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Menopausal Status in Breast Cancer Patients with Past Chemotherapy Determines Long-Term Hypoactive Sexual Desire Disorder

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Introduction

Sexual changes in women treated for breast cancer often become a problematic aspect of quality of life. Patients experience a wide variety of sexual difficulties including dyspareunia, fatigue, vaginal dryness, decreased sexual interest or desire, decreased sexual arousal, numbness in previously

sensitive breasts, difficulty achieving orgasm, and lack of sexual pleasure [1–3]. It appears that younger women, in particular, experience difficulties related to the loss of reproductive function and relationship problems, in addition to more abrupt vaginal changes than older women [4,5]. This is of general importance as there are 25,100 estimated new breast cancer cases in women younger than 45 years in the United States for the year 2009, which is almost 10% of all expected new breast cancer cases (American Cancer Society: Cancer facts and figures 2009–2010, http://www.cancer.org).

Sexual problems among women treated for breast cancer appear to be much more prevalent when patients have received chemotherapy that is frequently associated with abrupt menopause [6–8]. The prevalence rates of sexual dysfunction after breast cancer have not been determined conclusively due to methodological issues (assessment instruments, samples sizes and heterogeneity, and time of follow-up) [9]. A lack of or a reduction in sexual interest was found in 23–64% and arousal difficulties and/or lubrication problems in 21–48% of breast cancer survivors [10–15].

Long-term sexual dysfunction in breast cancer patients with chemotherapy has been reported by several authors but sexuality among healthy women may also decline as they age [11]. Ganz et al. have published data from a large study of disease-free survivors of breast cancer, which showed that 5–10 years following diagnosis, women were still experiencing sexual difficulties including vaginal dryness, reduced frequency of sexual activity, and reduced breast sensitivity; however, impaired sexual desire and dyspareunia were not a common problem [8]. Other authors also reported a worsening of sexual functioning such as vaginal dryness, inability to relax and enjoy sex, difficulties becoming aroused, and problems achieving orgasm, but did not find a lack of sexual interest [16].

Very little is known about the long-term prevalence of hypoactive sexual desire disorder (HSDD) in patients of younger age with breast cancer. HSDD is the most common sexual complaint in women, with reports of prevalence estimates among females in the general population ranging from 5% to 46%. In the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, HSDD is defined as "persistently or recurrently deficient (or absent) sexual fantasies and desire for sexual activity" that result in "marked distress or interpersonal difficulty" [17]. In premenopausal women with a current age of 30–50 years, the prevalence of HSDD was reported to be 7% [18] and 14% [19]; among surgically menopausal women, the rate was 26% [19]. The Sexual Interest and Desire Inventory-Female (SIDI-F) was developed as a clinician-administered assessment tool to quantify severity of HSDD. The SIDI-F has the highest specificity to focus on major clinical complaints among women with HSDD as compared to a number of other instruments measuring sexual functioning [20,21]. Women with HSDD were reported to have a mean SIDI-F score of 20.4 (standard deviation [SD]: 6.0) and patients with no sexual dysfunction of 44.7 (SD: 3.0) [20]. A cut-off score of 33 was found to delineate these two groups [22].

In a prospective study to examine the sexual effects of adjuvant gonadotropin-releasing hormone agonist (GnRHa) therapy through the use of self-administered questionnaires, the addition of endocrine treatment did not further increase the high level of sexual dysfunction in patients treated with chemotherapy [7]. In contrast, among patients who did not receive chemotherapy, GnRHa therapy produced a significantly higher level of dysfunction from 1 to 2 years after treatment, as compared with those who received no endocrine treatment [7].

We therefore evaluated the long-term frequency of HSDD in young patients with breast cancer treated with chemotherapy and eventual endocrine therapy in a controlled cross-sectional study with a validated instrument for the quantification of HSDD. To our knowledge, this is the first controlled study in which the SIDI-F has been applied in young breast cancer patients after chemotherapy and adjuvant endocrine therapy.

Aims

The aim of the study was to examine the effect of past chemotherapy and adjuvant endocrine therapy on sexual desire in young women with breast cancer and past chemotherapy. Our hypothesis is that ovarian failure caused by chemotherapy and eventual endocrine treatment negatively affects sexual desire.

Methods

In this controlled cross-sectional study at the tertiary care oncology center of the University of Munich, Campus Grosshadern, conducted in 2008, 47 women with malignant or benign breast disease were included. The medical ethics committee of the University of Munich approved the study. Thirty-four patients had breast cancer primarily treated with surgery and chemotherapy and

subsequent endocrine therapy, and 13 patients had breast surgery due to benign breast disease with no further therapy, that served as controls. The mean age of breast cancer patients and controls at the time of the study was 42.3 (range 29–46) years and 39.8 (range 34–46) years, respectively, which did not differ significantly (*t*-test: $P = 0.07$).

The majority of patients with breast cancer (25/34) and with benign breast disease (12/13) had breast-conserving surgery (i.e., lumpectomy). The technique for lumpectomy was similar for both benign and malignant tumors: the site of incision depended on the position of the tumor. To avoid deformities after lumpectomy and to achieve optimal plastic results, defects were minimized by glandular adaptation. In patients with breast cancer, sentinel node biopsy, and if indicated, axillary dissection was carried out. All patients with breast-conserving surgery had postoperative local radiation treatment. Mastectomy was performed in 9/34 breast cancer patients and in 1/13 patients with benign tumors. This includes removal of the areola-nipple complex with a spindle-shaped skin area and of the mammary gland. The patients' mean age at breast surgery was 37.4 (range 25–43) years in the cancer group and 35.2 (range 26–42) years in the control group. The mean time interval between surgery and study participation was 4.8 (range 2.3–8.4) years in the cancer group and 4.5 (range 2.2–8.0) years in the control group. Standard chemotherapy regimes were used containing cyclophosphamide in combination with methotrexate and fluorouracil (CMF; n = 1), anthracyclines in combination with cyclophosphamide without (n = 9) or with taxanes (n = 14).

All participating women were heterosexual. Sixty-five percent (22/34) of the breast cancer patients (n = 34) were married, 18% (6/34) had a permanent partner, and 18% (6/34) had no permanent partner. Ninety-two percent (12/13) of the control patients (n = 13) were married and 8% (1/13) had a permanent partner.

Recruitment

In 2008, we sent letters of invitation to 50 breast cancer patients and 22 patients with benign breast disease, which were previously treated at our tertiary care center and met the inclusion criteria (see below) 2–4 weeks before the planned interview. Thirty-five breast cancer patients and 13 patients with benign breast disease arranged for an appointment with our medical and psychological staff. All patients gave informed consent. One breast cancer patient was excluded from the study because of anticipated bias in the interview due to private contact with a member of the study staff (see also Figure 1).

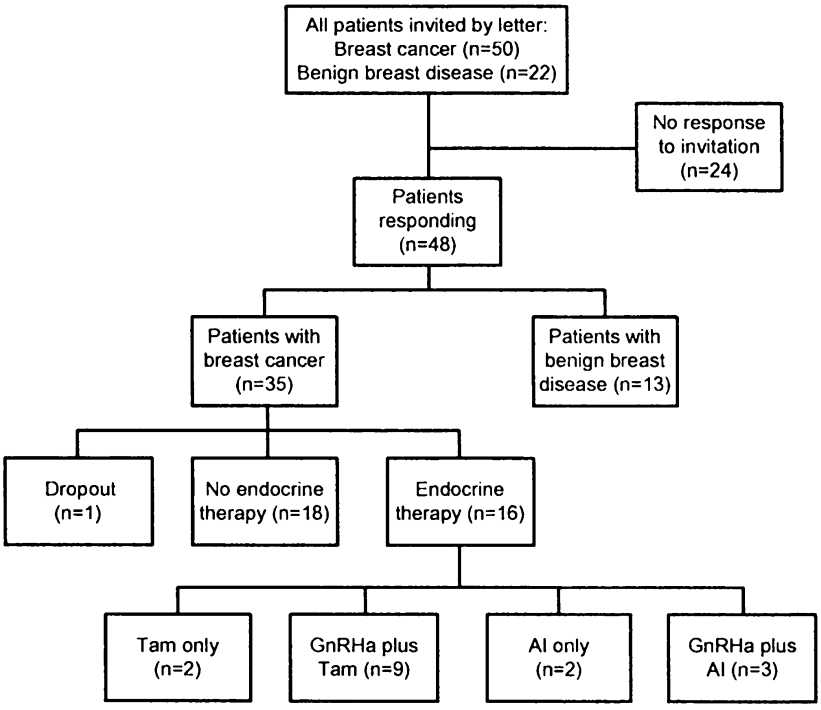

Figure 1 The flow diagram of the study design. Tam: Tamoxifen; GnRHa: Gonadotropin-releasing hormone agonist; AI: aromatase inhibitor.

Sexual Interest and Desire Inventory-Female (SIDI-F)

This study employs a standardized questionnaire (SIDI-F) on HSDD, as previously described [19]. A single psychologist and certified psycho-oncologist with more than eight years of experience in counseling cancer patients and investigating survivorship issues conducted the interviews. The interviewer has extensive training and experience with testing. In addition, baseline demographic data and data on actual gynecological history were collected by medical personnel. The SIDI-F was developed as a clinician-administered assessment tool to quantify the severity of symptoms in women diagnosed with HSDD [21]. The SIDI-F is a 13-item scale with a separate module that includes five additional items that do not contribute to the total score. The dimensions of the test fall into five categories: (i) sexual desire (e.g., levels of sexual fantasies, affirmative and aversive thoughts about sex, motivation to seek sexual activity, desire experienced once involved and aroused); (ii) aspects of sexual dysfunction that might be comorbid with or predispose an individual to dysfunction of desire (e.g., pathological aversions, arousal difficulties, orgasmic difficulties, sexual pain); (iii) sexual behavior (e.g., initiations, frequency of sexual activity); (iv) sexual relationship (e.g., sexual satisfaction); and (v) complicating psychiatric and physical health issues (e.g., dysphoric mood). The inventory bypasses self-rating by patients to avoid subjectivity, possible unfamiliarity with some of the concepts to be assessed, and possible failure to master the complexity of some of the items. It is essential that clinicians ask additional questions to those contained in the inventory to probe for an unambiguous answer from the patient for each item [20].

Blood Sampling and Hormone Assays

Blood samples (10 mL) were obtained for hormone assays independent of menstrual status and day of the menstrual cycle. The blood was centrifuged at 3,500 rpm for 10 minutes. The serum was stored in 1.5-mL polypropylene tubes at –20°C until measurement. Serum estradiol concentrations were measured by a specific enzyme immunoassay kit (DSL-10-4300 ACTIVE Estradiol EIA Kit; Diagnostic Systems Laboratories Deutschland GmbH, Sinnsheim, Germany). The sensitivity of the estradiol assay was 5 pg/mL. Testosterone concentrations (data not shown) were analyzed by an electro-chemiluminescence immunoassay (ECLIA; Testosterone Cobas, implemented on the Elecsys Immunoanalyzer-System; Roche Diagnostics, Mannheim, Germany). The sensitivity of the testosterone-assay was 0.1 ng/mL.

Inclusion Criteria

The inclusion criteria were a maximum age of 46 years at the time of the interview and a history of breast cancer primarily treated by surgery and chemotherapy, or of benign breast disease treated with surgery, more than 2 years before. Participants were included whether or not they were currently in a relationship or currently sexually active. Current menopausal status was documented but had no influence on inclusion.

Main Outcome Measures

The SIDI-F interview was conducted in 35 women with breast cancer and breast surgery 2–8 years after chemotherapy was completed. As controls, 13 women with benign breast tumors and breast surgery 2–5 years before with no systemic therapy were included. Women with breast cancer were divided into subgroups according to eventual adjuvant endocrine therapy at the time of the interview (see Figure 1): (i) no actual endocrine therapy (n = 18); (ii) tamoxifen only (n = 2); (iii) GnRHa plus tamoxifen (n = 9); (iv) aromatase inhibitor (AI) only (n = 2); or (v) GnRHa plus AI (n = 3).

Statistics

All data were collected in a blinded form and entered in SPSS for Windows (SPSS Inc., Chicago, IL, USA). Analyses were carried out according to a pre-established analysis plan. Statistical analyses were conducted using SPSS for Windows using version 16.0. For all comparisons of mean values, independent *t*-test was used, considering $P < 0.05$ as statistically significant. For subgroup examinations, the multiple test procedure was based on the Bonferroni test [23].

Results

Mean total scores on the SIDI-F were not statistically different in the breast cancer group as compared to the benign breast disease group (for details see Table 1). Subgroup analysis revealed differences of the mean total SIDI-F scores depending on the endocrine therapy, but statistical analysis did not show significant differences (for details see Table 2).

Table 1 Mean total scores and scores for individual items (with standard deviations) on the SIDI-F obtained from women with no sexual dysfunction, as previously published by Clayton et al. 2006 [20], benign breast disease and menorrhea, breast cancer with menorrhea, and breast cancer patients with amenorrhea. Cut-off indicating sexual dysfunction <33.

	No sexual dysfunction (Clayton et al. 2006) [20]	Benign breast disease (all with menorrhea) (n = 13)	Breast cancer patients with menorrhea (n = 9)	Breast cancer patients with amenorrhea* (n = 24)	*P* value
Relationship-Sexual	3.7 (0.9)	3.6 (1.0)	3.3 (1.1)	3.1 (1.4)	0.662
Receptivity	4.5 (0.7)	2.6 (1.5)	3.4 (1.0)	2.3 (1.8)	0.078
Initiation	2.7 (0.6)	1.1 (1.0)	1.6 (1.1)	1.0 (1.0)	0.248
Desire-Frequency	4.1 (0.8)	2.7 (1.5)	4.2 (0.7)	2.3 (1.9)	0.006
Affection	4.5 (0.9)	4.2 (1.2)	4.8 (0.4)	4.0 (1.0)	0.031
Desire-satisfaction	3.9 (0.2)	3.5 (1.3)	3.3 (1.0)	2.5 (1.7)	0.152
Desire-distress	3.9 (0.2)	3.4 (1.3)	3.6 (0.9)	3.2 (1.2)	0.328
Thoughts positive	4.1 (0.6)	2.8 (1.4)	3.9 (0.8)	2.8 (2.5)	0.059
Erotica	1.9 (1.0)	1.2 (1.0)	1.8 (1.0)	1.4 (1.1)	0.321
Arousal-frequency	2.8 (0.5)	2.2 (1.1)	2.4 (0.5)	2.1 (1.1)	0.419
Arousal ease	2.7 (0.5)	1.9 (0.7)	2.6 (0.5)	1.9 (1.0)	0.026
Arousal continuation	2.8 (0.4)	2.2 (1.1)	2.4 (0.7)	1.9 (1.1)	0.130
Orgasm	3.1 (0.9)	2.8 (2.1)	3.1 (0.6)	2.3 (1.7)	0.202
Total score	44.7 (3.0)	34.0 (9.4)	40.4 (5.6)	30.7 (11.3)	0.020
Relationship-general	3.7 (0.7)	3.9 (0.4)	3.8 (0.4)	3.6 (1.1)	0.484
Thoughts-negative	2.0 (0.0)	1.8 (0.4)	2.0 (0)	1.9 (0.6)	0.491
Pain	2.7 (0.6)	2.7 (1.1)	2.8 (0.4)	2.8 (1.0)	0.854
Mood	5.0 (0.2)	4.4 (1.2)	4.6 (0.7)	4.6 (1.0)	0.930
Fatigue	3.4 (0.7)	3.0 (1.0)	2.3 (1.1)	3.2 (1.0)	0.061

Underlined numbers indicate scores that differ statistically significantly.
*Only one patient with breast cancer had a hysterectomy and has been excluded form the group "breast cancer with amenorrea."

In contrast, in breast cancer patients with the induction of menopause by chemotherapy or GnRHa therapy, the SIDI-F scores were significantly lower (30.7) as compared to breast cancer patients who remained premenopausal (40.4; see also Table 1).

The mean scores for the individual items on the SIDI-F and for the items on the separate diagnostic module of the SIDI-F were similar and not statistically different between the three subgroups, controls with benign breast disease and breast cancer patients with or without menorrhea, except for three items: "Desire-Frequency," "Affection," and "Arousal Ease" had statistically higher scores indicating better function in breast cancer patients with menorrhea compared to those with amenorrhea (for details see Table 1).

Table 2 Mean SIDI-F scores in the different groups and subgroups of patients

Patient groups	Mean SIDI-F score (SD)
Breast cancer (n = 34)	32.9 (11.2)
No adjuvant endocrine therapy (n = 18/34)	36.2 (9.6)
Adjuvant therapy endocrine therapy (n = 16/34)	29.1 (11.9)
Tam only (n = 2/34)	37.5 (3.5)
AI only (n = 2/34)	34.0 (9.9)
GnRHa (n = 12/34)	26.9 (12.6)
GnRHa plus Tam (n = 9/34)	28.1 (13.9)
GnRHa plus AI (n = 3/34)	23.3 (9.0)
Benign breast disease (n = 13)	34.0 (9.4)

Tam = tamoxifen; GnRHa = gonadotropin-releasing hormone agonist; AI = aromatase inhibitor; SD = standard deviation; SIDI-F = Sexual Interest and Desire Inventory-Female.

The mean estradiol levels in the breast cancer group (44.5 pg/mL; SD: 51.4 pg/mL) were significantly lower ($P = 0.01$) compared to the mean estradiol levels in the benign breast disease group (all with menorrhea; 105.3 pg/mL; SD: 70.4 pg/mL). Within the breast cancer group, mean estradiol levels for patients with amenorrhea and intact uterus (24.9 pg/mL; SD: 29.2 pg/mL) were significantly lower ($P = 0.02$) compared to the mean estradiol levels of patients with menorrhea (91.3 pg/mL; SD: 65.6 pg/mL). Testosterone levels between groups and subgroups did not differ statistically significantly (data are not shown).

Discussion

Key Results

In this study, we investigated the effects of past chemotherapy of adjuvant endocrine therapy on sexual desire in young patients with breast cancer. The key results of the study are the following: (i) chemotherapy does not significantly impair long-term sexual desire and function as measured by SIDI-F compared to a control group with comparable breast surgery but no malignant disease or systemic therapy, unless permanent menopause was induced; (ii) subgroup analysis comparing

either the use of adjuvant endocrine therapies or the absence of any adjuvant therapy revealed lower total mean scores on the SIDI-F indicating poorer sexual desire and function, without reaching statistical significance; in the GnRHa group, the mean SIDI-F score was 26.9 compared to 36.2 in the breast cancer group with no adjuvant endocrine therapy; and (iii) there is a statistically significant association between menopausal status and mean SIDI-F scores; amenorrhea induced by past chemotherapy or adjuvant GnRHa therapy was associated with lower sexual desire (SIDI-F score: 30.7) as compared to breast cancer patients with menorrhea (SIDI-F score: 40.0).

Limitations and Generalizability

Bias may have occurred during recruitment of patients. Even though the rate of response was similar in patients with breast cancer (35/55 = 63%) and benign breast disease (13/22 = 59%), it cannot be excluded that, mainly, patients with more sexual complaints responded to our invitation. This does not necessarily affect the controlled setting of the study but may reduce the generalizability of our results, which is also limited by the relatively low number of patients in this study.

A possible limitation of the study arises due to the fact that the SIDI-F scores may have been negatively biased in the group of breast cancer patients due to a higher rate of mastectomy compared to the control group. Although breast-conserving therapy could be carried out in the majority of patients, mastectomy was necessary in 9/34 patients (26%) with breast cancer and in 1/13 patients (8%) with benign breast disease. Bias may also have occurred as intracycle variability of estradiol levels [24] was not recorded. Our study protocol did not specify a particular cycle day for venipuncture in the menstruating women. However, in patients with amenorrhea, estradiol levels were low and variability is unlikely in these patients.

In this study, women with breast cancer all had treatment with standard chemotherapy regimes containing CMF, anthracyclines in combination with cyclophosphamide without or with taxanes. In consideration of the recommendations on fertility preservation of the American Society of Clinical Oncology, all standard chemotherapy regimes in this study bear a comparable intermediate risk (20–79%) of permanent amenorrhea, taking into account that almost three-fourths (25/34) of the patients were younger than 40 years at the time of chemotherapy [25]. We therefore did not expect heterogeneous effects on sexual function and sexual desire in our study population. As a standard treatment with chemotherapy used, generalizability to a population of women with breast cancer is expected.

A further limitation of the study is that a wide variety of hormonal therapies have been applied. A greater sample size may have shown differences between the respective hormonal therapies.

It is assumed that a woman's sexual desire, arousal, and orgasm can be influenced by the quality of the committed relationship [26], partner sexual functioning, and overall health [27]. In our study, we indirectly investigated partner issues through the SIDI-F items "Relationship-Sexual" and "Relationship-General." Even though mean scores for these two items were similar and not statistically different for the three subgroups of controls and breast cancer patients with and without menorrhea, it is a possible drawback of our study that no additional information on such partner issues was gathered. However, the SIDI-F has been shown to be a reliable and valid measure of HSDD severity, independent of relationship issues [20].

A limitation of the current study was the relatively small sample size including the control group. The possibility cannot be ruled out that nonsignificant differences of sexual interest between the therapeutic subgroups were a reflection of low statistical power. The use of a cross-sectional research design is a limitation, since it cannot provide information about the course of sexual problems in breast cancer survivors. For future studies, a prospective, longitudinal design with a large, well-defined group of women should be used in which sexual function is assessed at specified time points during the course of the chemotherapy and for several years following the completion of active treatment. Such a study design would also allow separation of the impact of chemotherapy-induced menopause from that of later adjuvant endocrine therapy.

Interpretation

In accordance with our results, in another study with mainly premenopausal patients, high-dose or conventional chemotherapy did not have long-term effects on sexual activity as measured by a self-report questionnaire [28]. Berglund et al. showed that the use of chemotherapy was in fact not associated with changes in sexual frequency, but with continued problems regarding sexual function and fear [5]. The same authors reported that the addition of GnRH agonist treatment in

breast cancer patients with no former chemotherapy produced a significantly higher level of sexual dysfunction 1–2 years after treatment, as compared with those who received no endocrine therapy [7]. In our study, subgroup analysis also revealed greater sexual dysfunction as measured by lower mean total scores on the SIDI-F in patients with GnRH agonist treatment, but failed to reach statistical significance. Berglund et al. explained this effect by the possible disruption of ovarian hormone synthesis with lower circulating levels of estrogen and/or androgens [7]. Accordingly, we found statistically significant lower estradiol levels in breast cancer patients with amenorrhea compared to those with menorrhea.

In this study, amenorrhea induced by past chemotherapy or adjuvant GnRHa therapy was significantly associated with lower sexual desire as compared to breast cancer patients with menorrhea. Similar to our results, Yang et al. demonstrated that premature menopause in Asian women with breast cancer and chemotherapy was associated with increased prevalence of moderate-to-severe problems in sexual interest in 1-year follow-up, but sexual interest was not significantly impaired in patients without induction of menopause [15].

Patients with breast surgery due to benign breast disease served as the control group, in order to exclude disturbed body image as a possible bias for low sexual desire. Reportedly, significant psychosexual and body image problems occur in patients treated for breast cancer whether status/postmastectomy or breast-conserving therapy [11,13,29,30].

Endocrine therapy with nonsteroidal aromatase inhibitors in patients treated for breast cancer has been associated with increased vaginal dryness and dyspareunia, particularly in patients of younger age [16,31,32]. Glaus et al. found a symptom cluster of hot flashes, weight gain, tiredness, reduced sexual interest, and vaginal dryness in women with breast cancer undergoing hormonal treatment [14]. It has been argued that severity of vaginal dryness mediates the relationship between breast cancer status and sexual functioning [16].

Patients at our institute are discouraged from the use of systemic or local estrogens. Although the use of specific hormone replacement (most commonly local estrogen and less commonly systemic estrogen with or without an androgen, progesterone, or the addition of an androgen in an estrogenized woman) may be highly effective, the concern remains that in patients with estrogen-sensitive breast cancer, including those receiving anti-estrogenic adjuvant therapies, the use of estrogens may be attended with potential risk of relapse [33]. Our patients were therefore advised to use nonhormonal alternatives such as moisturizers and precoital vaginal lubricants [34]. However, we are aware that in well-informed patients with severely symptomatic vaginal atrophy that fails to respond to nonhormonal options, menopausal hormone replacement or prescription vaginal estrogen therapy may be considered after informed consent; such women were not included in this study.

Breast cancer patients, with menorrhea or amenorrhea, and patients with benign breast disease had mean scores for the item "pain" that were similar to previously published scores for patients with no sexual dysfunction [20]. According to our data, decreased sexual desire in breast cancer patients with amenorrhea can therefore not necessarily be explained by increased dyspareunia. In the separate diagnostic module of the SIDI-F, the item "mood" was investigated (Table 1). There is no evidence for a different level of depression in the group of breast cancer patients vs. patients with benign breast disease. Mean levels are similar or slightly lower compared to those of women without a sexual disorder as previously published [20]. In our study, breast cancer patients with menorrhea became more easily aroused and had a stronger desire to engage in sex compared to those with amenorrhea. However, it cannot be concluded from our data that undisturbed arousal is a precondition of normal sexual desire. Future studies should investigate partner health and functioning, and general health concerns, and provide more detailed information on the level of dyspareunia, any vulvo-vaginal tissue symptoms, and the use of vaginal lubricants and moisturizers.

Conclusions

In conclusion, chemotherapy in young breast cancer patients does not significantly impair long-term sexual desire as compared to patients with benign breast disease, unless permanent menopause is induced. Patients with menopause permanently induced by chemotherapy or related to use of gonadotropin-releasing hormone agonists show significantly reduced sexual desire as compared to menstruating patients with past chemotherapy. A limitation of the study is its small sample size. Future studies with a prospective, longitudinal design in a large, well-defined group of women should assess

sexual function at specified time points during the course of the chemotherapy and for several years following the completion of active treatment.

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Appendix 1

Questions asked in the Sexual Interest and Desire Inventory—Female (SIDI-F) and in the SIDI-F Diagnostic Module (DM) (http://www.bestsexualadvice.com)**:**

Item 1: Relationship—sexual:
How satisfied are you with the sexual aspect of your relationship with your partner?
Sexual activity (non-scored item):
Over the past month, approximately how many times did you engage in sexual activity either alone or with your partner?

Item 2: Receptivity
Over the past month, when your partner approached you for sex, how often did you accept?
When you accepted, what was your level of enthusiasm?

Item 3: Initiation
Over the past month, how frequently did you do anything to encourage sex with your partner?

Item 4: Desire—frequency
Over the past month, how frequently have you wanted to engage in some kind of sexual activity, either with or without a partner? How strong was your desire to engage in sex?

Item 5: Affection
Over the past month, how often have you wanted physical affection other than sex, for example touching, holding, kissing? How intense would you say was your desire for physical affection?

Item 6: Desire—satisfaction
Over the past month, how satisfied were you with your overall level of sexual desire/interest?

Item 7: Desire—distress
Over the past month, when you thought about sex or were approached for sex, how distressed (worried, concerned, guilty) were you about your level of desire?

Item 8: Thoughts—positive
How often have you thought about sex over the past month? When you thought about sex, what was your level of interest/strength of desire in having sex?

Item 9: Erotica
Over the past month, how did you react to sexually suggestive material (e.g., love scenes in movies and on television, erotic pictures/stories in magazines/books)?

Item 10: Arousal—frequency
Over the past month, when you had sex, how often did you become aroused (sexually excited, wet, lubricated, etc.)?

Item 11: Arousal Ease
Over the past month, when you had sex, how easily did you become aroused (sexually excited, wet, lubricated, etc.) in response to sexual stimulation?

Item 12: Arousal continuation
Over the past month, once you started to become sexually aroused, did you want to receive more stimulation? If yes, how strong was your desire to be further/more sexually stimulated?

Item 13: Orgasm
Over the past month, when you had sex, how often did you have an orgasm? How easy was it for you to have an orgasm?

DM Item 1: Relationship—general
How satisfied are you with your relationship as a whole?

DM Item 2: Thoughts—negative
Over the past month, including this interview, when you think about having sex, do you feel any of the following negative feelings: turned off, anxious, repulsed, sick?

DM Item 3: Pain
Over the past month, did you experience genital pain during sex?

DM Item 4: Mood
Over the past month, how has your mood been? Have you experienced any feelings of: sadness, hopelessness, helplessness, worthlessness? How often have you had such feelings?

DM Item 5: Fatigue
Over the past month, did you experience fatigue, tiredness, or loss of energy? How often did you experience fatigue, tiredness, or loss of energy?