66.3 %)		
Overall		**0.008**
1 versus 0	2.40 (1.47, 3.90)	**<0.001**
2 versus 0	1.36 (0.87, 2.10)	0.177
1 versus 2	1.79 (1.00, 3.23)	0.067

OR odds ratio, *CI* confidence interval, *FH* family history, *BC* breast cancer, *RBE* radiological breast examination, *SE* self examination

Statistically significant data (the level of significance *p* < 0.05) are highlighted in bold

We observed a similar pattern in the analysis of tumor size. The tumors of patients with positive FH for BC were significantly smaller compared to tumors of patients with negative FH and, again, this positive effect was primarily determined by the patients with first-degree BC affected relatives. In contrast, patients who had only second-degree BC affected relatives had similar tumor sizes to patients without a FH for BC. These findings are consistent with those of Tracy et al. [6], who also showed that the degree of

Table 5 Tumor size according to FH of BC. I. All patients; II. Tumors found by self-examination

	MD (95 % CI)	*p* value
All patients		
Degree of relationship		
0. no FH: 26.4 mm		
1. First-degree FH: 19.3 mm		
2. Second-degree FH: 26.3 mm		
Overall		**0.001**
1 versus 0	−7.1 (−11.0, −3.2)	**<0.001**
2 versus 0	−0.1 (−5.3, 5.0)	0.960
1 versus 2	−6.9 (−13.0, −0.9)	**0.025**
Number of affected relatives		
Overall		**0.019**
1 affected relative: 21.3 mm		
≥1 affected relative: 23.4 mm		
≥1 versus 1	2.2 (−4.7, 9.1)	0.535
Age of the affected relative at the time that her BC was diagnosed		
0. no FH: 26.4 mm		
1. FH, <50 years: 18.4 mm		
2. FH, ≥50 years: 21.0 mm		
Overall		**0.001**
1 versus 0	−8.0 (−13.1, −3.0)	**0.002**
2 versus 0	−5.4 (−9.6, −1.1)	**0.013**
1 versus 2	−2.7 (−3.6, 8.9)	0.403
II. Tumors found by self-examination		
Degree of relationship		
0. no FH: 30.6 mm		
1. First-degree FH: 22.5 mm		
2. Second-degree FH: 31.0 mm		
Overall		**0.041**
1 versus 0	−8.1 (−14.4, −1.7)	**0.013**
2 versus 0	0.5 (−6.9, 7.8)	0.902
1 versus 2	−8.5 (−17.6, −0.6)	**0.044**
Number of affected relatives		
Overall		0.082
1 affected relative: 24.5 mm		
≥1 affected relative: 32.5 mm		
≥1 versus 1	8.1 (−3.2, 19.3)	0.160
Age of the affected relative at the time that her BC was diagnosed		
0. no FH: 30.6 mm		
1. FH, <50 years: 23.9 mm		
2. FH, ≥50 years: 22.9 mm		
Overall		**0.026**
1 versus 0	−6.6 (−15.0, 1.6)	0.114
2 versus 0	−7.6 (−14.0, −1.3)	**0.019**
1 versus 2	1.0 (−8.9, 11.0)	0.841

MD mean difference, *CI* confidence interval, *FH* family history, *BC* breast cancer

Statistically significant data (the level of significance *p* < 0.05) are highlighted in bold

relationship between relatives with BC affected the likelihood of using BC screening. Furthermore, the authors found that BC death in a family is a stronger predictor for the use of BC screening.

Our results confirm the findings of recent studies, which showed that women with affected first-degree relatives were more likely to have smaller carcinomas and more often early disease stage [7–9]. Furthermore, our study confirms data from other studies which showed no significant differences with regard to tumor size and stage between patients who had only second-degree relatives affected with BC and patients without FH for BC [7, 8].

The phenomenon that patients with a first-degree BC affected relative had smaller tumors at diagnosis might be explained by more diligent use of BC screening amongst women who considered themselves to be at increased risk of developing the disease. However, we also observed this phenomenon in patients who detected their tumors by self-examination. In these cases, the personal experience of having a close family member with BC was so influential that they became more aware of the necessity of self-examination and perceived changes earlier, thus leading to the identification of smaller tumors. Sinicrope et al. [12], who examined communication about BC prevention between BC affected mothers and their daughters, found that BC prevention behaviors were associated with corresponding advice such as to have a mammogram (51 %) and perform BSE (39 %). Interestingly, the increased awareness of BC risk does not result in a behavioral change to a more preventive lifestyle, such as weight control or reduction of alcohol consumption [13].

The data regarding the relationship between FH of BC and tumor characteristics are inconsistent. Some recent studies found that women with a positive FH had tumors with a generally more favorable prognostic profile [8, 9], while others suggested that the characteristics of BC in patients with a positive FH do not differ substantially between those with and without relatives affected by BC (overview in [3, 8]); further studies showed that FH was associated with an increased risk of triple negative and HR-negative/HER2-expressing BC [14]. In our study, women with a positive FH had tumors with more favorable prognostic profiles as assessed by tumor size, disease stage, histologic grading, HR status and triple negative subtype. Malone et al. [8] reported in a recently published study, which examined a population-based cohort of younger BC patients, that those with a first-degree FH, compared with their counterparts without such a FH, had a better prognosis (40 % reduction in the risk of dying). The fact that patients with a positive FH have BC screening more often and might have more favorable tumor characteristics, support data which demonstrated a better prognosis for BC patients with a positive FH.

There are particular factors which must be considered in the interpretation of our findings. In the canton of Basel and the adjoining region of Northwestern Switzerland, there is no publicly funded organized mammography screening program. All interested and motivated women, however, have free access to mammography. In such an environment, the utilization of RBE for early BC detection is strongly dependent on the women's motivation and own initiative (opportunistic screening) as well as the recommendation by her physician. For the purpose of our study, i.e. to test whether the knowledge and experience of a BC in the family increases BC awareness, a patient-driven screening setting is better suited than a general screening setting. Furthermore, the referral practice for mammography, particularly in younger women, might be influenced by physicians who are aware of the positive FH of their patients. However, this motivating impact is hard to assess in individual cases.

In the future, the impact of FH on BC screening may become less important due to the broader acceptance and use of general screening programs. Furthermore, in Western countries, the number of potential female relatives who could potentially develop BC is reduced simply through the development of generally smaller, nuclear families.

Strengths and limitations

During the last decade, there have only been a few studies which evaluated the impact of FH on BC detection and tumor size in BC patient cohorts [7–9]. However, most of them reported only data on tumor size and stage [7], or tumor size and pathological/biological features [9] but did not consider tumor detection method. Malone et al. [8] applied a more comprehensive approach and reported both tumor size/stage and detection method. However, the authors, whose findings were in part similar to our study, restricted their analysis to younger patients (≤45 years) and did not study a current cohort (they ascertained BC cases diagnosed between 1983 and 1992). To our knowledge, our study is the first comprehensive analysis of the impact of FH on BC detection and tumor size based on a more recent population-based cohort (1990–2009), which does not exclusively consider a subgroup of younger BC patients. By analyzing a cohort with a broader age segment, we could demonstrate that the positive effect of first-degree relationship is not only present in younger women (BC patients ≤45 years represent approximately only the youngest 15 % of a Western BC cohort) but also in patients in whom BC is usually diagnosed (the median age of the entire cohort of the BC patients documented in our Swiss database was 61 years; patients ≤70 years of age comprise 73 % of the entire cohort of BC patients). Our findings are strengthened

by the ability to consider not only degree of relationship but also to assess the confounding effects of number of affected relatives and the age of the affected relative at the time that her BC was diagnosed. We deliberately did not consider BRCA1/BRCA2 mutation carrier separately. Due to the infrequent nature of BRCA1/BRCA2 mutations, even in women with a first-degree history, these mutations do not play an important role in the general behavior of women regarding mammography screening [8].

The following limitations of our study must be considered. Firstly, our study comes from a single region of a small country with a high socioeconomic status and all inhabitants have universal access to health care. Secondly, our study relies on information obtained by patients' self-reporting of FH. It is possible that in some cases the patients failed to accurately recall their FH or the complete FH might not be known to all women. Yoon et al. [15] reported that although 96 % of the respondents of a national survey in the USA believed that their FH information is important for their own health, <30 % had actively collected such information from relatives. Furthermore, the entire FH regarding malignant diseases may not always be known, since such topics might either not be discussed or purposely concealed from the rest of the family.

Conclusions

Women with a first-degree relative affected by BC or a relative who was diagnosed with BC at younger age have been sufficiently touched by that experience to prompt them to be more diligent in attending mammography screening, and thus be diagnosed earlier, than someone who has not had this experience. The increased awareness of BC risk, probably a result of personal experience from a close relative, decreases if the relationship is more distant. In patients who have only second-degree relatives, the tumors are diagnosed similarly often by RBE and are of a similar size compared to BC patients without FH.

Conflict of interest The authors declare that they have no conflict of interest.

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