

Impaired of Sexuality in Premenopausal Breast Cancer Patients

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Abstract

Introduction: The treatment modalities for Breast cancer may impair the sexual function of women, especially in the pre-menopausal period. Treatment in this group of women has a huge impact in quality of life. The main objective of this study was to evaluate the prevalence of sexual dysfunction (SD) after treatment for breast cancer among women who were premenopausal at the diagnosis of neoplasia. **Material and Methods:** All women diagnosed with premenopausal breast cancer at one outpatient clinic from March 2019 to September 2020 were selected. Participants answered two sexual function questionnaires (the Female Sexual Function Index [FSFI-19] and Female Sexual Quotient [QS-F]) and a quality of life [QOL] questionnaire [EORTC QLQ-C30]). Sociodemographic and tumor characteristics were also studied. **Results:** Fifty-eight pre-menopausal women were included. Sexual dysfunction (SD) was observed in 43 participants (74.1%) according to the FSFI-19, while 31 (53.4%) had SD according to the QS-F. The functional and general health scales of the EORTC QLQ-C30 were positively related to the FSFI-19 and QS-F scores, while the symptom scale was negatively related to the FSFI-19 and QS-F scores. There was no relationship between chemotherapy, hormone therapy, or surgery with the FSFI-19 and QS-F scores. A diagnosis of depression was negatively related to the total FSFI-19 scores. **Conclusion:** Pre-menopausal breast cancer women showed high rates of female SD. None breast cancer treatment modality was related to SD. The only studied variable associated with SD was depression.

Keywords

Breast Cancer, Sexuality, Quality of Life, Sexual Dysfunction, Premenopausal Period, FSFI-19, QS-F, EORTC QLQ-C30

1. Introduction

According to GLOBOCAN data, breast cancer is the most frequent malignancy among women, second only to non-melanoma skin cancer [1]. In Brazil, breast cancer accounts for approximately 30% of all cases of cancer in females; more than 60,000 cases were diagnosed between 2019 and 2020 [2]. Early diagnosis and advances in its treatment have caused an important decline in mortality, with a consequent increase in survival rates, which can exceed 90% in cases of localized disease [3]. Given this, issues related to the quality of life (QOL) and sexual function have gained a prominent role in recent years.

Sexuality is a complex phenomenon that involves organic and psychoactive processes and is influenced by multiple factors, including biological, social, psychological, historical, and cultural ones [4]. According to the World Health Organization, sexuality influences the physical and mental health of human beings, and for this reason, it constitutes an important aspect of women's lives and is one of the factors to be evaluated when studying the QOL of women with breast cancer [5].

Numerous studies have shown that the diagnosis and treatment of breast cancer can impair sexual function through several mechanisms, such as ovarian failure, altered perception of body image, intimacy, and the relationship between the couple [6] [7] [8]. With a prevalence of 23% - 85%, sexual morbidity is among the main side effects of breast cancer diagnosis and treatment [9]. In this context, premenopausal patients deserve a prominent role, since they tend to be more vulnerable to body changes resulting from surgical treatment and ovarian function changes resulting from systemic treatment [10].

Surgical management, which includes conservative surgery and mastectomy, with or without reconstruction, can have psychological effects, such as a feeling of loss of femininity and negative body image, in addition to physical effects, such as pain and decreased breast sensitivity [4] [11]. Studies evaluating breast surgery and sexual dysfunction (SD) in these women are quite contradictory in correlating the type of surgery with the worsening or not of sexual function, but there seems to be some advantage for women undergoing conservative surgery and mastectomy with reconstruction [12]-[17]. Systemic treatment, in turn, interferes with sexual function by inducing early ovarian failure. In this context, the decrease in ovarian hormone production ends up causing numerous symptoms, such as hotness, emotional lability, insomnia, decreased sexual desire, and vaginal dryness [6] [11]. In addition, the use of hormone therapy in cases of luminal tumors contributes to vaginal dryness and consequent dyspareunia ob-

served in this group of women.

To study the sexual function of premenopausal women, a cross-sectional study was conducted with the main objective of estimating the prevalence of SD in this group. Two questionnaires, the Female Sexual Function Index (FSFI-19) and Female Sexual Quotient (QS-F), were applied to evaluate SD. The effect of different modalities of systemic and surgical treatments in the SD was also studied.

2. Material and Methods

2.1. Population

All women diagnosed with premenopausal breast cancer from March 2019 to September 2020 attending two outpatient breast clinics, the Hospital de Clínicas de Porto Alegre and in a private clinic, located in Erechim, RS/Brazil, were included in the study. Male patients and patients diagnosed with carcinoma in situ or metastatic disease were excluded. After agreeing and signing the informed consent form, participants answered self-report questionnaires of sexual function, QOL, and sociodemographic characteristics. This study was approved by the Research Ethics Committee of HCPA (CAAE: 03399218.9.0000.5327).

2.2. Research Instruments

The FSFI-19 is a 19-item instrument that has been validated as a tool for assessing the sexual function of women with cancer and has been recognized as the main means for the study of sexuality in this population. It accesses six sexual domains or dimensions, including desire, arousal, lubrication, orgasm, satisfaction, and pain. SD is identified when the sum of the total score is <26.55 , with higher scores indicating better sexual function [18] [19].

The QS-F is an instrument developed by a Brazilian research group of the Faculty of Medicine of the University of São Paulo. It consists of 10 questions, and the higher the value is, the higher the sexual performance/satisfaction. A cutoff point of 60 was established as a screening for female SD [20].

The EORTC QLQ-C30 is an instrument developed by the European Organization for Research and Treatment of Cancer. It is composed of 30 items with the objective of evaluating general aspects of the QOL of cancer patients and is divided into three scales: general health, functional, and symptoms. The results range from 0 to 100, and the higher the score is, the better the overall and functional health status, but the worse the symptoms [21] [22].

Clinical and pathological characteristics, surgical and systemic treatments were also studied and correlated with SD.

2.3. Statistical Analysis

Data analyses were made through the Statistical Package for Social Sciences (SPSS) for Windows, version 18.0. The quantitative variables were expressed as mean \pm standard deviation (SD) or median and interquartile range [IQR], percentiles 25 - 75, defined by the Shapiro-Wilk normality test. The qualitative va-

riables were described by absolute (n) and relative (%) frequency. Spearman correlations were conducted between the variables of interest. The level of significance adopted for all analyses was established at 5%.

3. Results

3.1. Clinical and Pathologic Characteristics

A total of 58 patients were included. Sociodemographic characteristics were shown in **Table 1**. Most of the patients (56.9%) were from Porto Alegre. The mean age of the diagnosis was 46 years (29 - 55 years). Forty-nine (84.5%) patients had a steady partner for the last year. The comorbidities rates and birth control methods were showed in **Table 2**. The two more prevalent comorbidities were systemic arterial hypertension (31%) and depression (31%). Sixty-one percent of the patients not used birth control method. Tumor characteristics, surgical and systemic treatment were presented in **Table 3**. Twenty-four (41%) patients had tumors less than 2 cm and 23 (39.7%) had axillary involvement. Mastectomy with immediate reconstruction was performed in 31 (51.4%) patients.

Table 1. Sociodemographic characteristics.

Variable	Total (N = 58)
Origin—n (%)	
Erechim	25 (43.1)
Porto Alegre	33 (56.9)
Age (years)—md [IQR] (minimum - maximum)	46.00 [40.00 - 50.00] (29.00 - 55.00)
Race/color—n (%)	
White	52 (89.7)
Negress	5 (8.6)
INO	1 (1.7)
Marital status—n (%)	
Steady partner	49 (84.5)
No steady partner	6 (10.3)
Single	1 (1.7)
Widow	2 (3.4)
Education—n (%)	
Incomplete high school	8 (13.8)
1 st degree complete	7 (12.1)
2 nd degree incomplete	4 (6.9)
Complete 2 nd degree	16 (27.6)
Incomplete superior	6 (10.3)
Graduated	9 (15.5)
Postgraduate	8 (13.8)
Profession—n (%)	
Employee	53 (91.4)
Unemployed	4 (6.9)
Pensioner	1 (1.7)

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Religion—n (%)	
None	4 (6.9)
Catholic	37 (63.8)
Evangelical	8 (13.8)
Spiritist	5 (8.6)
Afro-Umbanda	1 (1.7)
Other	3 (5.2)

Data expressed as absolute (n) and relative (%) or median (md) and interquartile ranges [IQR, percentiles 25 - 75 percentiles]. Legend: INO—information not obtained.

3.2. Assessment of Sexual Function

The scores of the FSFI-19 and QS-F questionnaires, as well as the prevalence of SD, according to each instrument are presented in **Table 4**. The median score on the FSFI-19 scale was 19.10 [5.20 - 27.00], with 43 women (74.1%) diagnosed with SD according to the cutoff point < 26.55. On the QS-F scale, the median score was 55.00 [34.00 - 80.00], with 31 women (53.4%) diagnosed with SD according to the cutoff point < 60. Women who were sexually inactive were excluded in the last 4 weeks, the results of the sexual function according to the FSFI-19 are presented in **Table 5**.

3.3. Factors Related to Sexual Function

The results of Spearman's correlations are presented in **Table 6**. The FSFI-19 and QS-F scores were positively related to each other. The functional and general health scales of the EORTC QLQ-C30 were positively related to the FSFI-19 and QS-F scores, while the symptom scale was negatively related to these same

Table 2. Comorbidities and birth control methods.

Variable	Total (N = 58)
Systemic arterial hypertension—n (%)	18 (31.0)
<i>Diabetes mellitus</i> —n (%)	6 (10.3)
Thyroid disease—n (%)	6 (10.3)
Depression—n (%)	18 (31.0)
Neurological diseases—n (%)	3 (5.2)
Rheumatological diseases—n (%)	1 (1.7)
Gastrointestinal diseases—n (%)	4 (6.9)
Contraceptive method—n (%)	
None	35 (60.3)
Copper IUD	12 (20.7)
Combined oral contraceptive	1 (1.7)
Condom	7 (12.1)
Tubal ligation	3 (5.2)

Data expressed as absolute (n) and relative (%) or median (md) and interquartile ranges [IQR, 25 - percentiles 75]. Legend: INO—information not obtained. IUD—intrauterine device.

Table 3. Tumor characteristics, surgical and systemic treatment.

Variable	Total (N = 58)
Age at diagnosis (years)—mean \pm SD (minimum - maximum)	41.85 \pm 6.38 (28.00 - 52.00)
Age at diagnosis—n (%)	
29 - 35 years	13 (22.4)
36 - 40 years	11 (19.0)
41 - 45 years	18 (31.0)
46 - 50 years	16 (27.6)
Tumor size—n (%)	
T1	24 (41.4)
T2	22 (37.9)
T3	7 (12.1)
T4	3 (5.2)
INO	2 (3.4)
Lymph node involvement—n (%)	23 (39.7)
Hormone receptors—n (%)	37 (63.8)
HER2 hyperexpressed—n (%)	6 (10.3)
Type of surgery—n (%)	
Sectorectomy	23 (39.7)
Mastectomy without reconstruction	3 (5.2)
Mastectomy with reconstruction	30 (51.7)
INO	2 (3.4)
Chemotherapy—n (%)	
Geral	48 (82.8)
Adjuvant chemotherapy	24 (41.4)
Neoadjuvant chemotherapy	25 (43.1)
Radiotherapy—n (%)	39 (67.2)
Hormone therapy—n (%)	
Tamoxifen	33 (56.9)
Aromatase inhibitor	5 (8.6)

Data expressed as absolute (n) and relative (%) or averages and standard deviations (\pm SD).

Table 4. Total scores FSFI-19 and QS-F (n = 58.00).

Variable	Total (N = 58)
FSFI-19	
Total Score—md [IQR] (minimum - maximum)	19.10 [5.20 - 27.00] (1.20 - 34.00)
Total Score—n (%)	
<26.55	43 (74.1)
\geq 26.55	15 (25.9)
QS-F	
Total Score—md [IQR] (minimum - maximum)	55.00 [34.00 - 80.00] (2.00 - 96.00)

Continued

Standardized Score—n (%)	
82 - 100	14 (24.1)
62 - 80	11 (19.0)
42 - 60	18 (31.0)
22 - 40	7 (12.1)
0 - 20	8 (13.8)
Score—n (%)	
<60	31 (53.4)
≥60	27 (46.6)

Data expressed as absolute (n) and relative (%) or median (md) and interquartile ranges [IQR, percentiles 25 - 75].

Table 5. Scores of FSFI-19.

Variable	Total (N = 42)
FSFI-19	
Total Score—md [IQR] (minimum - maximum)	23.16 ± 7.13 (2.00 - 34.00)
Total Score—n (%)	
<26.55	27 (64.3)
≥26.55	15 (35.7)

Total scores FSFI-19—Participants of active sex life in the last 4 weeks (n = 42.00, 72.4%). Data expressed as absolute (n) and relative (%) frequencies, means and standard deviations (± SD) or medians (md) and interquartile ranges [IQR, percentiles 25 - 75].

Table 6. Correlations between FSFI-19 and QS-F.

Variable	Total Score (N = 58)			
	FSFI-19		QS-F	
	ρ	*p-value	ρ	*p-value
Total Score FSFI-19	-	-	0.726	≤0.05
Total Score QS-F	0.726	≤0.01	-	-
Total Score EORTC QLQ-30	0.549	≤0.01	0.333	0.013
Score EORTC—Functional Scale	0.424	≤0.01	0.393	≤0.01
Score EORTC—Symptom Scale	-0.307	≤0.05	-0.285	≤0.05
Score EORTC—Global Health Scale	0.549	≤0.01	0.333	≤0.05
Depression	-0.322	≤0.05	-0.221	0.096
Age at diagnosis	-0.114	0.479	-0.226	0.156
Tumor size	-0.047	0.731	-0.101	0.461
Lymph node involvement	0.195	0.147	0.136	0.313
Hormonal receptors	0.036	0.796	0.020	0.886
HER2 hyperexpressed	0.344	0.092	0.423	≤0.05
Adjuvant chemotherapy	-0.016	0.905	-0.077	0.570

Continued

Neoadjuvant chemotherapy	0.102	0.450	0.109	0.421
General chemotherapy	0.079	0.559	0.034	0.804
Hormone Therapy	0.158	0.239	0.089	0.508
Sectorectomy	0.118	0.387	0.165	0.224
Mastectomy with reconstruction	-0.092	0.499	-0.048	0.726
Simple mastectomy	0.202	0.136	0.004	0.977
Sexual activity last 4 weeks	0.740	≤0.01	0.458	≤0.01

scores. There was no relationship between chemotherapy, hormone therapy or the type of surgery with the FSFI-19 and QS-F scores. A diagnosis of depression was negatively related to the total FSFI-19 scores.

4. Discussion

SD is very common among patients with breast cancer. Sexuality-related issues tend to be underestimated in clinical practice, and the impairment of sexual function can negatively influence the QOL of these women. Our findings of SD in premenopausal breast cancer patients are in line with other published studies. When we used the FSFI-19 score, we found a prevalence of 74.1% of SD (*i.e.*, 74.1% of the patients had a score < 26.55, which is the cutoff point for diagnosis of SD), with a median of 19.1. Raggio *et al.*, showed a prevalence of 60% of SD among patients with breast cancer of all ages using the same evaluation instrument [23]. In a more recent meta-analysis evaluating only young breast cancer patients, a mean score of 19.28 was found for the FSFI-19 questionnaire 8. As the FSFI-19 score assesses sexual function in the last 4 weeks, this analysis was also performed in the subgroup of participants who denied an active sexual life in the last month. In this analysis, 42 (72.4%) women were included, and a prevalence of SD of 64.3% was found (*i.e.*, 64.3% of the patients in this subgroup had a score < 26.55), with a mean score of 23 [16]. Patients without an active sexual life in the last 4 weeks opted for the alternatives with a score of “0” in some questions of the FSFI-19. This fact could have contributed to reducing the final score of the FSFI-19 in this subgroup of women. As the other questionnaire used in the study does not restrict sexual activity in the last 4 weeks, we chose to also use the group of all patients in the score FSFI-19 to do the correlation analyses.

In the evaluation of sexual function through the QS-F questionnaire, we found a prevalence of SD of 53.4% (*i.e.*, 31 participants had a score below the cutoff point of 60), with a median score of 55. Unlike the FSFI-19, the QS-F does not restrict sexual life to the last 4 weeks. For this reason, no additional analysis was performed for this score. Our study was the first study to apply QS-F for assessing sexual function in premenopausal women with breast cancer.

Several studies have proven that different therapeutic modalities for breast cancer cause impairment to sexuality [10] [24] [25] [26]. Systemic treatment is a

predictor for SD in these women because it induces early ovarian failure and causes a decrease in estrogen intake in the target organs. Besides this, surgical treatment has been associated with an altered perception of femininity and body image, which makes them feel less sexually attractive [14] [17]. In our study, a significant portion of the participants underwent adjuvant chemotherapy (41.4%) or neoadjuvant chemotherapy (43.1%) and/or hormone therapy (65.5%). Besides that, slightly more than half of the participants underwent mastectomy with reconstruction (51.7%), 39.7% of participants had a sectorectomy and only 5.2% of participants underwent mastectomy without reconstruction. We did not demonstrate a relationship between chemotherapy, hormone therapy, or surgical modality with the FSFI-19 or QS-F scores. We believe that the failure to detect negative correlations between these treatments and the sexual function scales is due to the small sample size of our study.

The presence of comorbidities is of paramount importance when assessing sexuality in general. Correlation between depression and the use of antidepressant drugs with SD have already been demonstrated [27] [28]. Depression ($n = 18$) was one of the comorbidities most prevalent findings of our study, being associated with a negative relationship with the FSFI-19 score ($p \leq 0.05$). In addition, all women who report depression as a comorbidity in this study were using antidepressants. Between 10% and 16% of the general population had been through an episode of depression, and it is known that depressive disorders can cause loss of interest or pleasure, anhedonia, decreased activity, and difficulty concentration. These symptoms are often accompanied by a reduction in sexual desire and, consequently, sexual dysfunction [29]. According to Waldinger, the prevalence of SD in women with major depressive ranges from 40% to 65% [29]. Mitchell *et al.*, in a British survey of 6669 women, found current depression to increase the risk of sexual dysfunction with an odds ratio of [3] [12] [30]. In addition to that, a recent systematic review about the prevalence of symptoms of depression after breast cancer treatment found that this rate varied from 9.4% to 66.1% among this population [31]. Regarding the use of antidepressants, a recent study about their use and its side effects was conducted by Cartwright *et al.* and found that 71.8% of users of antidepressants reported sexual problems [32]. Another study that evaluated the correlation between antidepressants and SD was conducted by Lorenz *et al.* The study reviewed 3 meta-analyses and found that SD attributable to antidepressants was approximately 40% [33].

Nowadays, there is an increment of the studies correlating QOL with the post-treatment sexuality of breast cancer [34]. When we correlated the QOL index with the FSFI-19 and QS-F scores, these two variables were positively related to both the FSFI-19 and QS-F scores ($p \leq 0.01$ for both). Conversely, when we evaluated the symptom scale, this scale was negatively related to both the FSFI-19 and QS-F scores ($p \leq 0.05$ for both). In a retrospective multicenter study by Mayer *et al.*, 396 BC patients were compared to 60 healthy women in terms of sexual function and QOL, using FSFI-19 and EORTC QLQ C30 questionnaires

to assess sexual function and QOL, respectively. They found that sexual activity was associated with a better QOL ($p = 0.004$). Our data corroborate these previous findings that the best QOL culminates in better sexual function [35].

5. Conclusion

In this study, we could demonstrate a high prevalence of SD in premenopausal women with breast cancer. Despite this, we could not demonstrate a correlation between the type of surgery and systemic treatment with SD. The only correlation we could demonstrate was a high association with SD and depression, and with SD and QoL scores. More studies are necessary to better understand the real impact of breast cancer treatment on the patient's sexuality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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