ORIGINAL ARTICLE

Breast Cancer Morbidity

Questionnaire Survey of Patients on the Long Term Effects of Disease and Adjuvant Therapy

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SUMMARY

Background: Many women have symptoms of various kinds after being treated for breast cancer. It is unclear how frequently these different side effects of treatment arise.

Methods: All women who underwent surgery for breast cancer and subsequently received adjuvant systemic treatment in a single certified breast-cancer center from 2006 to 2010 were asked to fill out a standardized questionnaire. Medical data were retrieved from their charts and statistically analyzed together with the questionnaire responses. The questionnaire was also given to an age-adjusted control group.

Results: 734 questionnaires were filled out and returned (response rate, 70%). The mean interval from the diagnosis of breast cancer to the time of response to the questionnaire was 38 months. The median age at time of response to the questionnaire was 65 years (range, 30 to 91 years). The distribution of UICC stages at the time of initial diagnosis was as follows: I 46%, II 42%, III 12%. 78% of the patients underwent breat conserving surgery, 85% had radiotherapy, 85% had antihormonal treatment, and 49% had chemotherapy. 91% were satisfied or very satisfied with the outcome of surgery. 34% reported operation site pain; 35% reported limitations of shoulder or arm function. Younger patients suffered from emotional sequelae more than older ones did. 25% reported a change in their relationship with their spouse. Before being diagnosed with breast cancer, 9% had consulted a psychiatrist or psychotherapist; after the diagnosis, 19% did. 14% had taken psychoactive medication before the diagnosis, and 26% did afterward.

Conclusion: Treatment for breast cancer has negative physical, emotional, and social effects on many patients. They suffer these effects to varying degrees depending on age, type of surgery, and systemic treatment.

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Many women with breast cancer suffer from pain, postmenopausal symptoms, psychosocial stress, depression, sleep disorders, or fatigue (1–3). Although the majority are again taking an active part in life by around a year after their diagnosis, many symptoms persist for months or even years after the end of treatment (4). Particularly in view of the fact that patients often receive treatment that was not strictly necessary, the long-term effects are of considerable importance.

Various systemic treatments have been linked with secondary neoplasia, although the overall risk is judged to be slight (5, 6). The incidence of lymphatic edema increases up to 2 years after operation and is estimated at 16 to 21% (7). Radical surgery has been described as a risk factor (7), and meanwhile researchers are questioning the advisability of such extensive interventions (8). Cardiotoxicity is not only a treatment-limiting factor, but has also been identified as a long-term complication of oncological therapy (9).

Literature reports vary as to the frequency of cognitive impairments, the prevalence of which is stated to be between 16% and 50% (10). According to a recent review, from an objective viewpoint the influence of treatment on cognitive function is overestimated (5). The data on psychological impairments are also inconsistent: A meta-analysis restricted to studies that had used psychiatric interviews for diagnostic purposes showed that—following ICD criteria—anxiety (prevalence 10%) and depression (16%) were less widespread than commonly thought (11). While cancer patients still had higher rates of anxiety than healthy persons years after the disease, increased rates of depression did not persist as long (12).

Moreover, some subgroups suffer more serious impairments than others. While it is often assumed that older women tolerate the treatment less well than the young, in fact large studies have shown the opposite (4). Women under 50 years of age tend to report symptoms such as pain, forgetfulness, problems with their body image, and hot flashes (13). An epidemiological study identified diagnosis at young age, presence of chronic comorbidity, and low socioeconomic status as risk factors for greater difficulty regaining quality of life (1).

We set out to investigate the impact of disease and treatment on women's lives in various areas and uncover interrelationships.

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TABLE 1

Characteristics of the survey participants

Patients with invasive breast cancer		
Sex		
Female	N = 734	100%
Age at time of survey		
Median		65 years
Range		30–91 years
<60 years	n = 236	32%
60–70 years	n = 253	34%
>70 years	n = 245	33%
Menopausal status at time of diagnosis		
Premenopausal	n = 113	15%
Postmenopausal	n = 621	85%
Tumor location		
Left	n = 380	52%
Right	n = 332	45%
Bilateral (simultaneous)	n = 22	3%
Histology		
Ductal invasive	n = 541	74%
Lobular invasive	n = 106	14%
Other/mixed forms	n = 87	12%
Grading		
G1	n = 92	13%
G2	n = 428	59%
G3	n = 210	29%
Stage at time of diagnosis according to Union Internationale Contre le Cancer (UICC)	n = 332	46%
I	n = 302	42%
II	n = 84	12%
II		
Time from diagnosis to survey		
Mean		38 months
Range		10–70 months
≤ 25 months	n = 189	26%
26–38 months	n = 178	24%
39–51 months	n = 193	26%
≥ 52 months	n = 170	23%
Control group (no breast cancer in previous 5 years)		
Sex		
Female	N = 302	100%
Age at time of survey (stratified according to age distribution of patients)		
Median		65 years
Range		35–92 years
<60 years	n = 90	30%
60–70 years	n = 111	36%
>70 years	n = 101	33%

Methods

A scanner-readable standardized questionnaire was sent to all women with breast cancer who had undergone surgery at the Marienhof Breast Center in Koblenz, Germany, and proceeded to receive adjuvant systemic treatment. The survey contained questions designed to yield information on psychological, physical, cognitive, and social changes. Details of the patients' medical treatment were transferred from their charts to a database and linked with the survey data.

A computer-aided standardized telephone survey was carried out in an age-matched control group of n = 302 women who did not have breast cancer. These women were recruited by a market research institute, stratified by age group. The sample size was estimated a priori (14).

The medical data of responders (patients who completed the questionnaire) and nonresponders were compared to enable assessment of systematic selection effects. A nonresponder analysis could not be carried out for the control group.

Statistical evaluation was performed by means of SPSS 19. All patients had given written consent for pseudonymized use of their data. Frequencies, statistical measures of central tendency, and correlations were calculated. Statistical significance ($\alpha < 0.05$) was tested using the appropriate procedures. The women's responses regarding satisfaction with the outcome of surgery were evaluated by logistic regression, and further multiple analyses were carried out. Only seldom were data missing; whenever this was the case, correspondingly lower numbers of cases were included in the analyses.

Results

Around 250 women each year undergo surgical treatment at the Marienhof Breast Center, one of the largest of its kind in the German federal state of Rhineland–Palatinate. Their systemic treatment takes place in close cooperation with the patients' office-based oncologists.

A total of n = 1 272 patients were available for analysis, of whom 222 were ineligible for the following reasons:

- Ductal carcinoma in situ (DCIS) (n = 154)
- Primary metastasis (n = 35)
- Deceased (n = 27)
- Male (n = 6)

The remaining n = 1 050 patients received the questionnaire together with a letter inviting them to complete it. The response rate was 70%; 734 questionnaires could be analyzed. The median age at the time of the survey was 65 years (range 30 to 91 years). The participants' characteristics are displayed in *Table 1*.

There were no significant differences between responders and nonresponders with regard to age (p = 0.412), diagnosis, or treatment. The mean time between diagnosis and completion of the questionnaire was 38 months (standard deviation 16 months).

Surgery

The mean number of operations per patient, including secondary resection and lymph node surgery, was 1.4. The median cumulative hospital stay was 9 days (range 1 to 35 days). The surgical and systemic treatments administered are detailed in *Table 2*.

Satisfaction with treatment outcome

The patients were asked to report their satisfaction with the results of surgery on a four-point scale from "very satisfied" (1) to "not at all satisfied" (4). Ninety-one percent of the responders were "satisfied" or "very satisfied" with the outcome; the mean satisfaction score was 1.6. Patients with breast-conserving surgery were much more satisfied than those with mastectomy (mean 1.5 [95% confidence interval (95% CI) 1.48–1.58] versus 2.0 [95% CI 1.85–2.11]). The mean satisfaction scores for UICC stages I, II, and III were 1.5 (95% CI 1.45–1.60), 1.7 (95% CI 1.59–1.76), and 1.9 (95% CI 1.69–2.04), respectively. No significant differences were determined among the different age groups. Logistic regression analysis showed that the type of operation had a significant effect, but none of the other variables had any predictive value.

Postoperative pain, arm swelling, and functional impairment

Thirty-four percent of the responders reported operation site pain. Seventeen percent suffered swelling of the arm, with considerable variation among subgroups with regard to type of operation, lymph node surgery, age, and systemic treatment *(Table 3)*. Lymph drainage was (still) carried out in 25% of cases overall, with the highest rates among patients with axillary dissection (36%) and taxane-based chemotherapy (35%).

Antihormonal treatment

While 83% of the patients reported receiving antihormonal treatment, analysis of their medical records yielded a figure of 85%. Comparison of the subjective and objective data showed 92% correspondence (Cohen's kappa 0.700).

The mean number of substances administered was 1.3, with tamoxifen given most frequently (53%). Eleven percent of the women ended the endocrine therapy prematurely, mainly owing to pain and general adverse effects.

Cognitive, physical, and psychological impairments

Cognitive, physical, and psychological impairments were also classified on a four-point scale. Possible answers to the question "How much do you suffer from…?" ranged from "not at all" (1) to "very much" (4).

Comparison with an age-matched control group of women without breast cancer showed clearly that the patients suffered impairments in various areas of life. Their scores were higher in all areas, and the differences between the mean values of the two groups were all highly significant ($p < 0.001$) *(Table 4)*. The mean values for the different time quartiles (time between diagnosis and survey) did not differ significantly.

TABLE 2

Medical treatment data of the patients surveyed

Neoadjuvant chemotherapy (N = 734)		
Yes	n = 24	3%
No	n = 710	97%
Type of surgery (N = 733)		
Breast-conserving	n = 572	78%
Mastectomy	n = 161	22%
Secondary resection necessary		
Total (N = 734)	n = 141	19%
Breast-conserving (n = 572)	n = 121	21%
Mastectomy (n = 161)	n = 20	12%
Postoperative radiotherapy		
Total (N = 734)	n = 623	85%
Breast-conserving (n = 572)	n = 546	95%
Mastectomy (n = 161)	n = 77	48%
Lymph node surgery (N = 733)		
Sentinel node biopsy	n = 400	55%
Axillary dissection	n = 314	43%
None	n = 19	3%
Adjuvant chemotherapy (N = 732)		
Yes	n = 362	49%
No	n = 370	51%
Taxane-based chemotherapy protocol (N = 362)		
Yes	n = 218	60%
No	n = 102	28%
Unknown	n = 42	12%
Adjuvant antihormonal treatment (N = 734)		
Yes	n = 621	85%
No	n = 113	15%

Employment

Forty-four percent of the responders were in employment before their illness; of these, 57% had jobs involving manual labor. Overall, 66% returned to work (69% for breast-conserving surgery, 55% for mastectomy). Sixteen percent of those who returned to their previous employment reported disadvantages, with a higher rate for manual than for nonmanual labor (23% versus 7%; chi-square test <0.001). Sixty-six percent worked the same number of hours as before their operation, while 27% worked less.

Relationship with partner

For 75% of the patients who were living with a partner, the quality of the relationship was not affected by their illness. Improvement and deterioration of the relationship were each reported by 12%. The greatest changes were in those under 60 years of age *(Table 5)*.

Psychiatric treatment and psychotherapy

The proportion of patients undergoing psychiatric treatment and psychotherapy more than doubled as a result of the breast cancer (increase of 10.5%; *Table 6*). The greatest increase (21.8%) was observed in those under 60 years of age.

Consumption of psychopharmaceuticals increased from 14% of patients before the illness to 26% thereafter. The highest rate prior to cancer treatment was

TABLE 3

Patients' subjective symptoms: operation site pain, arm swelling on treated side, and functional impairments of shoulder and/or arm

	Operation site pain	Arm swelling on treated side	Impairments of shoulder/ arm function
TOTAL (N = 730)	34%	17%	35%
Type of surgery			
Breast-conserving (n = 570)	35%	14%	32%
Mastectomy (n = 160)	30%	26%	47%
	χ^2 test: p = 0.283	χ^2 test: p<0.001	χ^2 test: p<0.001
Lymph node surgery			
Sentinel node biopsy (n = 397)	31%	8%	27%
Axillary dissection (n = 313)	35%	29%	46%
	χ^2 test: p = 0.264	χ^2 test: p<0.001	χ^2 test: p<0.001
Adjuvant chemotherapy			
Yes (n = 362)	38%	22%	41%
No (n = 367)	29%	11%	28%
	χ^2 test: p = 0.012	χ^2 test: p<0.001	χ^2 test: p<0.001
Age group			
<60 years (n = 236)	44%	20%	45%
60–70 years (n = 252)	30%	15%	33%
>70 years (n = 242)	27%	16%	27%
	χ^2 test: p < 0.001	χ^2 test: p = 0.297	χ^2 test: p<0.001

among those over 70, but the postoperative increase was greatest in women under 60.

Discussion

Many women with breast cancer consciously choose a form of treatment with more pronounced adverse effects. In one survey more than half of those questioned were of the opinion that chemotherapy would be justified even if the survival advantage were merely 1 day or 0.1% (15). In reaching a joint decision on the best treatment, it is therefore essential to weigh up the whole spectrum of potential benefits and risks in order to achieve maximal benefit with no impact on the patient's quality of life (5)—the primary goal of any treatment (16).

We will now discuss the potential consequences of the disease and the treatment, bearing in mind that in real life the individual areas cannot be cleanly separated; interactions must be assumed.

Physical symptoms

Compared with the normal population, breast cancer patients have higher rates of pain and hot flashes (17). In addition, symptoms of fatigue are more frequent and more severe (18). A meta-analysis showed that 33% of all cancer patients still suffer from pain after the conclusion of curative treatment (19). Ten to 50% of all patients develop lymphatic edema (1), which in turn affects the ability to perform the tasks of daily life and thus leads to potentially serious impairments (20, 21).

Around one third of the women in our survey still suffered operation site pain an average of 38 months after diagnosis. This corresponds well with rates reported in the literature. Although only a small proportion of patients describe their pain as severe, it impairs their quality of life. Our findings confirmed previous reports that mastectomy results in more functional impairments in performing physical activities than breast-conserving surgery (22). The elevated risk of lymphatic edema after axillary dissection (1, 23) was also corroborated. Women engaged in manual labor experience more disadvantages in the workplace than those in nonmanual occupations, presumably because they are physically weaker after their illness.

A longitudinal analysis showed that the type of operation exerts considerable influence on satisfaction with the outcome of surgery: Patients treated by mastectomy felt less attractive than those with breast-conserving interventions and were less satisfied with the cosmetic outcome (24). Our results confirm these findings. From the patient's viewpoint, breast-conserving surgery should be preferred whenever it can be medically justified.

Cognitive impairments

A number of reviews and meta-analyses have found a connection between adjuvant chemotherapy and cognitive impairments (10, 25–31). The consistent nature of the findings speaks for a stable effect that may have a dramatic impact on the patient's quality of life (31). Sixteen to 50% of patients are affected by so-called "chemobrain" (10). In other words, they believe their cognitive ability has been negatively impacted even though the long-term impairments are objectively often no more than moderate and lack clinical significance (5, 25). Subjective disorders of memory, attention, or concentration frequently stand in contrast to objective neuropsychological test results in the normal range (10, 31, 32).

TABLE 4

Perceived impairments (mean values)*

	Breast cancer patients (N = 734)		Age-matched control group (N = 302)	
	Mean	**95% Confidence interval**	**Mean**	**95% Confidence interval**
Forgetfulness	2.0	1.94–2.06	1.7	1.59–1.75
Word-finding disorders	1.8	1.76–1.88	1.5	1.40–1.55
Concentration disorders	1.9	1.84–1.96	1.4	1.32–1.46
Depression	1.7	1.62–1.75	1.2	1.16–1.28
Anxiety	1.9	1.82–1.96	1.4	1.30–1.46
Fatigue	2.3	2.23–2.37	1.7	1.63–1.83
Sleep disorders	2.3	2.24–2.40	1.9	1.82–2.05
Hot flashes	2.2	2.11–2.27	1.4	1.34–1.51

* Comparison of mean values for breast cancer patients and a healthy age-matched control group.
The question "How much do you suffer from…?" was answered by giving a value on a four-point scale from "not at all" (1) to "very much" (4)

TABLE 5

Changes in relationship with partner*

Relationship ...	... has improved	... is unchanged	... has deteriorated
TOTAL (n = 553)	12% (n = 69)	75% (n = 415)	12% (n = 69)
Type of surgery			
Breast-conserving (n = 433)	13% (n = 56)	75% (n = 323)	12% (n = 54)
Mastectomy (n = 119)	11% (n = 13)	76% (n = 91)	13% (n = 15)
χ^2 test: p = 0.841			
Adjuvant chemotherapy			
Yes (n = 291)	12% (n = 36)	70% (n = 205)	17% (n = 50)
No (n = 261)	13% (n = 33)	80% (n = 209)	7% (n = 19)
χ^2 test: p = 0.002			
Age groups			
<60 years (n = 205)	19% (n = 39)	60% (n = 123)	21% (n = 43)
60–70 years (n = 200)	13% (n = 26)	78% (n = 155)	10% (n = 19)
>70 years (n = 148)	3% (n = 4)	93% (n = 137)	5% (n = 7)
χ^2 test: p<0.001			

* Only patients in a stable relationship

TABLE 6

Proportion of women receiving psychotherapy/psychiatric treatment or psychopharmacological treatment before and after breast cancer and changes in prevalences in percentage points

	Psychotherapy/psychiatric treatment			Psychopharmaceuticals		
	Before diagnosis	After surgery	Change	Before diagnosis	After surgery	Change
TOTAL (N = 724)	9%	19%	+10.5	14%	26%	+12.5
Adjuvant chemotherapy						
Yes (n = 359)	9%	24%	+14.3	14%	29%	+15.4
No (n = 363)	8%	15%	+ 6.9	14%	24%	+ 9.7
Age groups						
<60 years (n = 234)	11%	33%	+21.8	10%	30%	+20.0
60–70 years (n = 251)	10%	18%	+ 8.4	10%	21%	+ 9.4
>70 years (n = 239)	5%	7%	+ 1.6	20%	28%	+ 8.5

The results of our survey confirm that breast cancer patients suffer more than control persons from subjective memory, concentration, and word-finding disorders. It could not be established whether these experienced deficits might be objectively measurable.

Psychological impairments

Patients can be burdened by psychosocial distress, anxiety, and depression for months or even years after diagnosis and beyond the end of their treatment (2); the prevalences vary considerably among the published studies, ranging from 5 to 50% (3). While many patients experience "normal" stress, a subgroup suffers clinically significant depression (33).

The patients in our survey also perceived more pronounced psychological impairments than a healthy control group. All differences were highly significant, so that an association between disease, treatment, and psychological stresses can be discerned.

Impact on relationship and sexuality

Breast cancer apparently has no impact on the quality of the patient's relationship with her partner (17). In most cases the couples adapted well, or at least there was no deterioration, and occasionally the relationship even became stronger (3).

The quality of a couple's relationship is enormously important for the patient's sexual health (34). Short-term negative consequences of surgery and adjuvant systemic treatment on the sex life are well documented (35); the influence of chemotherapy is especially significant (5). The findings regarding long-term effects are inconsistent, however (35). Current data indicate that sexual dysfunction is not a persistent problem for all breast cancer patients. However, women who have existing relationship problems and/or have undergone systemic treatment are at increased risk (3). The problems are more severe if the treatment has induced premature menopause (5).

This age dependence is compatible with the findings of our survey, in which young women most frequently described changes in the relationship with their partner. These developments were not always negative, however; some patients experienced a strengthening of the relationship. It can be assumed that these were the relationships where the partners talked to each other more.

Overall, the consequences of falling ill with cancer were more severe for young women than for their older counterparts. This effect has also been found in other studies (1). One plausible explanation is certainly that younger women have to overcome greater challenges at work and in their private life. Another possible reason is the coincidence of cancer treatment with menopausal symptoms (17). Other risk factors include type of surgery, lymph node treatment, and systemic therapy, which in turn depend on the extent of the disease and the presence of comorbidities.

From the woman's subjective viewpoint, breast cancer and its treatment have many explicit long-term consequences, some of them serious. It is therefore all the more important to recognize impairments affecting the patient's daily life and provide appropriate treatment. On the physical side the options include physiotherapy and lymph drainage, while in the psychic sphere self-help groups, relaxation techniques, and psychotherapy or psychopharmacotherapy may be beneficial. Exercise programs help to reduce fatigue (Nyrop KA, et al.: Feasibility and promise of a self-directed walking program to reduce joint pain among older breast cancer patients on adjuvant aromatase inhibitors. [Abstract P3–08–10, San Antonio Breast Cancer Symposium 2013]), and rehabilitation measures can be helpful in many ways.

Strengths and limitations

The strength of our survey lies in the matching of objective treatment data with the patients' subjective assessment. The high response rate and the results of the nonresponder analysis indicate that the data are valid and representative. Further strong points are the relatively large sample, the fact that all medical treatment took place in the various departments of one single breast center, and a "normal" age distribution, because all patients were included in the analysis.

The survey of a healthy, age-matched control group enabled comparison of the patients' impairments with a "gold standard." This was the only way to judge the significance of the findings. It should be mentioned that the women in the control group were questioned by telephone interview, so distortions owing to the use of two different survey techniques are conceivable. Another limitation is that no nonresponder analysis could be carried out for the control group. The choice of the telephone interview method was ultimately pragmatic, because it was quick and relatively inexpensive. Further weaknesses arise from the monocentric and cross-sectional design of the study, which permits no causal conclusions.

Conclusion

Adjuvant breast cancer treatment leads to long-lasting physical, psychological, and social impairments in a considerable proportion of patients. The extent to which the women are affected depends on their age, the type of surgery, and the type of systemic treatment. Identification and targeted treatment of these impairments must form an integral part of high-quality postoperative care.

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Conflict of interest statement
The authors declare that no conflict of interest exists.

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KEY MESSAGES

- Subjective satisfaction with the outcome of surgery depends almost exclusively on the type of intervention: women treated with breast-conserving surgery are much more satisfied than those who undergo mastectomy.
- Compared with healthy controls, breast cancer patients experience physical, psychological, and social impairments.
- Identification and targeted treatment of these impairments must form an integral part of high-quality postoperative care.
- Younger women, particularly those who have not yet reached the menopause, suffer more severe consequences of breast cancer and thus represent a particular risk group.
- Before commencing any program of treatment with potentially severe adverse effects, the patient should be informed in detail of the possible long-term consequences.

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