

Breast Cancer Patients' Fear of Treatment: Results from the Multicenter Longitudinal Study BRENDA II

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Keywords

Breast neoplasms · Oncology · Prospective studies · Anxiety · Fear

Summary

Background: Fear of cancer treatment can become overwhelming. It is important to understand what patients are mainly afraid of and what factors are correlated with intense fear of treatment. **Methods:** Patients with primary breast cancer ($n = 761$) completed questionnaires about fear of treatment before surgery (t_1), and before (t_2) and after (t_3) adjuvant treatment. Psychological co-morbidity was assessed using the Patient Health Questionnaire. Logistic regression identified predictors of intense fear of treatment. **Results:** Patients were most afraid of chemotherapy (mean score 3.5), and fear remained high throughout follow-up; fear of radiotherapy and of surgery was lower and decreased over time (from 2.7 to 2.2, $p < 0.0001$; and from 2.6 to 2.2, $p < 0.0001$, respectively). Patients with psychological co-morbidity (odds ratios (OR) 1.7–3.0) and those who had heard reports of negative experiences with cancer treatments from others (OR 3.8–16.2) were more likely to have intense fear of all the treatments. Patients with a previous cancer less often expressed fear of surgery (OR 0.6, 95% confidence interval 0.4–1.0). **Conclusion:** Fear of treatment, especially of chemotherapy, is prevalent in many patients with primary breast cancer. Patients with psychological co-morbidity and those who have heard reports of negative experiences with cancer treatment are at higher risk of experiencing intense fear.

Introduction

Fear is one of the most common and distressing psychological reactions in cancer patients. Many experience this fear as overwhelming, especially at the time of diagnosis [1, 2]. However, also in the outpatient aftercare [1, 3], and even years after completion of treatment, survivors report increased levels of fear [4–6]. Burgess et al. [4] found that 33% of patients with early breast cancer suffered from clinically relevant symptoms of anxiety and/or depression at the time of cancer diagnosis, and 15% later on.

Many studies investigating fear in cancer patients so far have focused on anxiety in terms of mental health or on fear of progression [5, 7–10]. However, patients are not only afraid of the malignant disease itself but also of the treatments involved in cancer care. Such fears can result in delay of treatment and/or refusal of follow-up tests [11], which in turn diminishes the odds of survival [12–14]. A meta-analysis including 8,781 women with breast cancer estimated that 34% were symptomatic for ≥ 3 months before seeing a doctor [12]. It is therefore of great importance to better understand what patients are mainly afraid of and what factors are correlated with intense fear of treatment and might hinder a patient's decision to seek help.

This study set out to examine the following questions in a large cohort of patients with primary breast cancer:

- i) What are breast cancer patients most afraid of: surgery, lymphadenectomy, radiotherapy, chemotherapy, or endocrine therapy? How does fear of treatment develop over time?
- ii) What do patients associate with mastectomy versus breast-conserving surgery?

iii) Which media do patients use to seek information about breast cancer treatment? Is the use of public media for seeking information correlated with fear of treatment?

iv) What factors are associated with intense fear of treatment?

Methods

Data Collection

In a prospective multicenter cohort study, patients with primary breast cancer were sampled consecutively over a period of 4 years (2009–2012). Patients were approached before surgery (t1), before initiation of adjuvant treatment (t2), and after completion of adjuvant radio- and/or chemotherapy (t3).

Patients were eligible for this study if they had been diagnosed with primary breast cancer (histologically confirmed). Exclusion criteria were: metastatic or recurrent disease at baseline, bilateral breast cancer, primary occult disease and phylloides tumor, inability to complete a questionnaire, and no written informed consent.

Following a consultation, each patient was informed about the study by her doctor and asked to participate. If she agreed, the doctor handed over the first series of questionnaires, and interviewed the patient. Follow-up interviews were performed by trained study nurses. We collected data at 4 hospitals all of which are breast cancer centers certified by the German Cancer Society. Ethical approval was obtained from the Ethics Committee of Ulm University.

Instruments

Clinical data were obtained from the medical records by trained data managers. The patient's individual risk was defined according to the Nottingham Prognostic Index [15] based on the size of the lesion, number of lymph nodes involved, and tumor grade. Missing values on any of the 3 parameters were imputed using the mean.

Previous malignant diseases in the patient's personal or family history were documented by the doctor after he/she had taken the medical history of the patient.

Demographic data such as age and education were provided by the patient.

We elicited *fear of treatment* by asking: 'How much are you afraid of the following treatments: surgery, lymphadenectomy, radiotherapy, chemotherapy, endocrine therapy?' Responses were collected on a 4-point Likert scale ranging from 1 ('not afraid at all') to 4 ('very much afraid'). Subsequently, responses were dichotomized into 'intense fear' (response 4) versus 'no intense fear' (responses 1–3).

Potential *sources of fear* were considered to be negative experiences of friends and/or family, and negative associations with certain treatments.

Patients reported on 4-point Likert scales ('not at all' to 'very often') the frequency of hearing about negative experiences with treatments (surgery, lymphadenectomy, radiotherapy, chemotherapy, and endocrine therapy) from friends and/or family.

Negative associations with surgery were elicited by asking 'What do you associate with breast-conserving therapy?' and 'What do you associate with mastectomy?'. Patients indicated on a 4-point Likert scale whether the following 4 associations were relevant for them regarding these 2 types of surgery: mutilation, pain, reduced sexual attraction, and change in body image.

Seeking for information through public media was ascertained by asking 'Have you searched for information about your disease and treatment in the following media: internet, newspapers, brochures, television, radio?'. Response categories were yes/no.

Patient involvement in care was measured using the Patient Involvement in Care Scales (PICS) [16] adapted for Germany [17]. The PICS are composed of 3 subscales: The Doctor Facilitation Subscale, containing items such as 'My doctor encouraged me to talk about personal concerns related to my medical symptoms', measures perceived doctor support. The Patient Information Subscale assesses the activities on the part of the patient in seeking information, e.g., 'I asked my doctor a lot of questions about my medical symptoms'. The Patient

Table 1. Sample characteristics

	n	%
Total	761	100
Age, years		
< 40	40	5.3
40–49	157	20.6
50–59	207	27.2
60–69	215	28.3
70–79	118	15.5
≥ 80	24	3.2
Education, years		
< 10	353	46.4
≥ 10	399	52.4
Unknown	9	1.2
Nottingham Prognostic Index		
Low risk	66	8.7
Medium risk	348	45.7
High risk	249	32.7
Very high risk	98	12.9
Treatment received		
Breast-conserving surgery	634	83.3
Mastectomy	127	16.7
Chemotherapy, neoadjuvant	39	5.1
Chemotherapy, adjuvant	333	43.8
Radiotherapy	672	88.3
Endocrine therapy	619	81.3
Herceptin	88	11.6
Psychological comorbidity		
Psychological condition present at baseline	162	21.6

Decision-Making Subscale ascertains the involvement of patients in treatment decisions, e.g., 'I suggested a certain kind of medical treatment to my doctor'. Notably, this scale does not assess shared decision-making but the efforts a patient puts into being involved in decision-making.

We measured *mental health* using the Patient Health Questionnaire (PHQ) [18], a self-administered instrument assessing mental disorders according to the criteria of the 10th revision of the International Classification of Diseases (ICD-10). The PHQ has been validated, using the Structured Clinical Interview [19], as the gold standard [18].

Statistical Analysis

Absolute and relative frequencies were calculated for categorical variables, and mean scores for continuous variables, to describe the sample. Changes in fear and search for information over time were analyzed using matched-pairs signed-ranks tests.

Associations of fear of treatment with search for information through public media was investigated using Spearman's rank correlation tests. The role of potential predictors of intense fear of treatment was estimated using logistic regression analyses with age, clinical prognosis, previous cancer in family or personal history, negative experiences with that treatment of friends and/or family, psychological co-morbidity, and patient involvement in care as predictors. All variables were entered simultaneously into the models. Fear of all 5 treatments was analyzed as an outcome variable before that treatment started, i.e. fear of surgery and lymphadenectomy was analyzed at t1, fear of radiotherapy and chemotherapy at t2, and fear of endocrine therapy at t3.

As this is an exploratory study, we do not employ the term 'statistically significant' but discuss differences that are conspicuous in size and likely not to be due to random variation only. Statistical analyses were performed using STATA 12.1 (StataCorp LP, College Station, TX, USA).

Results

Sample

During the study period, 857 patients with primary breast cancer were treated at the collaborating clinics; 92 declined participation, and 1 patient was excluded because of dementia, resulting in a total of 764 patients (89% participation rate). Data on fear of treatment were available for 761 patients; this group was used for data analysis. Non-participants were on average older than participants (median age 67 vs. 58 years); the Nottingham Prognostic Index, however, did not differ between participants and non-participants.

All patients received surgical care, 83% breast-conserving surgery and 17% mastectomy (table 1). The type of surgery was related to age: those ≥ 75 years old received mastectomy in 30% of all cases, those < 75 years old in only 15%. The median time between t1 and t2 was 24 days, and the median time between t2 and t3 was 7 months. At t2, 653 (86%) patients participated, and 628 (83%) at t3.

Fear of Treatment

At baseline, patients were most afraid of chemotherapy (67% of all patients said they were very much afraid of chemotherapy), followed by lymphadenectomy and radiotherapy (fig. 1). Over time, fear of treatment decreased especially regarding radiotherapy (on average from a score of 2.7 at baseline to 2.2 after completion of adjuvant therapy, $p < 0.0001$) and surgery (from 2.6 to 2.2, $p < 0.0001$) whereas fear of chemotherapy remained at a high level throughout follow-up (from 3.5 to 3.4, $p = 0.23$).

Potential Sources of Fear

On average, not many patients had heard of negative experiences with cancer treatments from friends and/or family. Most frequent were negative stories about chemotherapy (average score 2.2), least frequent stories about endocrine therapy (average score 1.5).

Patients had greater concerns regarding mastectomy than breast-conserving therapy (fig. 2). For example, 50% of patients agreed completely that mastectomy is associated with mutilation whereas only 8% made this association with breast-conserving therapy. Over time, negative associations regarding breast-conserving therapy decreased slightly whereas they remained relatively stable or even increased for mastectomy.

Search for Information in Public Media

The most frequently searched source of information was brochures ($> 50\%$ at all times), followed by internet and newspapers (fig. 3). Less than 10% of patients gained information from radio shows. Over time, patients increased their efforts to gain information through public media ($p < 0.0001$). Some patients used no public media at all (e.g., 29% at t1), some used more than 3 sources (e.g., 10% at t1). On average, 1–2 sources were used.

There was no evidence that type or amount of sources used were correlated with fear of any cancer treatment (data not shown).

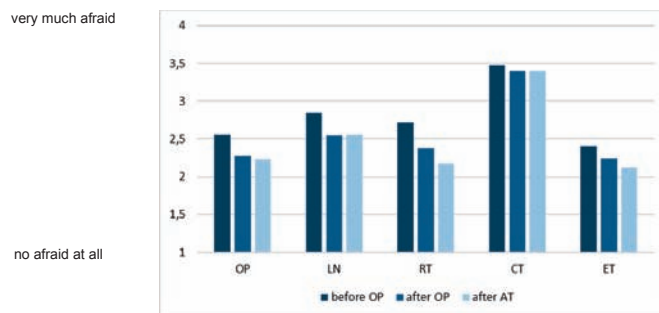


Fig. 1. Fear of breast cancer treatments over time. OP = Surgery; LN = lymphadenectomy; RT = radiotherapy; CT = chemotherapy; ET = endocrine therapy; AT = adjuvant therapy (chemotherapy and/or radiotherapy).

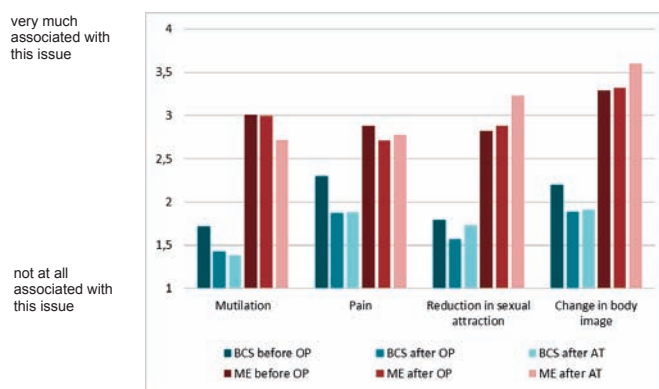


Fig. 2. Associations patients have with 'breast-conserving therapy' and 'mastectomy' over time. BCS = Breast-conserving therapy; ME = mastectomy; OP = surgery; AT = adjuvant therapy (chemotherapy and/or radiotherapy).

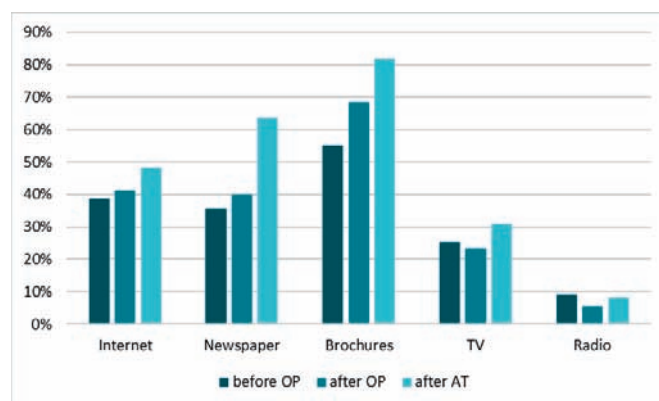


Fig. 3. Search for information through public media over time. OP = Surgery; AT = adjuvant therapy (chemotherapy and/or radiotherapy); TV = television.

Predictors of Intense Fear

Patients with poor mental health and those who had repeatedly heard negative stories about a treatment from friends and/or family more often had intense fears (table 2). This applied to all types of treatment. For example, poor mental health doubled the odds of

Table 2. Predictors of intense fear of breast cancer treatments

	Fear of surgery		Fear of lymphadenectomy		Fear of radiotherapy		Fear of chemotherapy		Fear of endocrine therapy	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age \geq 65 years	0.7	(0.5; 1.1)	1.0	(0.7; 1.4)	1.5	(0.9; 2.4)	1.3	(0.9; 1.8)	0.4	(0.2; 0.9)
NPI 2 vs. 1	0.6	(0.3; 1.1)	1.1	(0.6; 2.0)	1.0	(0.4; 2.3)	0.6	(0.3; 1.1)	0.4	(0.2; 1.0)
NPI 3 vs. 1	0.5	(0.2; 0.9)	0.8	(0.4; 1.5)	1.0	(0.4; 2.4)	0.4	(0.2; 0.8)	0.7	(0.3; 1.5)
NPI 4 vs. 1	1.0	(0.5; 2.1)	1.2	(0.6; 2.4)	1.7	(0.6; 4.3)	0.5	(0.2; 1.0)	0.4	(0.1; 1.2)
Psychological comorbidity	3.0	(2.0; 4.5)	1.7	(1.1; 2.5)	1.8	(1.1; 3.0)	2.1	(1.3; 3.4)	1.8	(1.0; 3.2)
Cancer in personal history	0.6	(0.4; 1.0)	0.7	(0.5; 1.1)	1.1	(0.7; 1.9)	1.1	(0.7; 1.7)	1.2	(0.6; 2.2)
Cancer in family history	0.9	(0.6; 1.4)	0.9	(0.6; 1.2)	0.7	(0.4; 1.1)	1.1	(0.7; 1.6)	1.2	(0.7; 2.3)
Repeated reports of negative experiences with this treatment from others	3.8	(1.8; 8.2)	6.0	(2.8; 13.1)	9.3	(4.4; 19.5)	5.1	(2.8; 9.3)	16.2	(5.5; 47.6)
Doctor facilitation	1.2	(0.9; 1.6)	0.9	(0.7; 1.2)	1.2	(0.9; 1.8)	1.0	(0.7; 1.3)	0.8	(0.5; 1.3)
Patient information	0.9	(0.7; 1.2)	1.3	(1.0; 1.7)	1.1	(0.8; 1.5)	1.1	(0.9; 1.5)	1.0	(0.7; 1.5)
Patient decision making	1.0	(0.8; 1.3)	0.9	(0.8; 1.2)	1.0	(0.8; 1.4)	1.0	(0.8; 1.3)	1.2	(0.9; 1.8)

OR = Odds ratio; CI = confidence interval; NPI = Nottingham Prognostic Index. Higher values indicate higher risk of dying.

intense fear of chemotherapy and tripled the odds of fear of surgery. Patients who had heard reports about negative experiences from others about lymphadenectomy were 6 times more often very afraid of lymphadenectomy than other patients.

Patients with cancer in their personal history were less afraid of surgery (odds ratio (OR) 0.6, 95% confidence interval (CI) 0.4–1.0), but fear of any other cancer treatment was not decreased.

Not surprisingly, older patients were less afraid of endocrine therapy (OR 0.4, 95% CI 0.2–0.9). Overall, there was no evidence that involvement of the patient in her care is related with intensity of fear with the exception that patients asking the doctor a lot of questions about symptoms and treatment were more afraid of lymphadenectomy (OR 1.3, 95% CI 1.0–1.7).

Discussion

This study set out to better understand breast cancer patients' fears regarding cancer treatment, and factors correlated with intense fears. We found that patients were most afraid of chemotherapy. Moreover, this fear did not decrease over time in contrast to fear regarding other treatments such as radiotherapy or surgery. Similarly, negative experiences with cancer treatment reported in social circles mainly related to chemotherapy. It seems that chemotherapy is seen as the treatment with the most negative consequences, both short- and long-term. Indeed, chemotherapy is often associated with decreased quality of life, both short- and long-term [20]. Given the long duration of this treatment (usually about 6 months), it is not surprising that patients remember its side effects very well. However, only few patients discontinue chemotherapy despite the detrimental effects on quality of life.

In the past, radiotherapy often had severe side effects and thus also quite a negative image [21]. Nowadays, fear of radiation is still prevalent, not only among patients but also the general public [22]. However, modern radio-oncology techniques have reduced side effects considerably, and our findings suggest that this has translated into decreased fear of radiotherapy compared to the past.

Fear is a normal reaction in the face of a cancer diagnosis. Without fear, people would not take action and seek medical help [23]. However, when fear becomes intense and overwhelming, it is usually very distressing for patients. Some people deal with such intense fear by denying everything that might contribute to it [24, 25], which in turn can result in delay of diagnostic and treatment procedures up to declining all medical care [26].

Therefore, healthcare providers should support patients in their coping with fear, not only because it is a distressing feeling but also to improve adherence to treatments. The question arises as to how this can be achieved. Providing more information on breast cancer treatment does not necessarily translate into reduced fear [26]. We also saw in our study that neither search for information through public media nor a patient's motivation to seek information from her doctor were related to the level of fear. This may be because the relationship between amount of information and fear is complex. Many patients feel safer when they are informed comprehensively about the disease and treatment [27, 28]. However, if they understand from the doctor's explanations only that their situation is difficult or hopeless, they may try to avoid this information [29]; and if this is not possible, anxiety increases even more. We saw in our study that psychological disorders were associated with fear of cancer treatment throughout all types of treatment. Thus, clinicians seeking to ease a patient's fear will best succeed when targeting her emotional state and not (only) the

amount of information provided. Needless to say, if the patient wants more information, it should of course be provided. If, however, she feels already overwhelmed by information, it will make her feel even more uncomfortable if the doctor continues to break bad news.

Guidelines explaining how doctors should talk to cancer patients [30, 31] therefore recommend they should start a consultation with i) creating a trusting relationship and ii) asking the patient how much information she needs at the moment. Both features are essential in reducing fear of treatment.

From a psychological point of view, having intense fear of treatment could also reflect a coping mechanism within the patient. As fears regarding the disease itself could be experienced as overwhelming, projecting this fear onto a concrete issue such as the treatment may make it more manageable, resulting in reduced anxiety.

Another finding from our study is that bad experiences with cancer treatment reported by friends or relatives are highly related with fear of treatment. Clinicians can target this issue by exploring together with the patient the stories she has heard, and subsequently analyze which of her fears are 'realistic' and which are not.

While interpreting the results of our study, its limitations should be taken into account. First, only patients with primary breast cancer were included. Patients with metastatic disease may experience other levels of fear, and there might be different predictors of intense fear in that group of patients. Secondly, patients participating in the study were younger than patients who declined. As we have seen that younger age was associated with more intense fear of endocrine treatment, presumably because side ef-

fects are more detrimental for premenopausal women, the overall level of fear of endocrine therapy found in our study is likely to be overestimated for the entire group of primary breast cancer patients.

Another limitation is that fear of endocrine treatment could only be measured at the beginning of this treatment. As it usually takes 5 years before anti-hormonal treatment is discontinued (nowadays up to 10 years in high-risk patients), we would need a follow-up of 5 years or more to be able to fully judge the level of fear for this treatment. Moreover, the instrument used to assess fear of treatment had not been validated before. It was developed specifically for this study, and seems to have good face validity. However, a comprehensive validation would have increased the validity of our findings.

In conclusion, fear of treatment, especially of chemotherapy, is prevalent in many patients with primary breast cancer. Patients with psychological co-morbidity and those who have repeatedly heard reports of negative experiences with cancer treatment in their social circles are at higher risk of intense fear.

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Disclosure Statement

The authors declare no competing interests.

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