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Short term psychological distress in patients actively approached for genetic counselling after diagnosis of breast cancer

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ABSTRACT

This prospective study assessed anxiety, depression and breast cancer-specific distress in recently diagnosed breast cancer patients before and after an active approach for genetic counselling at the beginning of adjuvant radiotherapy (mean: 52 days after surgery). Patients completed the hospital anxiety and depression scale (HADS) and the impact of event scale (IES). Psychological distress did not increase after the approach. High anxiety decreased in the comparison group ($n = 182$), whereas breast cancer specific distress decreased in the approached group ($n = 220$). It is concluded that breast cancer patients can be approached for genetic counselling shortly after surgery without additional short-term psychological burden. Patients who are young, single with little social support, less optimistic, use an avoiding coping style, experience a lower quality of life or who are highly distressed prior to approach for genetic counselling, need extra attention. Medical history did not prove to be relevant.

1. Introduction

An estimated 5–10% of all breast cancers are probably due to an autosomal dominant inherited genetic default.[1] Genetic testing became available for breast cancer patients and their family members after the identification of two breast cancer susceptibility genes, *BRCA1* and *BRCA2*. Inherited *BRCA1* and *BRCA2* mutations are associated with an increased risk for breast and ovarian cancer.[2]

Psychological distress after diagnosis and surgery for breast cancer has been well recognised and widely investigated.[3] Psychological distress was found in 20–30% of breast cancer patients within the first year after diagnosis. Burgess *et al.*[4] identified anxiety and depression or both in nearly 50% of breast cancer patients in the year following the diagnosis. In addition, high levels of intrusive thoughts and avoidance were noted in 18% and 14%, respectively, of breast cancer patients six weeks after surgery.[5] The psychological impact of genetic counselling and testing on unaffected women with a family history of breast cancer has been widely investigated as well. Non-carriers derive psychological benefits from genetic testing, while no adverse effects are observed amongst carriers.[6]

Little is known, however, about the psychological impact of genetic testing on breast cancer patients who participate in DNA testing for themselves or at the request of a healthy

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family member. A few studies concerning genetic testing in breast cancer patients found that patients diagnosed less than one year before testing demonstrated higher general anxiety and breast cancer-specific distress prior to genetic counselling and more depression after testing than patients diagnosed long ago.[7] Patients diagnosed less than one year before testing seemed as interested in genetic testing as patients diagnosed more than one year before testing and showed more interest in testing when advised by a physician.[8] So far, psychological distress during genetic counselling after a recent diagnosis with breast cancer in such an early stage of primary treatment has not yet been assessed.

We previously studied a hospital-based series of recently diagnosed breast cancer patients for predictive factors associated with *BRCA1* and *BRCA2* mutations.[9] After active approach for genetic testing, a substantial portion of participants dropped out during the genetic counselling protocol. The reasons for dropping out were not thoroughly studied, although the main reason given was patients' concern for the additional psychological burden imposed by genetic testing.

The present prospective study was initiated to: (1) investigate the possible additional psychological burden from an active approach for genetic counselling in recently diagnosed breast cancer patients at the beginning of adjuvant radiotherapy; and (2) to identify characteristics of patients with high anxiety, depression and breast cancer specific distress after the approach. The women who were eligible for genetic counselling (see below) and who were approached at the beginning of adjuvant radiotherapy were expected to demonstrate higher psychological distress after approach than the women who were not eligible and not approached. The patients with high psychological distress at baseline were expected to portray high psychological distress after approach.[5,10] The patients with a low perceived level of social support and a less optimistic outlook on life were expected to have more difficulty with psychological adjustment to the approach for genetic counselling.[3,11] Patients with more maladaptive coping strategies were expected to have more difficulty as well.[12] Finally, breast cancer patients who had received a more extensive treatment were expected to experience more psychological distress after approach for genetic counselling.[13]

2. Materials and methods

2.1. Participants

The participating patients were recruited from all consecutive breast cancer patients referred to the University Medical Centre Utrecht for adjuvant radiotherapy between January 2002 and March 2004. The inclusion criteria were a first diagnosis of breast cancer, age between 18 and 75 years, and a good command of the Dutch language.

2.2. Procedure

Referred breast cancer patients were sent an introductory letter, an informed consent form, and a baseline questionnaire by mail prior to their first visit to the Department of Radiotherapy (T0). Patients were asked to complete this questionnaire before their first visit. During this visit (7–8 weeks after surgery), the radiation oncologist filled out a checklist, adapted from our previous study,[9] on the following factors presumed predictive for hereditary breast cancer: (1) age at diagnosis <40 years; (2) bilateral breast cancer; (3) multi-centricity or multi-focality of infiltrating carcinoma; (4) a personal history of ovarian cancer; (5) family members with breast cancer; and (6) family members with ovarian cancer. If the patient was diagnosed as positive for one or more of these predictive factors, then the radiation oncologist would inform her about the possible risk for hereditary breast cancer and offer to have a family pedigree drawn up to identify eligibility for further genetic counselling at the Department of Medical Genetics. If none of the predictive factors were diagnosed as, then the radiation oncologist would not offer pedigree analysis. Together with the checklist, the treating physician prospectively registered each patient's medical history including time since surgery, type of surgery (mastectomy *versus* lumpectomy), chemotherapy prior to radiotherapy (in case of four or more axillary lymph node metastases) and TNM stage.

Four weeks after the first visit, a research nurse explained to each participant from the approached group and the comparative group what further participation in the psychological study would involve and gave the opportunity to ask questions about the study. In addition, the approached patients were provided general information on the procedure of genetic counselling. The research nurse requested further participation in the study and provided a second informed consent form and questionnaire (T1). This questionnaire was returned by mail within ten days. The study flow scheme is shown in Fig. 1. This study was approved by the Medical Ethical Committee of the University Medical Centre, Utrecht.

2.3. Measures

T0 included questions on socio-demographics (age, marital status, age and sex of children, level of education and employment), number of first- and second-degree relatives with breast cancer, and involvement with family members with cancer. The following psychological characteristics were assessed:

Coping strategy was measured using the Utrecht Coping List (UCL).[14] This 15-item Dutch adaptation of the Westbrook Coping Scale[15] evaluates active coping (considers all aspects of a problem), social support seeking (shares concerns with others), avoidance (avoids difficult situations as much as possible), and the so-called palliative reactions (seeks distraction) using a four-point frequency scale ranging from 'almost never' to 'nearly always' (Cronbach's alpha was 0.67–0.84 in a random selection of Dutch cancer patients[14]) with higher scores indicating a more often use of a particular coping style.

Optimism was assessed using an 8-item subscale of the self-assessment questionnaire-Nijmegen (SAQ-N).[16,17] This four-point frequency scale ranges from 'almost never' to 'nearly always', with higher scores indicating a more optimistic outlook on life.

Quality of life was measured using the 2-item subscale of the quality of life questionnaire (QLQ) for cancer patients in general, developed by the European organisation for research

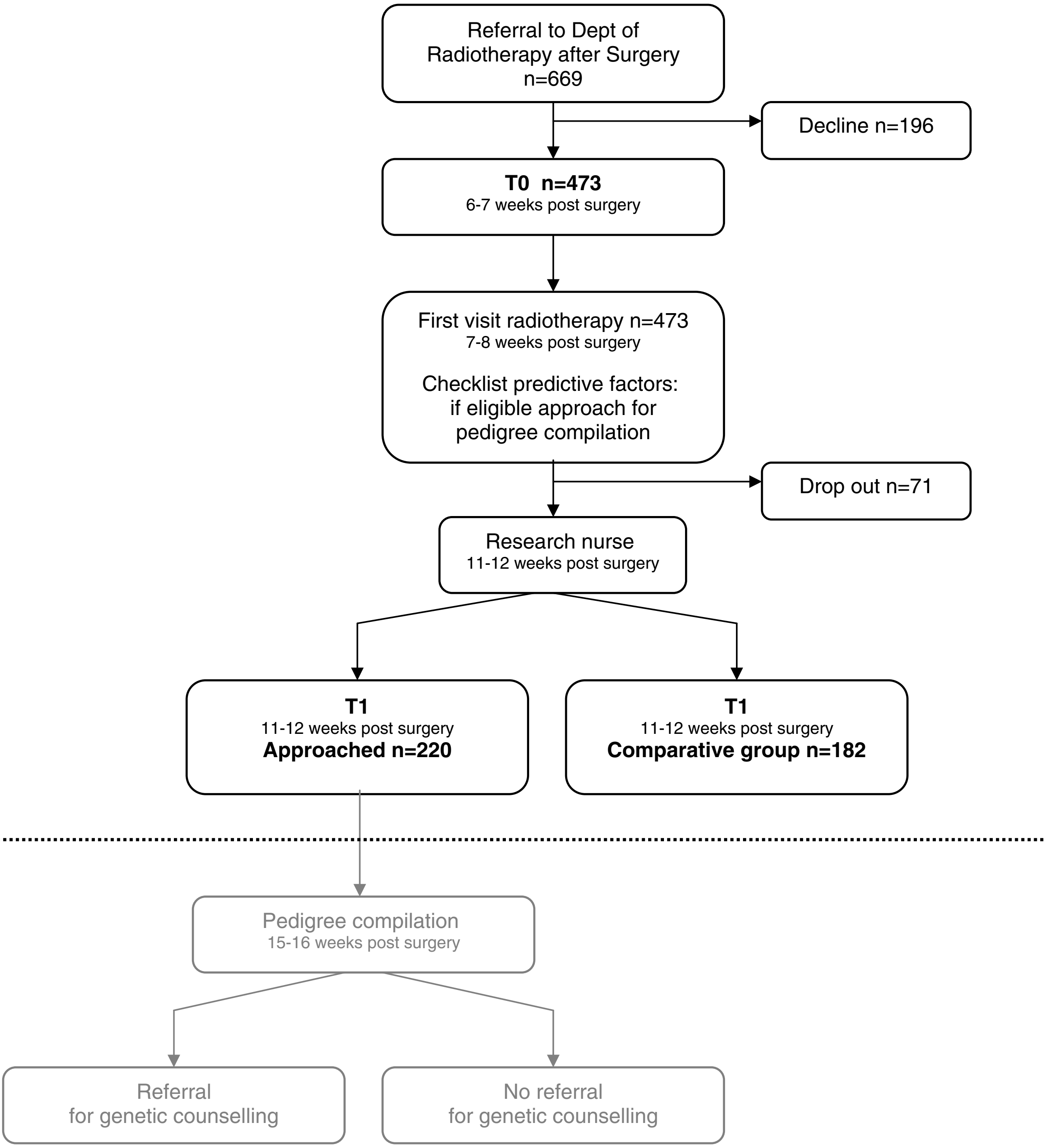

Fig. 1 – The study flow scheme.

and treatment of cancer (EORTC-QLQ).[18] Higher scores indicate a higher perceived quality of life.

Social support was noted using a self-designed single item inquiring whether the patients have someone to share their personal problems and feelings with. Three answers were possible: (1) no, (2) yes, with one person, and (3) yes, with more than one person.

2.3.1. *Two outcome measures were included in T0 and T1*

General anxiety and depression was measured using the hospital anxiety and depression scale (HADS)[19] consisting of two subscales of seven items each with four answer categories resulting in a total score ranging from 0 to 21. An anxiety score of >10 indicates abnormal anxiety and a depression score of >8 indicates abnormal depression.[20] A total score of >13 indicates an adjustment disorder.[21]

Breast cancer-specific distress was measured using the 15-item impact of event scale (IES)[22] with intrusion (the extent to which individuals are overwhelmed by thoughts and feelings about breast cancer; 7 items) and avoidance (the tendency to avoid thoughts and feelings about breast cancer; 8 items) as subscales. Each item was geared towards breast cancer as the distressing event. The total scores range from 0 to 75, with the subscale scores >8 indicating a moderate reaction and >19 indicating a clinically important reaction. A total score of 9–25 is indicative of moderate adaptation difficulties and >26 is considered indicative of clinical adaptation difficulties.[23]

2.4. Statistical analysis

The Statistical Package for Social Sciences (SPSS 11.0) was used to analyse the data.

The descriptive statistics were generated to describe the total sample and the sub-sample of eligible patients in terms of socio-demographics and medical history. The differences at T0 between participants and non-participants of the study, dropouts and participants, as well as differences between the participants eligible for pedigree analysis and the participants who were not were analysed using the χ^2-test on nominal variables and the Student's *t*-test on continuous variables. Differences between groups concerning percentages of patients with high distress were calculated using χ^2-tests. The within groups change of psychological distress was measured using McNemar comparisons of proportions. The differences between high- and low-distress groups at T1 were explored using univariate statistics (*t*-test for independent samples and χ^2-tests). The predictors of high psychological distress at T1 were identified using stepwise logistic regression models with HADS and IES total scores as dependent variables.

3. Results

3.1. Characteristics of the study group

Of the 669 breast cancer patients approached to take part in this psychological study, 473 patients (71%) returned T0 (Fig. 1). The 196 non-participants did not differ on mean age or medical history from participants, except on their eligibility for pedigree analysis. Of the non-participating group, 44% was eligible for pedigree analysis based on the presence of at least one predictive factor for hereditary breast cancer as opposed to 55% in the participating group ($\chi^2 = 6.21$, $p = 0.014$).

Seventy-one patients (15%) declined further participation after T0, resulting in full participation by 402 breast cancer patients (60% of those approached). The majority of the dropout group (46%) did not provide a motivation for withdrawal. Forty-four precent reported that the additional questionnaire was too burdensome at this stage of treatment. The patients who continued participation did not differ from the dropout group on socio-demographics, medical history and eligibility for pedigree analysis. Nor did these groups differ on mean level of general anxiety, depression or breast cancer-specific distress at T0. However, depression scores in the abnormal range were present in 25% of the dropout group compared to 12% in the participating group ($\chi^2 = 8.86$, $p = 0.005$).

Based on the presence of at least one predictive factor for hereditary breast cancer, 220 (55%) of 402 participating patients were found eligible for a pedigree analysis, while 182 (45%) presented no risk factors (Fig. 1, Table 1). As expected, patients approached for genetic counselling differed from the comparative group on socio-demographics pertaining to selection criteria for eligibility for pedigree analysis (eligible patients were younger ($t = 5.63$, $p = 0.000$) and had more first-degree ($\chi^2 = 71.67$, $p = 0.000$) and second-degree relatives with breast cancer ($\chi^2 = 84.57$, $p = 0.000$)). In addition, approached patients had a higher education ($\chi^2 = 12.58$, $p = 0.000$) and were more often employed before diagnosis ($\chi^2 = 13.06$, $p = 0.000$). With respect to psychological characteristics, the approached patients more often used a social support seeking strategy for coping ($t = -2.57$, $p = 0.011$) (Table 2). None of the approached patients had previously undergone genetic counselling.

Table 1 – The prevalence of predictive factors for hereditary breast cancer in 402 breast cancer patients treated with adjuvant radiotherapy

	n	%
Age at diagnosis <40 years	38	9.5
Bilateral breast cancer	2	0.5
Multicentricity	5	1.2
Multifocality	25	6.2
Ovarian cancer in personal history	2	0.5
Breast cancer in family	162	39.5
Ovarian cancer in family	12	2.9

At least one predictive factor was found in 220 patients.

3.2. General anxiety and breast cancer-specific distress

There were no differences in the percentage of patients from each group scoring above the clinically important cutoff score for general anxiety and depression or breast cancer-specific distress at T0 or at T1 (Table 3). Within group comparison

Table 2 – Socio-demographic, medical and psychological characteristics of breast cancer patients approached for genetic counselling and the comparative group

	Approached (*n* = 220)	Comparative (*n* = 182)	Range
Socio-demographics			
Mean age (range)	51 (24–74)	57 (40–74)[*]	
With partner	78%	74%	
With children	81%	82%	
Education ⩾high school	47%	30%[*]	
Employed	63%	45%[*]	
Medical history			
Mean days post operation (range)	55 (13–201)	56 (9–182)	
Mastectomy	17%	20%	
Prior chemotherapy	21%	19%	
First-degree relative bc[a]	35%	1%[*]	
Second-degree relative bc[a]	50%	7%[*]	
Involvement of cancer in the family	34%	29%	
Psychological resources (Mean, SD)			
Quality of life	70.6 (18.1)	73.5 (17.6)	0–100
Optimism	23.5 (4.3)	24.1 (4.6)	8–32
Coping strategy active	13.6 (3.1)	13.3 (3.5)	5–20
Avoiding	5.6 (1.4)	5.6 (1.6)	3–12
Social support	12.3 (3.2)	11.5 (3.2)[*]	5–20
Palliative	5.0 (1.3)	4.9 (1.3)	2–8

[a] Breast cancer.

[*] Significant difference $p < 0.05$; SD, standard deviation.

Table 3 – High anxiety, depression and breast cancer-specific distress scores in breast cancer patients approached for genetic counselling and the comparative group

		Approached, $n = 220$ (%)	Comparative, $n = 182$ (%)	Between group analyses χ^2	p
HADS total >13	T0	27	31	1.93	0.38
	T1	25	24	0.46	0.79
Anxiety >10	T0	13	12	0.20	0.38
	T1	10	7	1.80	0.12
Depression >8	T0	11	13	0.19	0.39
	T1	13	16	0.52	0.28
IES total >26	T0	54	50	0.67	0.24
	T1	45	42	0.54	0.26
Avoidance >19	T0	23	28	1.14	0.17
	T1	19	21	0.25	0.35
Intrusion >19	T0	21	17	1.63	0.13
	T1	16	12	0.54	0.26

T0, one week prior to radiotherapy, 6–7 weeks post surgery; T1, four weeks later, 11–12 weeks post surgery.

revealed in the approached group a significant decrease of patients with high levels of intrusive thoughts ($\chi^2 = 3.89$, $p = 0.049$) and total scores on breast cancer specific distress ($\chi^2 = 7.54$, $p = 0.005$). Within the comparative group, a significant decrease of patients with high anxiety ($p = 0.049$) was found and a trend towards a decrease in patients scoring above the total HADS cutoff score ($p = 0.050$). A trend towards decrease was also found for the number of patients from the comparative group with a high level of avoidance ($\chi^2 = 3.69$, $p = 0.053$). Both groups did not display a change in high depression.

3.3. *Characteristics of approached patients with high psychological distress*

The total cutoff scores for anxiety and depression and/or breast cancer-specific distress were used to dichotomise recently diagnosed breast cancer patients into a high distress group and a low distress group. At T1 the total scores above cutoff were identified in 55 (25%) of the approached patients for anxiety and depression and in 99 (45%) for total scores on breast cancer specific distress (Table 3), amounting to a total of 111 (50%) approached patients being in the high distress group. 43 (20%) of the approached patients scored high on both distress measures. High- and low distress groups were compared using: (1) socio-demographics (age, education, children and partner), (2) medical history (time since operation, mastectomy *versus* lumpectomy, chemotherapy prior to radiotherapy, node status and involvement with family members with cancer), and (3) psychological characteristics (level of distress at baseline, quality of life, optimism, coping style and social support).

Table 4 – The predictors of high psychological distress in recently diagnosed breast cancer patients approached for genetic counselling (n = 220) at 4 weeks follow-up: stepwise regression model

	Standardised final beta	Raw correlation	R^2	Increase R^2
Optimism	–0.32	–0.37	0.14	0.14
Quality of life	–0.20	–0.33	0.17	0.04
Social support	–0.18	–0.17	0.21	0.03
Partner	0.16	0.08	0.23	0.02
Age	0.15	0.12	0.24	0.02

No socio-demographics or medical history variables resulted in statistically different levels of anxiety, depression and/or breast cancer specific distress at T1. However, with respect to psychological characteristics, the approached patients with high distress at T1 reported at T0 a lower level of optimism ($t = 4.56$, $p = 0.000$), a lower perceived quality of life ($t = 6.17$, $p = 0.000$) as well as more use of an avoiding coping style ($t = -2.60$, $p = 0.010$). In addition, this group demonstrated higher anxiety, depression and breast cancer specific distress at T0 (HADS: $t = -9.801$, $p = 0.000$, IES: $t = -11.59$, $p = 0.000$).

High scores on anxiety, depression and breast cancer-specific distress at T0 were indicative for high scores on these distress measures at T1 (correlation 0.64–0.80). To identify other predictors for high distress at T1 in approached patients, the above comparison measures were entered into the stepwise regression model with the total scores on anxiety and depression and breast cancer specific distress as the dependent variable. The comparison measures accounted for 24% of the prediction of high distress at T1. Optimism and quality of life at T0 accounted for 17%, and social support, having a partner and age explaining an additional 7% (Table 4).

4. Discussion

This study was designed to identify the possible additional psychological burden from an active approach for genetic counselling in newly diagnosed breast cancer patients, several weeks after surgery. Overall this study showed no increase in psychological distress after the active approach for genetic counselling at the start of adjuvant radiotherapy. According to our expectations, the approached group did not display a decrease in the percentage of patients with high anxiety, while there was a decrease in the comparative group. However, the approached group did demonstrate a significant decrease in the percentage of patients with high breast cancer specific distress, not found in the comparative group. As expected, the approached patients with high distress were less optimistic, experienced a lower quality of life as well as less social support and more often used an avoiding coping style. In addition, highly distressed patients were younger and more often single. However, medical history did not prove relevant.

The overall decrease in the course of anxiety and breast cancer-specific distress after four weeks may be simply due to time elapsing since the cancer diagnosis and operation.[4,5] It could be that receiving the diagnosis of cancer had such an impact that the possibly hereditary nature could not have increased the experienced psychological distress during primary treatment. This impact might become more evident later on by further genetic counselling, testing of the *BRCA* genes and the disclosure of a DNA test result after the patients have adapted to their diagnosis. On the contrary, the level of anxiety, depression and breast cancer-specific distress may increase due to the evolving acute toxicity of the current radiotherapy treatment.[24]

The surprising significant decrease in the proportion of approached patients with high breast cancer specific distress, not found in the comparative group, may be due to the approached group's possible awareness of their family history. Accordingly, the approached group may have been more prepared than we had expected. Eligible patients may have considered the approach as a standard part of medical treatment as opposed to an unexpected approach. The offer of genetic counselling may have provided peace of mind through the unrealistic idea of future certainty concerning the possible hereditary nature of their breast cancer.[25]

As in other study groups, our patients showed a close relationship between baseline and follow-up measurements of anxiety, depression and breast cancer-specific distress.[5] The high correlation between baseline and follow-up measurements of distress may indicate underlying individual differences, independent of eligibility for pedigree analysis or an approach for genetic counselling.

Experienced distress in the first few years following a breast cancer diagnosis is not influenced by the patient's medical history.[26] Apparently, this is also the case for breast cancer patients approached for genetic counselling shortly after surgery. Studies on other risk factors for high distress following a breast cancer diagnosis are not consistent in their findings. More studies concerning risk factors for high distress after an approach for genetic counselling shortly after surgery are needed to compare findings and to gain insight into the risk factors for long-term distress.

Randall and colleagues[27] found comparable levels of intrusion and avoidance in breast cancer patients prior to the first appointment at a genetic clinic. This despite the longer time since diagnosis: 3 months to over 5 years after the diagnosis as opposed to the 11–12 weeks post surgery in the present study. Their study group consisted of breast cancer patients requesting genetic testing for hereditary breast cancer on their own initiative as opposed to the actively approached patients. The former group may well have started the adaptation process to the possible hereditary nature of breast cancer as opposed to actively approached patients, whom we assume were not expecting genetic counselling or testing. The similar levels of breast cancer-specific distress in these groups argue in favour of an early active approach of recently diagnosed breast cancer patients. An even earlier timing for mutation searching, right after diagnosis, prior to operation, and on behalf of the treatment decision-making process, may prove more desirable.[28,29] Mitchell and colleagues[30] also proposed rapid genetic testing in selected cases to facilitate urgent clinical management decisions. Additional research on potential benefits and risks of rapid genetic testing in the diagnostic phase of breast cancer is needed.

Underestimation of the impact of the approach for genetic counselling may be caused by self-selection within the study group. Participants who dropped out of the study after the baseline questionnaire more often reported high depression compared to the participating group. This group of dropouts may be particularly vulnerable and is not included in the present study population. Another possible selection is the significant difference between study participants and non-participants in their eligibility for pedigree analysis. The participants may have been more aware of and prepared for the possible hereditary nature of their breast cancer and therefore more likely to participate in a study geared towards this aspect. The approached breast cancer patients also had a higher education and were more often employed than the comparative group. Although a higher education may influence the choice of whether to participate in genetic counselling or whether to take part in a psychological study, there is no apparent explanation for the higher education level in the approached group, other than the simple fact of younger age possibly reflecting a difference in generation.

Despite the fact that no additional psychological distress is caused by the approach of eligible patients for genetic counselling at the beginning of adjuvant radiotherapy, extra attention may be needed for particularly vulnerable patients. In an attempt to identify patients vulnerable to high distress, clinicians should gear more questions towards anxiety, depression and breast cancer specific distress as well as the patients outlook on life and experience of the quality of life. Preferably they should do so by using standardised questionnaires. The identified patients may benefit from additional counselling by a genetic nurse. There is a need for further research using a truly experimental design geared towards the long-term impact of an active approach for genetic counselling on recently diagnosed breast cancer patients. The particular groups of interest are the approached breast cancer patients who choose not to take part in genetic counselling, and patients who initially opt for counselling, but drop out at a later stage.

Conflict of interest statement

None declared.

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