

Effects of Surgical and Adjuvant Therapies for Breast Cancer on Sexuality, Cognitive Functions, and Body Weight

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ABSTRACT

Introduction. Breast cancer and its treatment negatively affect the important aspects of a woman's life such as sexual health, cognitive functions, body image, and weight. Abrupt estrogen deficiency following chemotherapy and/or hormonal therapy plays an important role in worsening of sexuality.

Aim. To evaluate the impact of breast cancer treatment on sexual functioning, cognitive function, and body weight in premenopausal women.

Methods. Thirty-five women with a premenopausal diagnosis of breast cancer who are candidate to adjuvant treatment completed validated questionnaires on menopausal symptoms, sexuality, partner relationship, depression, body image, and cognitive functions after surgery (T0), then after chemotherapy or at least 6 months of endocrine therapy (T1), and after 1 year (T2). In addition, gynecological and dietological examinations were performed.

Main Outcome Measure. The following validated questionnaires were used: Greene Climacteric Scale, Beck Depression Inventory, Body Attitude Test, McCoy revised Italian version McCoy Female Sexuality Questionnaire, Cues for Sexual Desire Scale, Dyadic Adjustment Scale, Numeric Matrix Test and Rey auditory-verbal learning test, to measure cognitive functions, a recall 24 H questionnaire to evaluate food intake, Minnesota Leisure Time Physical Activity questionnaire and Eating Attitude Test-40, while anthropometric and plicometry data were assessed by a dietitian.

Results. Low levels of sexual functioning were registered at baseline; a further decrease in sexual activity, quality of the partnered relationship, desire, and arousability was demonstrated at T1 and T2. We found a significant increase in hot flushes and anxiety. Nonsignificant deterioration of body image was demonstrated. Although women reported losing memory and concentration, "chemobrain" effect was not demonstrated as cognitive tests improved after 6 months, probably because of "learning effect." Women who had undergone chemotherapy gained weight and fat disposition was typically android.

Conclusions. Young women undergoing adjuvant breast cancer therapy experience a heavy impairment in important quality of life domains as sexuality and targeted support interventions are needed. **Biglia N, Moggio G, Peano E, Sgandurra P, Ponzone R, Nappi RE, and Sismondi P. Effects of surgical and adjuvant therapies for breast cancer on sexuality, cognitive functions and body weight. J Sex Med 2010;7:1891–1900.**

Key Words. Breast Cancer Treatment Associated Sexual Function; Cognitive Functions; Body Weight; Adjuvant Therapy

Introduction

Breast cancer is the most common cancer in women. Approximately one of every eight women will develop breast cancer during her lifetime [1]. Earlier diagnosis and advances in adju-

vant treatments, such as chemotherapy (CT) and endocrine therapy (ET), have resulted in an increasing number of breast cancer survivors (BCS). That being so, many studies have focused on several aspects of Quality Of Life (QOL), including sexual well-being, cognitive function,

and body image. Breast cancer and its treatments have a negative impact on sexual functioning [2] with a significant rate of low sexual desire, decreased arousal and lubrication, painful intercourse, and impaired orgasm [3]. These sexual symptoms appear to be much more prevalent in women who received CT, regardless of the type of surgery [4], and among younger women who are more vulnerable to changes in ovarian function resulting from CT and/or ET manipulation, and to body image concerns after surgery [5]. Indeed, following mastectomy, women were more likely to report body image dissatisfaction than those with breast conservative treatment [6,7]. There is evidence for cognitive changes associated with cancer and its treatment [8], but data from the literature are not univocal. Some BCS treated with CT experience a cognitive decline, especially in domains of memory and attention. Persistent cognitive changes associated with CT and/or ET are often subtle but can impact on BCS' ability to function [9].

Breast cancer treatments have been shown to affect also metabolism and body weight. Weight gain is a common problem among women who receive adjuvant CT [10,11] and it was well-known since 1978 [12], in spite of the nausea, vomiting, and mucositis associated with CT. Apart from overeating, many reasons for weight gain can be hypothesized, including reduced physical activity and some unclear mechanisms related to CT. Weight gain may adversely affect the risk of malignancy recurrence, likely because of the higher estrogen levels deriving from the adipose tissue, to the reduction of sex hormone binding globulin and to the increased plasma levels of insulin-like growth factor (IGF) and insulin-like growth factor binding protein (IGFBP-3) [10].

This prospective study was designed to evaluate, on a convenient sample of premenopausal or early postmenopausal women, the general effects of breast cancer treatment on different aspects of QOL, including sexual function, cognitive function, and body image 1 year after surgery. Menopausal symptomatology, depression, and body weight have been also investigated. Here, preliminary results were reported.

Materials and Methods

Sample

Preliminary data after 1 year are available on 35 women with breast cancer who underwent surgical treatment at the Gynecological Oncology Unit of

the Institute for Cancer Research and Treatment of Candiolo (Turin, Italy) between January 2007 and September 2008. To be eligible, a woman had to be premenopausal or menopausal since less than 2 years at the time of the diagnosis, a candidate for CT and/or ET after surgery, and free from metastatic disease. The protocol was approved by the local university ethical committee.

Study Design

During the first visit after surgery for breast cancer (T0), a physician recorded the demographic characteristics of the women, including religion, histopathological characteristics of the tumor, and proposed adjuvant therapy. A complete gynecological examination was also performed, including Pap smear and vaginal culture. When a vaginal infection was detected, women were adequately treated and included in the study only after a subsequent vaginal culture was negative. Vaginal atrophy was subjectively and objectively evaluated during the gynecological visit by performing both the vaginal maturation index and the Vaginal Health Index Score (VHIS), which includes pH determination. Study measures were collected with specific validated instruments at baseline (T0), following adjuvant CT or after at least 6 months of ET (T1), and 1 year after surgery (T2). Below, we briefly described the instruments and measures used in the present study.

Instruments and Measures

Menopausal Symptomatology

Symptoms related to menopause were measured by the Greene Climacteric Scale (GCS) [13]. The scale yields three main independent measures regarding psychological, somatic, and vasomotor symptoms. Each symptom is rated by the subject according to its severity using a 4-point rating scale. The GCS can also be used to identify menopausal women who are severely and possibly clinically anxious (scored >10 in anxiety items), and/or depressed (scored >10 in depression items). Construct validity has been demonstrated in relation to life stress, bereavement, psychological treatment, and hormone replacement therapy in many publications.

Depression

The Beck Depression Inventory (BDI) [14] was used to specifically screen for depression. BDI is a 21-item self-report rating inventory assessing severity of depression, introduced by Beck et al. in 1961 and revised in 1971. The score range on each

of the 21 questions is between 0 and 3, and each range of total score is associated to a physiological condition: a score below 4 means possible denial of depression, faking good; 5–9 means ups and downs that are considered normal; 10–18 is defined as mild to moderate depression; between 19 and 29 is moderate to severe depression; and 30–63 means severe depression. A meta-analysis of studies on the revised BDI's psychometric properties reported high content validity, high validity in differentiating between depressed and nondepressed people, and high internal consistency [15].

Body Image

Satisfaction with body and body image was obtained with the Body Attitude Test (BAT), a 20-item questionnaire based on 5-point Likert-type scale, revised from the initial version with 39 items [16]. The BAT allows a complete evaluation: it measures different dimensions of body experience as familiarity with the body, attention to body size, and confrontation of body appearance. The original questionnaire has good psychometric characteristics and Santonastaso et al. validated the Italian version in both clinical and nonclinical samples (Cronbach's alpha resulted 0.91 e 0.92, respectively) [17].

Sexual Functioning

Sexual functioning was measured by the McCoy-revised Italian version [18] McCoy Female Sexuality Questionnaire (MFSQ) and the Cues for Sexual Desire Scale (CSDS) [19]. The first was derived from the original MFSQ and it was translated and validated by Rellini et al. [20]. The MFSQ was selected because it permits the assessment of sexual functioning associated with hormonal fluctuation (e.g., menopause). Eighteen of the original 19 items of the MFSQ are scored on a 7-point Likert scale and one item asks for frequency of intercourse. Seventeen items are grouped into five factors derived from a principal component analysis and two items were added at a later time to measure "attractivity." The five factors comprise: sexual interest (four items), satisfaction with frequency of sexual activity (three items), vaginal lubrication (three items), sex partner (three items), and orgasm (four items). A two-factor solution identified by principal component analysis provided the best solution and the two factors were labeled sexuality and partnership. Moreover, in the Italian version, four items were eliminated from the questionnaire (items 3, 6, 16, and 17).

The CSDS [19] was created by McCall and Meston as a multidimensional assessment tool of

cues associated with sexual desire in women. It considers the contextual nature of sexual desire and it draws attention to potential individual differences in the various factors that can contribute to sexual desire. The original 125-item questionnaire was reduced to 40-item scale and then validated in women with and without hypoactive sexual desire disorder. The CSDS includes four factors described as: Emotional Bonding Cues, Erotic/Explicit Cues, Visual/Proximity Cues, and Romantic/Implicit Cues. The response choices were listed on a 5-point Likert scale. There is, however, no Italian validation of the translated version we have used in the present study.

Partner Relationship

Partner relationship and marital distress was measured by the Dyadic Adjustment Scale (DAS) [21]. The DAS has been used in over 1,000 published studies in order to evaluate relationship distress. The total score on the DAS ranges from 0 to 150. Of the 32 items, 27 are 6-point Likert-type scales, one is a 7-point Likert-type scale, and the two remaining items call for yes/no responses. Individuals scoring less than 100 are considered to have poor dyadic adjustment and are classified as relationally distressed. The author derived the following four subscales from factor analysis: Dyadic Satisfaction, Dyadic Consensus, Dyadic Cohesion, and Dyadic Affectional Expression.

Cognitive Function

Selective visual attention was measured by the numeric matrix test [22]. Three matrices were shown to a patient: every matrix is made of 13 rows of 10 numbers (0–9) each, placed by chance. The subject must mark the same number as printed above the matrix ("5" in I, "2-6" in II, "1-4-9" in III) every time it appears. Matrix must be shown from the easiest to the most difficult. Sum of right answers (0–60 for all the three matrices), false answers (0–279), and omissions were calculated. Population mean score of right answers is 47.39 (± 9.76).

The Rey auditory-verbal learning test [23] was used to evaluate the verbal memory and ability to learn. In the first part of the test, the clinician repeats five times a list of 15 words; the patient is then asked to tell all words she remembers. This part is useful to evaluate the immediate recall (IR) ability. The score, i.e., the total number of recalled words, ranges from 0 to 75. After 15 minutes, the delayed recall (DR) ability is evaluated: the patient is newly asked to repeat as many words as she can

recall from the list. The score is corrected for age and education and the cutoff is 28.5 for IR and 4.7 for DR.

Nutritional Assessment

Nutritional evaluations were performed by a dietitian at baseline and after 6 and 12 months in order to assess body weight and metabolism changes.

- A recall 24 H questionnaire or a daily diary was used to evaluate food intake.
- The Minnesota Leisure Time Physical Activity questionnaire (MLTPAQ) [24] was administered in order to determine the physical activity level over the past 12 months. It measures lifestyle physical activities, including household, gardening, and other yard work activities. The MLTPAQ yields an average daily expenditure of physical activity (kcal/day), in terms of metabolic equivalents (METs) (1 MET corresponds to an energy expenditure of 1 kcal/kg/h). Patients were grouped as sedentary (<10 MET h/week), moderately active (10–40 MET h/week), and active (>40 MET h/week).
- Eating disorders were assessed by the Eating Attitude Test-40 (EAT-40) [25]; it is a widely used, standardized, and self-reported questionnaire designed to assess pathological eating behaviors, attitudes, and thoughts. Answer options for 40 questions ranging from 0 to 3, with higher scores indicative of clinical levels of eating disorders. Scores equal to and higher than 30 were regarded as indicative of clinical eating disorder.
- Anthropometric and plicometry data were collected by a dietitian. The anthropometric measures obtained included height, weight, body mass index (BMI), skinfold measurements (mm) in predetermined sites such as biceps, triceps, subscapular, suprailiac, and circumference measurement of arm.

Statistical Analyses

All analyses were performed using the Statistical Package for Social Science, version 13.0 for Windows (SPSS Inc, Chicago, IL, USA). Dependent-samples *t*-test was used to compare changes in parameters across the time. The Shapiro–Wilk test was used to confirm that the sample origins from a normal population. When normality of data was not confirmed, the Wilcoxon Signed-Rank test was used. Variables were compared with Pearson chi-square test or Fisher exact test, as appropriate. A two-sided Type I error rate of 0.05 was used throughout data analysis.

Results

We reported a preliminary analysis on 35 patients. A 1-year follow-up is available in 21 women, while in 14 women, data are available following 6 months after surgery. The socio-demographic data and clinical characteristics of the study sample are summarized in Table 1.

The mean age of patients was 45.7 ± 3.6 (range 40–50 years). Thirty-one women were married and our study population had an average level of education (only five women graduated). At the enrollment, each woman was premenopausal, with the exception of three early postmenopausal women (less than 2 years before the diagnosis). During the study period, the entire sample entered iatrogenic menopause as a consequence of adjuvant CT or gonadotropin releasing hormone (GnRH) analogues. Almost the entire study sample (91.4%) underwent breast conservative surgery, while 97.2% received CT regimen containing anthracycline +/- taxane. Most women (85%)

Table 1 Sample characteristics at baseline

Characteristic	No.	%
Level of education		
High school or less	13	37.1
College	17	48.6
University	5	14.3
Current partner status		
Married	31	88.6
Nubile	1	2.8
Separated	3	8.6
Religious belief		
Believer	33	94.3
Nonbeliever	2	5.7
Stage of disease		
Localized, negative lymph nodes	18	51.4
Localized, positive lymph nodes	17	48.6
Type of surgery		
Lumpectomy	32	91.4
Mastectomy	3	8.6
Sentinel lymph node	18	51.4
Axillary dissection	17	48.6
Type of chemotherapy		
None	1	2.8
FEC	17	48.6
FEC + T	17	48.6
Radiotherapy		
Yes	31	88.6
No	4	11.4
Hormone therapy		
None	4	11.4
Tamoxifene	28	80
Aromatase inhibitors	3	8.6
GnRH analogues	27	77.1
Immunotherapy		
None	32	91.4
Trastuzumab	3	8.6

FEC = fluorouracil (5FU), epirubicin, and cyclophosphamid. FEC + T = fluorouracil (5FU), epirubicin, cyclophosphamid, and taxotere. GnRH = gonadotropin releasing hormone.

began ET with tamoxifen after CT and about 77% entered GnRH-analogue-induced menopause. A minority (four patients) had insensitive hormonal cancers and therefore were not subsequently treated with ET. Three postmenopausal women before surgery were candidate to be treated with aromatase inhibitors. Finally, trastuzumab was dispensed to two women with human epidermal growth factor receptor 2 (HER2/neu) amplification.

Menopausal Symptomatology—GCS

Climacteric symptoms worsened after CT, but especially when women started ET.

As expected, vasomotor symptoms increased significantly during the study period: score of subscale including hot flushes and nocturnal sweating increased from 0.454 ± 1.214 at T0 to 3.273 ± 2.412 at T1 and increased further to 4.545 ± 2.207 after 1 year. Score related to level of anxiety (1–6 items) was higher at the end of CT compared with basal time (4.727 at T0 and 6.091 at T1, $P = 0.04$); anxiety persisted also 1 year after surgery (score = 6.364 at T2, $P = 0.025$).

Scores of depression and urogenital symptoms worsened ($+1.091 \pm 3.208$ at T1 and $+1.364 \pm 2.541$ at T2), without reaching statistical significance. Somatic problems, like headache, dizziness, and muscular pain seemed to improve, but not significantly, 6 months (score lower than 0.727 ± 2.724) and 1 year (score lower than -1 ± 2.683) following surgery (Table 2).

Depression—BDI

Total mean BDI score increased at the end of CT ($+0.727 \pm 2.24$) and after 1 year from surgery ($+0.909 \pm 1.700$) as compared with baseline, without reaching statistical significance ($P = 0.307$ and 0.106). However, a lower mood level was detected in 63.6% of the study population. Women complained of different disturbances including irritability, retardation in daily activities, and episodes of crying; 90.9% of the sample reported more fatigue at T1.

Body Image—BAT

BAT subscales analyses “Attention to body size” and “Comparison of body appearance” ($+1.273 \pm 7.47$ and $+0.909 \pm 2.879$, respectively, $P > 0.05$) increased after the end of CT or after 6 months of ET, with a further not statistically significant increase after 1 year of follow-up ($+2.182 \pm 7.026$ and $+1.364 \pm 2.111$, respectively, $P > 0.05$).

“Familiarity with the body” improved, as indicated by the decreased mean score (-0.818 ± 2.523 at T1 and -1 ± 1.897 at T2 in comparison with baseline), without reaching statistical significance.

Sexual Functioning—MFSQ and CSDS

At T0, 77.1% of the sample referred sexual activity during the previous 4 weeks, with a reduction to 37.1% at T1 and to 34.3% at T2.

Moreover, half of the sample provided MFSQ scores below the normal range, already at baseline. Both MFSQ subscales declined following 6 months and 1 year of adjuvant therapy: mean score related to sexuality domain was significantly impaired after 1 year of follow-up (-12.7 , $P = 0.022$), while score concerning partnership decreased significantly (-4.1 at T1, $P = 0.007$, and -5.4 at T2, $P = 0.002$).

At baseline, the study sample reported very low CSDS scores. Emotional Bonding, Visual/Proximity, and Romantic/Implicit subscales scores did not change during the first year of adjuvant therapy. Only Romantic/Implicit stimuli significantly increased in power of evoking interest in sexual activity after 6 months from surgery ($+0.154 \pm 0.197$, $P = 0.026$). There is a trend to a decrease of Erotic cues (-0.145 ± 0.413 at T1 and -0.264 ± 0.403 at T2). All data related to MFSQ and CSDS analyses are shown in Table 3.

Partner Relationship—Spanier’s Dyad Scale

Total mean score of DAS changed from 100.2 ± 18.2 at baseline to 107.3 ± 16.042 at T1

Table 2 Greene Climacteric Scale scores modification at 6 months (T1) and 1 year (T2) of follow-up

	Mean scores (\pm SD)			Δ T0-T1 (\pm SD)	P value	Δ T0-T2 (\pm SD)	P value
	T0	T1	T2				
Anxiety	4.727 (4.125)	6.091 (3.27)	6.364 (3.107)	+1.364 (1.912)	0.040	+1.636 (2.063)	0.025
Depression	4.545 (3.856)	5.636 (3.443)	5.909 (3.33)	+1.091 (3.208)	0.286	+1.364 (2.541)	0.105
Somatic symptoms	4.273 (5.217)	3.545 (3.142)	3.273 (3.228)	-0.727 (2.724)	0.397	-1 (2.683)	0.245
Vasomotor symptoms	0.454 (1.214)	3.273 (2.412)	4.545 (2.207)	+2.818 (2.359)	0.003	+4.091 (2.211)	0.000
Urogenital symptoms	3.364 (3.749)	3.636 (3.042)	4.091 (3.145)	+0.273 (2.901)	0.762	+0.727 (2.76)	0.403

Table 3 Modification of McCoy Female Sexuality Questionnaire (MFSQ) and Cues for Sexual Desire Scale (CSDS) during the study period

MFSQ and CSDS subscales	Mean scores (\pm SD)			Δ T0-T1 (\pm SD)	P value	Δ T0-T2 (\pm SD)	P value
	T0	T1	T2				
M Sexuality	32.30 (21.802)	21.80 (18.996)	19.6 (17.122)	-10.500 (14.827)	0.052	-12.7 (14.545)	0.022
F S Partnership	22.00 (10.842)	17.90 (11.93)	16.6 (11.815)	-4.100 (3.725)	0.007	-5.4 (4.115)	0.002
C Emotional bonding	2.018 (0.558)	2.209 (0.453)	2.109 (0.450)	+0.191 (0.604)	0.319	+0.091 (0.298)	0.336
S Explicit/erotic	1.900 (0.654)	1.755 (0.505)	1.636 (0.476)	-0.145 (0.413)	0.270	-0.264 (0.403)	0.055
D Visual/proximity	1.264 (0.277)	1.400 (0.343)	1.300 (0.253)	+0.136 (0.307)	0.172	+0.036 (0.121)	0.341
S Romantic/implicit	1.864 (0.367)	2.018 (0.354)	2.136 (0.364)	+0.154 (0.197)	0.026	+0.273 (0.162)	0.000

and to 106.6 ± 17.102 at T2. It is worth mentioning that these values are slightly higher than 100, the cutoff value for hypothesizing a poor dyadic agreement and a disorder in relationship. However, there is a trend to an increase of each subscale score (Dyadic Satisfaction, Consensus, Cohesion, and Affectional Expression) over time, without reaching statistical significance.

Cognitive Function—Numeric Matrix Test and Rey Auditory-Verbal Learning Test

Selective visual attention did not deteriorate during the first 6 months of treatment for breast cancer and after 1 year from surgery. Each patient, after adjusting for age and level of education, reported score higher than 47.39 ± 9.97 (the cutoff of normality). At T0, women detected a mean number of 54.5 ± 4.552 out of 60 (90.8%), 54.1 ± 4.095 (90.1%) at T1 and 54.3 ± 4.001 (90.5%) at T2.

Mean number of immediate recalled words increased from 46 ± 6.983 at T0 to 50.67 ± 5.808 at T1 and to 50.7 ± 5.655 at T2 ($P = 0.033$ and 0.028). The same was true for the 15 Rey's words (deferred recall, after 15 minutes); indeed, patients recalled a greater number of words (+9.3% at T1 and +9.1% at T2) in comparison with baseline ($P = 0.025$ and $P = 0.017$, respectively) (Table 4).

Nutritional Assessment

EAT-40 administration identified only three women with a score close to 30, indicative of clinical eating disorder.

With regard to physical activity, only four women reported to practice regularly at T0: three of them did not discontinue their physical activity during the first year of adjuvant treatment for breast cancer and they reported an improvement in fatigue in the 6 months after the end of CT.

Half of them reported to walk or to move for housekeeping activities, but they admit a reduction during CT. As far as the MLTPAQ results were concerned, only one woman could be considered moderately active (10–40 MET h/week) and the other 32 as sedentary (<10 MET h/week).

Mean body weight of study population significantly increased after 6 months of therapy for breast cancer ($P = 0.035$). The only woman losing weight in 6 months was the one who did not receive CT. On average, weight gain in chemotherapy-treated patients was 2.07 ± 2.65 kg at T1 and 2.02 ± 2.15 kg at T2. Mean BMI increased significantly ($P = 0.039$) from 26.15 ± 4.2 to 26.93 ± 5.1 . At T0, 50% of women treated with CT were in the normal range of weight (BMI 18.5–24.9); 30% were overweight (BMI 25–29.9), and 20% were obese (BMI > 30). After 6 months

Table 4 Modification of cognitive function tests (Number Matrix Test and Rey auditory-verbal learning test [RAVLT]) during the study period

Test for cognitive function	Mean scores (\pm SD)			Δ T0-T1 (\pm SD)	P value	Δ T0-T2 (\pm SD)	P value
	T0	T1	T2				
Number Matrix Test	54.50 (4.552)	54.10 (4.095)	54.3 (4.001)	-0.400 (2.716)	0.653	-0.200 (1.751)	0.726
RAVLT immediate recall	46 (6.983)	50.67 (5.808)	50.7 (5.655)	+4.67 (5.886)	0.033	+4.7 (5.695)	0.028
RAVLT deferred recall	10.25 (1.592)	11.65 (1.414)	11.61 (1.390)	+1.400 (1.646)	0.025	+1.36 (1.481)	0.017

Table 5 Analyses of mean scores and difference in time of anthropometric measurements

	Mean scores (\pm SD)			Δ T0-T1 (\pm SD)	P value	Δ T0-T2 (\pm SD)	P value
	T0	T1	T2				
Body weight	65.19 (11.841)	67.26 (14.092)	67.21 (14.142)	+2.07 (2.647)	0.035	+2.02 (2.803)	0.049
Arm circumference	28.911 (3.391)	29.611 (3.672)	29.778 (3.743)	+0.700 (0.589)	0.007	+0.867 (0.659)	0.004
Subscapular	19.389 (9.751)	20.178 (9.508)	20.211 (9.621)	+0.789 (0.611)	0.005	+0.822 (0.79)	0.014
Suprailiac	24.5 (9.985)	27.711 (9.259)	27.7 (9.36)	+3.211 (3.539)	0.026	+3.2 (3.476)	0.025
Triceps	26.678 (7.234)	27.611 (7.687)	27.767 (7.52)	+0.933 (0.716)	0.004	+1.089 (0.562)	0.000
Biceps	19.155 (9.231)	19.833 (9.035)	19.755 (8.972)	+0.6778 (0.796)	0.034	+0.6778 (0.705)	0.034

of CT, percentages of normal (30%) and overweight (50%) patients were reversed, while the percentage of obese women did not change. Analyses of plicometry measures at T0 and T1 showed that both the four measured skinfolds (subscapular, suprailiac, triceps, biceps) and arm circumference significantly increased (Table 5). Suprailiac skinfold increased more than the others, from mean value of 24.5 ± 9.985 mm at T0, to 27.711 ± 9.259 mm at T1 and to 27.7 ± 9.36 mm at T2.

Discussion

Psychological consequences in breast cancer survivors have been neglected in medical literature for a long time [26] and sexual dysfunctions in women with breast cancer were mentioned in the 1970s for the first time.

Our present work is a preliminary report on the modifications of different aspects related to QOL (sexual dysfunction, menopausal symptomatology, cognitive impairment, partner relationship, body image, and weight problem) affecting young women in the first year after breast cancer surgery and adjuvant therapy.

Breast cancer patients enrolled were premenopausal or early postmenopausal; the majority of them underwent iatrogenic menopause by using adjuvant CT or GnRH analogues. This study population could be considered psychologically and cognitively healthy, with the only exception of one woman in which diagnosis of anxiety disorder could be hypothesized.

A significant increase in anxiety after the first semester of adjuvant treatment for breast cancer as compared with baseline emerged and was confirmed after 1 year of follow-up. Anxiety might be related to QOL deterioration following CT and to newly experienced menopausal status. Moreover, most of the women reported an oppressive worry about disease recurrences during the interview.

Vasomotor symptoms started or increased in number and severity during CT: hot flushes and

nocturnal sweating became annoying symptoms in everyday life of many patients. However, our sample defined hot flushes as mild or moderate, and only in one case was it necessary to prescribe a treatment for improving quality of sleep. Somatic symptoms included in GCS, such as headache, dizziness, and muscular pain, did not change during the first year after surgery.

Many studies suggested [27] that the onset of vaginal dryness as a consequence of abrupt menopause is one of the most important factors influencing sexual functioning. However, our findings, including the gynecological exam, the VHIS evaluation, and urogenital GCS scores did not support these data, likely because of the young age and the short duration of time since menopause.

In the present study, mean score of BDI did not significantly change overtime, even if a trend to depressive mood was present in 60% of the patients reporting an increase of irritability and of episodes of crying in the first 6 months after surgery during CT. Knowing that depression is highly related to loss of desire, physicians need to discuss the relevance of such comorbidity in modulating intrapersonal and interpersonal issues [28].

We found that relationship with body and physical appearance did not change over 6 months and 1 year of therapy: Body image was not significantly changed in comparison with baseline. This evidence may be related to breast conservative surgery with oncoplastic technique and with good aesthetical outcome that was performed in the majority of the women [29]. On the other hand, women on CT must cope with other changes in their physical appearance, such as alopecia, pallor, and weight change, far more obvious to casual observer than is mastectomy [30].

As far as sexual functioning is concerned, baseline scores were below the range of normality for half of the sample: it proved that sexual life was not satisfying, even before the beginning of adjuvant therapy for breast cancer. Sexual dysfunction in the premenopausal age range is common [31] but

these data are even more alarming, if we consider the further worsening of sexual activity of these young women after 6 months of treatment and also after 1 year from surgery. Similar patterns of sexual activity are reported by many authors and the impact of CT on menopausal status appears to be one of the most important factors: Ganz et al. [32] found that sexual functioning was most impaired for women no longer menstruating after CT, a finding also supported by Alder et al. [33]. The analysis of the CSDS revealed poor cues of sexual desire in our study sample suggesting a potential risk for developing a real sexual dysfunction, i.e., hypoactive sexual desire disorder. Ganz et al. [4] remarked that interest in sexual activity was one of the most relevant problems regarding QOL after surgery and that it remained altered over time. Indeed, after 1 year from cancer diagnosis, explicit erotic cues were even less effective in exciting sexuality as compared with baseline; on the other hand, romantic cues increased their power in inducing sexual desire. In spite of the potential limitations due to the use of a translated, not validated version of the CSDS, these results are in line with the idea that women facing a difficult situation, such as cancer, are in need for tenderness, counseling, and protection, more than physical passion.

No significant change in partner relationship were registered by DAS; at baseline, scores were very close to the low cutoff, meaning that partner relationship did not completely fulfill women's wishes, expectations, or needs even before breast cancer was diagnosed. Both marital status and the partners' difficulties in understanding the condition of the spouse could be associated with sexual problems [34].

Controversial data on cognitive dysfunction in women undergoing adjuvant CT for breast are reported in the literature. Some recent studies indicated a cognitive impairment in 15–50% of adult solid tumor survivors who had received CT [35]. Such cognitive deficits are diffused and involve especially the domains of attention, concentration, and visual memory. On the other hand, there are data to support a negligible cognitive dysfunction in a minority of patients or even an improvement, despite premature menopause and CT [36].

The etiology of cognitive impairment after CT remains unknown. Different mechanisms have been postulated: direct neurotoxic effects with injury to neurons or cells, oxidative stress and DNA damage, induced hormonal changes,

immune deregulation or release of cytokines, and blood clotting in central nervous system vessels.

In our study, we did not find a negative effect of CT on cognitive functions, but memory domain seemed to strengthen after 6 months of therapy and remained stable after 1 year. A possible explanation is the short time (6–12 months) elapsed between baseline examination and the repetition of tests after CT that allows a “learning effect”. Nevertheless, women reported a subjective feeling of memory impairment and difficulty in concentration, during and after CT; also if these problems were not detected by cognitive tests, they can strongly affect the perceived women's QOL. Furthermore, higher level of anxiety, fatigue, and emerging menopausal symptoms did not help concentration and memory in these patients.

Also, selective visual attention did not significantly change over 6 months of adjuvant therapy and after 1 year of follow-up. The performance of the sample in numeric matrix test was good, above general population mean, even at baseline.

In line with many authors [37], we found that body weight and BMI increased significantly after CT; while at baseline, half of women could be defined as normal. After 6 months, half of them was overweight and patients with BMI <19 decreased (minus 20%). The same was observed 1 year after surgery. Previous studies suggest that weight gain commonly ranges from 2.5 to 6.2 kg [15] and is especially pronounced among premenopausal women and among those who receive multiagent regimens. In our study, 34/35 women received CT and weight gain was of 2.07 ± 2.647 kg. Weight gain induced women to worry more about body size and comparison of body appearance.

Several findings, in which dietary data were collected using validated dietary methods do not support overeating as a cause [38]; authors focus on the possibility of decreased energy expenditure via reductions in physical activity. In this study, we did not find significant difference in physical activity performed by women at baseline and during follow-up. Unfortunately in our sample, 32 out of 35 women were sedentary and did not practice any physical activity; that being so, weight gain cannot be related.

Every measure of skinfolds statistically increased significantly at T1 and T2 as compared with basal value. Since suprailiac fold measure was the one which raised more, there was an accumulation of fat mass in the abdominal area, confirming that CT is responsible for android deposition

of fat and worn out of lean body mass [36,39]. Demark-Wahnefried et al. found that age-related changes in body composition are accelerated in patients who receive CT, and most of these changes occur within 6 months of diagnosis.

It has been demonstrated that android body fat distribution is associated with insulin resistance and it may act as late stage promoters of mammary carcinogenesis: android body fat distribution is, indeed, a critical prognostic anthropometric indicator related to survival from breast carcinoma.

Conclusion

Preliminary results of this study showed that adjuvant treatment for breast cancer in young patients has a strong negative impact on different QOL domains, especially on menopausal symptoms, sexuality, and body weight. On the contrary, no influence of standard CT regimens on cognitive functions was demonstrated.

Many studies about QOL and sexuality in breast cancer patients have already been published, but they usually focus on one specific aspect. Even if this is a preliminary report, based on a small number of patients, it is an attempt to consider prospectively all these variables together, taking into account also cognitive function, partner relationship, body weight, and body image aspects, in order to have a “360 degrees” view of patients treated for breast cancer. Although a longer follow-up is essential to evaluate if negative impact of CT would last over time, these data support the need for multidisciplinary approach to breast cancer patients after surgery, in order to assess new interventions [40] and to improve their sexuality and QOL.

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