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Research Article

Breast Cancer Survivors with Genitourinary Syndrome of Menopause Receiving Aromatase Inhibitors Are Willing to Sexual Assessment: Is a Dyspareunia Approach Enough?

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Objective. To assess the sexual health and interest of breast cancer survivors (BCSs) in a tailored evaluation of their sexuality. *Methods*. A descriptive analysis on baseline sexual assessment of female BCS with genitourinary syndrome of menopause (GSM) receiving aromatase inhibitors (AIs), who have participated on an ongoing double-blinded randomized controlled trial on the efficacy and safety of laser therapy (NCT04619485), was conducted. Epidemiological and BC variables, as well as mental, vaginal, and basic sexual health assessment (self-reported sexual activity and frequency, sexual behavior, type of sexual activity and relationship status, Female Sexual Function Index (FSFI), and Body Image Scale questionnaires and 2 visual analogue scales (VASs) about sexual life disturbance and dyspareunia) were recorded. An optional specialized sexual assessment was offered. *Results*. Among 83 participants, 67 (80.7%) wanted sexual counseling. Half of them had a body image alteration, and 74% worsened their sexual life after receiving BC diagnosis and treatments. The sexual activity rate was 71.1%. Sexually inactive women had higher impairment of FSFI desire dimension ($p = 0.0013$), dyspareunia ($p = 0.0114$), and unsatisfaction with their sexuality ($p = 0.0530$) compared to sexually active women. In sexually active women, the mean FSFI and all of its dimensions showed a lower score. The most frequent sexual behavior was a combination of nonvaginal and vaginal sex, despite the high intensity of dyspareunia (mean VAS ± SD: 7.1 ± 2.1). *Conclusion*. Most of the BCSs with GSM receiving AI were interested in a specialized sexual consultation. Sexual activity and function were impaired, either secondary to dyspareunia or to other biopsychosocial sexual factors.

1. Background

Sexuality is a central aspect of the human being [1] that may be affected in breast cancer survivors (BCSs) [2]. In a recent meta-analysis focused on sexual function among BCS, female sexual dysfunction (FSD) prevalence was 73.4% with a mean Female Sexual Function Index (FSFI) of 19.28 [3]. BC diagnosis and/or its treatments (surgery/chemotherapy/radiotherapy/hormonal therapy) may alter sexual health [4]. BCS receiving aromatase inhibitors (AIs) define one of the groups with greater

likelihood of complaining with severe genitourinary syndrome of menopause (GSM) and sexual impairment [5], being 3 out of 4 BCS with AI distressed by their sexual problems [6]. Only 52% of these women were sexually active when endocrine therapy began, and 79% of them developed new sexual problems [6]. However, these symptoms are often underreported, underdiagnosed, and undertreated [7]. Vulvovaginal health is a key factor for female pleasure, but the treatment of this condition is still a challenge in BCS population [8–11]. However, sexual health involves not only the genitalia but also aspects like intimacy, eroticism, reproduction, and body image. These aspects may be affected in BCS and could impact on other dimensions of female sexuality such as satisfaction, desire, arousal, and orgasm. Therefore, before recommending any intervention for sexual complaints in BCS with GSM, unmet needs should be taken into account.

Unfortunately, a specialized sexual assessment is not usually performed, with most studies focusing on generic questionnaires that do not measure the wide-ranging impact of the disease. A systematic review [12] of the existing scales to screen FSD in BCS identified the Arizona Sexual Experience Scale, FSFI, and Sexual Problem Scale as most closely meeting criteria for acceptable psychometric properties and incorporation of the DSM-5/ICD-10 criteria; however, all of them have limitations. Therefore, a combination of a quantitative and qualitative approach through validated questionnaires and sexual interviews would provide a deeper and more accurate explanation for changes in BCS sexuality.

The main goal of the present study was to evaluate sexual health quantitatively and qualitatively in terms of sexual activity and function in BCS with GSM receiving AI. In addition, we aimed to assess the interest of BCS in a tailored evaluation of their sexuality.

2. Methods

2.1. Study Design. This study represents a preliminary analysis of an ongoing prospective double-blind sham randomized controlled trial on the efficacy and safety of laser therapy among BCS (NCT04619485). Herein, we present a descriptive analysis of baseline sexual data aimed to get the picture of the sexual life of the participants before any intervention.

2.2. Participants and Procedures. Women attending the breast cancer unit at a tertiary university hospital, between October 2020 and September 2021, were included. Considering the FSFI score as the main variable of the study and using statistical software STATA to calculate sample size, accepting an alpha risk = 0.05 and a beta risk <0.1 in a bilateral contrast, with the common standard deviation assumed to be of 5 points and the minimum expected effect size of 4 points [13], we calculated a sample size of 33 subjects for each group. Considering a follow-up loss rate of 15%, the sample size should be 76 patients. Finally, 84 patients were included.

The inclusion criteria were as follows: female BCS receiving AI ± GnRH analogues; menopause, GSM signs/symptoms, dyspareunia, and vaginal pH ≥ 5; negative human papillomavirus; and willingness to have sex.

The exclusion criteria included the use of vaginal moisturizers and/or lubricants in the last month; vaginal hormonal treatment in the last 6 months; radiofrequency, laser treatment, hyaluronic acid, and lipofilling in the vagina in the last 2 years; and ospemifene treatment. In addition, women complaining with intraepithelial neoplasm of the low genital tract, active genital tract infection, current or past genital cancer, and pelvic organ prolapse stage ≥ II on examination were also excluded.

Written informed consent was obtained from all the participants, and the trial was approved by the ethical committee of the hospital (HCB/2019/0786).

2.3. Materials. Epidemiological variables, BC variables, and mental health status were recorded. Vaginal health was assessed with the Vaginal Health Index (VHI). A final score ≤15 is indicative of vulvovaginal atrophy (range 5–25) [14].

Sexual health was assessed with a self-reported FSFI questionnaire [15], a generic sexual questionnaire validated for cancer survivors [16] and for the Spanish population [17]. It assesses 6 sexual dimensions (desire, arousal, lubrication, orgasm, satisfaction, and pain) and global sexual function (range 2–36), being higher scores indicative of better sexual function. A cutoff ≤26.55 identifies women at risk of FSD [18]. A specific cutoff of ≤21.7 has also been proposed for the Spanish population [19]. Only desire domain can be effectively used in women who are not currently sexually active [20]. According to DSM 5, a sexual disorder should be considered in the presence of clinically significant disturbance. As FSFI does not report on disturbance, we also asked patients to fill in a visual analogue scale (VAS) (range 0–10) about disturbance by their sexual life, we classified disturbance as clinically significant when women scored >3. Dyspareunia was also assessed in all patients (sexually active and inactive) at the baseline visit according to their last vaginal sexual activities. Moreover, patients filled in the Spanish version of Body Image Scale (S-BIS) [21] (range 0–30); the higher the score, the greater the concern regarding body image. All participants reported on sexual activity/inactivity, no sexual activity/month, sexual behavior, and type of sexual activity and relationship status. This methodology allowed us to get a basic sexual assessment for the overall sample.

A specific appointment with two sexual medicine clinicians was offered as an optional visit to all the participants within the study to get a specialized sexual assessment. It included a sexual health semistructured interview to assess both their past and current sexual life as well as their future sexual expectations. FSD was considered when the woman reported clinically significant distress in relation with her sexual symptom. Satisfaction with sexual life was also recorded.

2.4. Statistical Analysis. Statistical analyses were performed with the Software for Statistics and Data Science release 15.1 (STATA, College Station, Texas: StataCorp LLC). A descriptive analysis of all data was performed.

Normal distribution of the sample was evaluated using the Shapiro–Wilk test. In normally distributed variables, parametric tests were used. In nonnormallly distributed

variables, nonparametric tests were used. Continuous variables were compared using the independent or paired-samples *T*-test/Wilcoxon signed-rank test and presented as mean ± standard deviation. $p < 0.05$ was considered statistically significant.

3. Results

We included 84 women until June 2021, but one withdrew their consent due to personal issues before the baseline assessment. Sample characteristics are described in Table 1. On average, patients had been diagnosed with BC 4.1 years before (between January 1992 and January 2021). Considering the surgical treatment, 41 participants (50%) had received conservative management, 10 (12.2%) mastectomy without immediate reconstruction (50% had undergone delayed breast reconstruction before the inclusion), and 31 (37.8%) mastectomy with immediate reconstruction. Only one-third of our sample had a metabolic disease. Two out of five women had a mental health issue, which was previous to the BC diagnosis in 54.5% of the cases, and one third of them had been receiving pharmacological management for this reason. Comparing sexually active to inactive women, a statistically significant difference on age, VHI, and mental health was found.

Basic sexual characteristics of our sample are described in Table 2. The sexual activity rate was 71.1%, being the most frequent sexual behavior, a combination of nonvaginal and vaginal sex. Solo-sex sexual activity was reported by one out of three of our patients (62.5% partnered women) including vaginal sex in 35.7% of them. All FSFI dimensions in sexually active women showed a lower score, especially pain (inclusion criteria) and desire. We also analysed intensity of dyspareunia among sexually active women with versus without GnRh analogues, but no statistically significant difference was found ($p = 0.677$). Sexually inactive women had a statistically significant higher impairment of FSFI desire dimension and dyspareunia VAS than their sexually active peers.

Women rejected sexual counseling ($N = 16$) due to personal beliefs, shame, or lack of motivation on sexuality. No statistically significant differences were found between women who accepted and rejected the specialized sexual assessment regarding baseline characteristics or basic sexual assessment (Appendices 1 and 2). Three women could not attend the specific sexual consultation, despite their initial interest. Regarding the sexuality of the evaluated women (Table 3), most of the patients reported worsening of their sexual life after BC diagnosis and treatments, while only 26% maintained their good sexual life. All women with previous FSD maintained their symptoms. Ten women reported a history of sexual violence, of whom one had suffered both child sexual abuse and partnered-related sexual violence. According to the qualitative body image assessment, half of those women had a body image alteration, comprising a combination of at least 2 dimensions in 4 of them (1 patient = genital + body image affected and 3 patients = breast + body image affected). Nonsexually active women were more unsatisfied with their past and current sexual life than their sexually active peers. According to the specialized sexual assessment, the sexual function of sexually active women was impaired in 72.1%, as they reported unsatisfaction with their sexual life. The FSD rate with the proposed FSFI Spanish cutoff was 70.2%, whereas it was 91.5% with the original cutoff.

We found some discrepancies between the basic sexual assessment with FSFI compared to the specialized sexual assessment in 32.8% of the women who attended sexual counseling. First of all, regarding sexual behavior: 6 women reported sexual inactivity on the FSFI despite they engaged in solo-sex sexual activity and 1 in partnered sexual activity, whereas 3 women reported FSFI as being sexually active but explained sexual inactivity (frequency = 0 and also in a sexual interview). We were able to repeat the FSFI questionnaire in almost all of these participants, except for 3 who were not included in the FSFI analysis. Second, regarding sexual function, 2 women reported FSFI referring to partnered sex but could not reflect solo-sex sexual response which was pleasurable. Nine women could not express in their answer to the FSFI questionnaire the difference in their sexual response depending on the kind of sexual activity (intercourse, manual stimulation, oral sex, use of lubricant, toy sex use, solo-sex…) but clearly stated having global pleasurable sexuality except for vaginal sex during the interview. One woman reported greater impairment during the interview, not only regarding dyspareunia as in FSFI but also lubrication and orgasm dimensions.

4. Discussion

4.1. Specialized Sexual Assessment. Broad literature has been published about sexual issues among BCSs and their interest on sexual health care. In a recent French cross-sectional observational study [22], the authors underlined that all patients, regardless of age, BC stage, and ongoing treatment, are concerned about the possible impact of BC treatments on sexual function and are interested in maintaining a good sex life. A systematic review [23], carried out to investigate facilitators to seeking help in BCS with sexual problems, found women who suggested easier access to sexual health services, more open provider-initiated discussions, and more easily accessible information for patients and their partners. According to that, it was not surprising that most of our patients decided to attend the specialized sexual assessment. The request for sexual attention was similar among sexually active and inactive women suggesting that sexual counseling should be offered to both.

To our knowledge, this is the first study on sexuality of BCS including sexual semistructured interviews instead of isolated validated sexual questionnaires prior to laser therapy for GSM [9, 24]. Most of the previous publications mainly focused on the FSFI questionnaire, which had clear limitations (e.g., not applicable in sexually inactive women in the last 4 weeks, heterosexual bias, sexuality focused on penile-vaginal intercourse, and solo sex not evaluated) [12, 25, 26]. Having implemented a combination of qualitative and quantitative methods to assess women's sexuality has allowed us to acknowledge the real impact on sexuality

Table 1: Baseline characteristics of the overall sample, as well as according to sexual activity.

		All patients ($N = 83$)	Sexually active ($n = 59$)	Non-sexually active ($n = 24$)	p value
Age (years), mean ± sd (range)		52.9 ± 8.6 (33–70)	**51.6 ± 8.7 (33–70)**	**56 ± 7.7 (42–67)**	**0.0361**
Ethnicity	(i) White/Caucasian, *n* (%)	77 (92.8)	55 (93.2)	22 (91.7)	0.562
	(ii) Latino American/Hispanic, *n* (%)	6 (7.2)	4 (6.8)	2 (8.3)	
Occupation	(i) Unemployed, *n* (%)	4 (5.1)	3 (5.5)	1 (4.3)	0.4913
	(ii) Employed, *n* (%)	39 (50)	27 (49.1)	12 (52.2)	
	(iii) Sick leave, *n* (%)	15 (19.2)	11 (20)	4 (17.4)	
	(iv) Incapacity, *n* (%)	9 (11.5)	5 (9.1)	4 (17.4)	
	(v) Retired, *n* (%)	11 (14.1)	9 (16.4)	2 (8.7)	
	Missing, *n*	5	4	1	
Smokers, *n* (%)		10 (12.1)	7 (11.9)	3 (12.5)	0.9367
Children	(i) No, *n* (%)	20 (24.4)	13 (22.4)	7 (29.2)	0.5230
	(ii) Yes, *n* (%)	62 (75.6)	45 (77.6)	17 (70.8)	
	Missing, *n*	1	1	0	
BMI (kg/m^2), mean ± sd (range)		24.5 ± 4.1 (18–40.9)	24.1 ± 3.8 (18–34.2)	25.6 ± 4.7 (19.1–40.9)	0.1158
Age of menopause (years), mean ± sd (range)		45.4 ± 6.4 (22.5–57)	45.1 ± 5.7 (31–56)	46.2 ± 8 (22–56)	0.4827
(i) Natural menopause, *n* (%)		29 (35.4)	17 (29.3)	12 (50)	0.0762
(ii) Induced menopause, *n* (%)		53 (64.6)	41 (70.7)	12 (50)	
Missing, *n*		1	1	0	
Serum oestradiol (pg/ml), mean ± sd (range)		13.0 ± 35.5	**7.2 ± 13.8**	**35.2 ± 7.3**	**0.03**
Metabolic diseases	(i) Hypertension, *n* (%)	18 (21.9)	14 (24.1)	4 (16.7)	0.56
	(ii) Diabetes, *n* (%)	4 (4.8)	3 (5.2)	1 (4.2)	0.66
	(iii) Dyslipidemia, *n* (%)	18 (21.9)	12 (20.7)	6 (25)	0.77
	Missing, *n*	1	1	0	
Mental health	(i) No mental health issues, *n* (%)	50 (60.3)	**41 (69.5)**	**9 (37.5)**	**0.023**
	(ii) Non-pharmacological management, *n* (%)	6 (7.2)	**3 (5.1)**	**3 (12.5)**	
	(iii) Pharmacological management, *n* (%)	27 (32.5)	**15 (25.4)**	**12 (50)**	
BC stage	(i) Stage I, *n* (%)	32 (38.6)	21 (35.6)	11 (45.8)	0.347
	(ii) Stage II, *n* (%)	43 (51.8)	32 (54.2)	11 (45.8)	
	(iii) Stage III, *n* (%)	7 (8.4)	6 (10.2)	1 (4.2)	
	(iv) Stage IV, *n* (%)	1 (1.2)	0	1 (4.2)	
Treatment modalities	(i) Hormonal therapy, *n* (%)	83 (100)	59 (100)	24 (100)	—
	(ii) GnRh analogues, *n* (%)	28 (34)	**24 (40.6)**	**4 (16.7)**	**0.04**
	(iii) Surgery, *n* (%)	82 (98.8)	59 (100)	23 (95.8)	0.539
	(iv) Chemotherapy, *n* (%)	67 (80.7)	49 (83.1)	18 (75)	0.4054
	(v) Radiotherapy, *n* (%)	60 (72.3)	43 (72.88)	17 (70.8)	0.8523
VHI, mean ± sd (range)		10.5 ± 3.4 (0–21)	**11.4 ± 3.5 (7.0–21.0)**	**8.9 ± 2.8 (0–14)**	**0.001**
Vaginal pH, mean ± sd (range)		7.7 ± 0.9 (5–9)	7.6 ± 0.9 (5–9)	7.8 ± 0.8 (6–9)	0.7118

The bold values indicate the significant difference.

Table 2: Basic sexual assessment of the overall sample, as well as according to sexual activity.

			All patients ($N = 83$)	Sexually active ($n = 59$)	Non-sexually active ($n = 24$)	p value
Sexually active women, n (%)			59 (71.1)	59 (100)	0	
Sexual frequency (times/month), mean ± sd (range)			2.5 ± 3.2 (0–16)	3.6 ± 3.2 (0–16)	0	
Missing, n			3	3		
Type of sexual activity	(i) None, n (%)		24 (32.4)	—	24 (100)	
	(ii) Solo sex, n (%)		11 (14.9)	11 (22)	—	
	(iii) Partnered sex, n (%)		26 (35.1)	26 (52)	—	
	(iv) Both, n (%)		13 (17.6)	13 (26)	—	
	Missing, n		9	9	—	
Sexual behavior	(i) None, n (%)		24 (32.4)	—	24 (100)	
	(ii) No vaginal sex, n (%)		15 (20.3)	15 (30)	—	
	(iii) Only vaginal sex, n (%)		4 (5.4)	4 (8)	—	
	(iv) Both, n (%)		31 (41.9)	31 (62)	—	
	Missing, n		9	9	—	
Relationship	(i) Single, n (%)		14 (17.7)	9 (16.1)	5 (21.7)	
	(ii) Partnered not cohabitant, n (%)		11 (13.9)	8 (14.3)	3 (13.1)	
	(iii) Partnered cohabitant, n (%)		54 (68.4)	39 (69.6)	15 (65.2)	0.078
	Missing, n		4	3	1	
FSFI*#	Dimensions mean ± sd (range)	(i) Desire	2.2 ± 0.9 (1.2–4.8)	**2.4 ± 1 (1.2–4.8)**	**1.6 ± 0.6 (1.2–3)**	
		(ii) Arousal	*2.9 ± 1.6 (0–6)*	3.6 ± 1.3 (0–6)	*1.2 ± 0.8 (0–2.4)*	
		(iii) Lubrication	*2.5 ± 1.7 (0–6)*	3.3 ± 1.4 (0–6)	*0.6 ± 0.7 (0–2.4)*	
		(iv) Orgasm	*2.8 ± 2 (0–6)*	3.8 ± 1.5 (0.8–6)	*0.4 ± 0.6 (0–2)*	
		(v) Satisfaction	*2.9 ± 2 (0–6)*	3.7 ± 1.6 (0.4–6)	*0.7 ± 0.6 (0–2)*	**0.0013**
		(vi) Pain	*1.7 ± 1.4 (0–6)*	2.3 ± 1.2 (0–6)	*0.3 ± 0.5 (0–1.2)*	
	Total score, mean ± sd (range)		*15 ± 7.8 (1.2–29.6)*	19 ± 4.9 (7.8–29.6)	*4.7 ± 2.7 (1.2–10.1)*	
	FSD rate, n (%)	(i) FSFI ≤ 26.55	*79 (95.2)*	54 (93.1)	*22 (100)*	
		(ii) FSFI ≤ 21.7	*64 (77.1)*	40 (68.9)	*22 (100)*	
VAS dyspareunia, mean ± sd (range)#			7.5 ± 2.3 (2–10)	**7.1 ± 2.1 (2–10)**	**8.6 ± 2.3 (3–10)**	**0.0114**
Missing, n			2	0	2	
VAS disturbance sexual life, mean ± sd (range)			6.3 ± 2.5 (0–10)	6.1 ± 2.6 (0–10)	6.9 ± 2.4 (1–10)	0.2695
(i) VAS > 3 (%)			62 (84.9)	44 (83)	17 (85)	0.8413
Missing, n			10	6	4	
BIS, mean ± sd (range)			10	10.6 ± 7.2 (1–29)	9.25 ± 6.8 (0–23)	0.4308

*3 FSFI questionnaires were excluded from the analysis because they corresponded to women whose sexual activity status did not correlate with the answers in the questionnaire #Significant differences have been adjusted by age for possible interactions, persisting statistically significant differences. Italic data: data which include nonsexually active women FSFI questionnaires were highlighted in italics, as it should not be considered for the interpretation of the results. The bold values indicate the significant difference.

after BC diagnosis and treatment. We found two out of three women who engaged in solo-sex sexual behavior had a partner. Moreover, most of the women with partnered sex and solo sex reported a pleasurable experience with the last one (mainly based on nonvaginal sexual activities). However, only a few sexually active couples in our sample had adapted their sexuality to the most pleasurable types of sexual activities without vaginal sex, despite the high intensity of dyspareunia, which can lead to sexual inactivity. That was in line with findings of Gilbert et al. [27] who found only 16% of participants were able to renegotiate their sexual relationship, having adherence to "coital imperative" and sexual relationship problems prior to cancer as the main difficulties.

In our sample, among 78.7% of women referred at baseline had some impairment in their sexuality and a quarter had a previous history of FSD. Moreover, dyspareunia reactivates negative emotions, feelings, and sensations in two out of ten women with a past history of sexual violence, presuming that this precedent could affect the evolution of sexual outcomes in these patients. Awareness of the information mentioned above is crucial when measuring sexual improvements after any therapy, as it is clear that women with a previous history of FSD might respond differently to interventions related to sexuality.

In addition, as it has been reported in other clinical conditions [28], a correlation between mental health status and sexual inactivity was found in our sample, especially in those patients with pharmacological management, a fact that raises awareness of the need for a multidisciplinary approach from a biopsychosocial perspective. Moreover, nearly, half of the participants developed their mental health issue after BC diagnosis and treatments; likewise, three-quarters of our sample worsen their sexual life in such a moment. So, for further studies, an early intervention from the beginning of the oncological process will be taken into account.

4.2. Sexual Activity. Nearly, one out of three BCSs with GSM receiving AI were nonsexually active, and among those who were sexually active, sexual frequency was low. These data are similar to the 32.9% rate of sexual inactivity in a case-control study [29], which showed that BCSs under hormonal treatment were characterized by diminished or absent sexual activity compared to the control group. In our study, age, severe GSM, and lower desire seemed to be related to sexual inactivity, whereas no correlation with body image or metabolic diseases was observed. However, factors for sexual inactivity or diminished usual sexual frequency could be diverse and probably multiple for each patient [30] and should be considered under a biopsychosocial framework.

Table 3: Specialized sexual assessment of women who attended the sexual counseling visit, as well as according to sexual activity.

			Accepted sexual counseling ($n = 67$)	Sexually active ($n = 48$)	Non-sexually active ($n = 19$)	p value
Sexual orientation	(i) Heterosexual, n (%)		60 (98.4)	42 (97.7)	18 (100)	0.705
	(ii) Bisexual, n (%)		1 (1.6)	1 (2.3)	—	
	(iii) Homosexual, n (%)		—	—	—	
	Missing, n		6	5	1	
Past sexual life[#]	(i) Satisfied sexual life, n (%)		50 (82)	**38 (88.4)**	**12 (66.7)**	**0.039**
	(ii) Unsatisfied sexual life, n (%)		11 (18)	**5 (11.6)**	**6 (33.3)**	
	Missing, n		6	5	1	
Current sexual life[#]	(i) Satisfied sexual life, n (%)		13 (21.3)	**12 (27.9)**	**1 (5.6)**	**0.018**
	(ii) Unsatisfied sexual life, n (%)		48 (78.7)	**31 (72.1)**	**17 (94.4)**	
	Missing, n		6	5	1	
Sex toy use	(i) None, n (%)		35 (57.4)	22 (51.2)	13 (72.2)	0.482
	(ii) Occasional (noneffective), n (%)		6 (9.8)	5 (11.6)	1 (5.6)	
	(iii) Occasional (effective), n (%)		11 (18)	8 (18.6)	3 (16.6)	
	(iv) Usually, n (%)		9 (14.8)	8 (18.6)	1 (5.6)	
	Missing, n		6	5	1	
History of sexual violence	(i) None, n (%)		30 (75)	20 (74.1)	10 (76.9)	0.09
	(ii) Child sexual abuse, n (%)		8 (20)	6 (22.2)	2 (12.5)	
	(iii) Partnered related, n (%)		2 (5)	0	2 (12.5)	
	(iv) Non-partnered related n (%)		1 (2.5)	1 (3.7)	0	
	Missing, n		27	21	6	
Qualitative body image	(i) Not affected, n (%)		30 (49.2)	20 (46.5)	10 (55.6)	0.278
	(ii) Genital image affected, n (%)		6 (9.8)	1 (2.3)	5 (27.8)	
	(iii) Breast image affected, n (%)		11 (18)	10 (23.3)	1 (5.6)	
	(iv) Body image affected, n (%)		18 (29.5)	15 (34.9)	3 (16.6)	
	Missing, n		6	5	1	
FSFI*[#]	Dimensions, mean ± sd (range)	(i) Desire	2.2 ± 1 (1.2–4.8)	**2.4 ± 1 (1.2–4.8)**	**1.6 ± 0.6 (1.2–3)**	**0.001**
		(ii) Arousal	*3 ± 1.6 (0–6)*	3.6 ± 1.3 (1.2–6)	*1.3 ± 0.7 (0–2.4)*	
		(iii) Lubrication	*2.7 ± 1.7 (0–6)*	3.4 ± 1.3 (1.2–6)	*0.6 ± 0.8 (0–2.4)*	
		(iv) Orgasm	*2.8 ± 2 (0–6)*	3.6 ± 1.5 (0.8–6)	*0.4 ± 0.6 (0–2)*	
		(v) Satisfaction	*2.7 ± 1.9 (0–6)*	3.4 ± 1.7 (0.4–6)	*0.8 ± 0.6 (0–2)*	
		(vi) Pain	*1.7 ± 1.3 (0–6)*	2.2 ± 1.2 (0–6)	*0.3 ± 0.5 (0–1.2)*	
	Total score, mean ± sd (range)		*15 ± 7.7 (1.6–29.6)*	18.6 ± 5.3 (7.8–29.6)	*5 ± 2.6 (1.6–10.1)*	
	FSD rate, n (%)	(i) FSFI ≤ 26.55	*63 (93.8)*	43 (91.5)	*17 (100)*	
		(ii) FSFI ≤ 21.7	*52 (78.1)*	33 (70.2)	*17 (100)*	

*We excluded 3 FSFI questionnaires from the analysis of those women whose sexual activity status does not correlate. [#]Significant differences have been adjusted by age for possible interactions, persisting statistically significant differences. Italic data: data which include nonsexually active women FSFI questionnaires were highlighted in italics, as it should not be considered for the interpretation of the result. The bold values indicate the significant difference.

4.3. Sexual Function. The mean FSFI total score and dimensions were lower, and the rate of sexual dysfunction was greater in BCS, comparing our results to published studies on healthy women [14, 18]. Among sexually active women, nearly, all of them (93.1%) were sexually affected according to the FSFI cutoff ≤26.55, whereas according to the Spanish cutoff (≤21.7), they were less than three-quarters (68.9%). In addition, neither of these rates correlated with sexual disturbance referred by our patients (83%), probably because FSFI does not reflect distress, reasons for sexual dysfunction, the partner's contribution, the role of artificial lubricants, solo-sexual expression, nonvaginal sex activities, and precancer functioning [31].

According to a systematic review and meta-analysis [9], which was focused on intravaginal energy-based devices and sexual health of female cancer survivors based on 8 articles and 274 patients (mostly BCS receiving CO_2 laser therapy), only 1 study with 8 participants provided specific data for each domain of women's sexuality. Recent publications [32, 33] have also included the score of each FSFI domain, showing a low score for all the dimensions at the baseline visit. Unfortunately, both studies reported FSFI scores of the overall sample, including sexually inactive participants (50% of both samples), a fact that drastically underestimates women's sexual functioning scores, increases the variance of total and domain scores, potentially inflates FSFI score differences between groups with and without FSD, and undermines the assessment of sexual dysfunction when using established clinical cutoffs [34]. Following Meston et al. [34] recommendations for studies that do not exclude sexually inactive women, the calculation of total FSFI scores and relevant domain scores (on all but the desire domain) should be limited to those who have not indicated a zero score on any of the FSFI items. Hence, we showed our sexual data for the overall sample but also according to the sexual activity of our participants. Despite the fact that, in our population, pain was one of the most impaired dimensions, similarly to desire, our results showed sexual arousal, lubrication, orgasm, and satisfaction were also affected, in line with previously published literature on BCS population [35, 36]; therefore, dyspareunia is not the only dimension which affects sexual function and sexual activity in BCS with GSM receiving AI.

Worthy of note is the importance of assessing body image self-perception as part of the comprehensive sexual care before any treatment. In line with previously published articles [2, 36], we found body image self-perception is affected in at least half of our sample. The specialized sexual assessment allowed us to better understand those women with affected body image. Despite breast image impairment is present in one-third of our participants, overall body image impairment (hair/weight/silhouette. . .) secondary to menopause or chemotherapy is most relevant from the patient's perspective.

4.4. Sexual Satisfaction. Only one in five women who attended the specialized sexual consultation had a satisfactory sexual life, a little bit below 30% found in the BEROSE study [22], a cross-sectional observational study among 318 BCSs. Similarly, in both studies, the satisfaction rate was higher before BC diagnosis (our study: 74.6%; BEROSE study: 83%). In their exploratory analysis, only tumor stage significantly affected satisfaction with current sexuality.

Among sexually active women who attended the specialized sexual assessment, nearly, three out of four were unsatisfied with their current sexual life (72.1%) which was similar to the FSD rate (70.1%) according to the FSFI Spanish cutoff (≤21.7). However, it did not correlate with the FSD rate according to ≤26.55 original cutoff (91.5%). These findings highlight how sociocultural differences may affect the interpretation of results from validated questionnaires; therefore, for a better assessment of sexuality, a combination of quantitative and qualitative measures, such as a clinical interview, should be recommended [31, 37]. There are an increasing number of publications which encourage us to investigate cross-cultural properties of FSFI and to assess the generalizability of the scoring approach across different countries and cultures [12, 34].

4.5. Study Strengths and Limitations. The main strength of our study lies in the combination of quantitative and qualitative sexual health assessment, which allowed us not only to evaluate sexually active participants (with and without partner) but also those nonsexually active. In addition, this qualitative analysis is essential to establish a framework that acknowledges the complex and multifactorial sexual impairment in BCS from a biopsychosocial perspective. Moreover, this analysis also benefits from the widespread sexual assessment previous to any intervention including past sexual life, unknown in most of the studies. Despite the FSFI questionnaire analysis being performed in the overall sample, this is the first study where sexually inactive subjects were excluded for the interpretation of FSFI results.

We are aware about some limitations:

(i) The sample of women reached may not represent the general population of BCS, as nowadays with BC molecular classification there are many patient profiles, defining those with GSM receiving AI a very specific subgroup, exposed to adverse effects regarding genital physiology and the central nervous system that impact on sexuality by multiple mechanisms. This fact may hinder to stablish causality and the generalization of our results.

(ii) Most of our participants were Caucasian, employed, and heterosexual, which may complicate the extrapolation of our results to a more diverse population.

(iii) The single-center design was also a limitation.

(iv) Even though within the sample size calculation, the small sample size may influence the interpretation of our results. However, it is worth noting there were some missing data regarding sexual outcomes.

(v) The use of the FSFI questionnaire to evaluate women's sexuality has some limitations as was discussed above despite that we decided to use FSFI,

since it is the mostly used by studies on sexual function in women with cancer [38]. However, to overcome the FSFI limitations, we also considered qualitative data, excluded sexually inactive women from result interpretation, and used not only the original cutoff of 26.55 but also the specific cutoff described for the Spanish population [18].

(vi) Androgens may play a role in female genital tissue improving GSM symptoms as it has an anti-inflammatory effect, as well as a positive effect on the vaginal muscles and mucosae [39–41]. Unfortunately, we have no data about androgen serum levels in our sample.

4.6. Conclusions. The findings of our study highlight that four out of five BCSs are interested in an evaluation of their sexuality, a piece of information which should be considered when planning the holistic approach to BCS by a multidisciplinary team, especially when there is an aim to treat a sexual symptom. Our study clearly underlined that the majority of BCSs with GSM receiving AI show affectation for their sexuality. These populations are at higher risk of FSD and sexual inactivity, either secondary to dyspareunia or to other sexual issues which affect desire, arousal, lubrication, orgasm, and/or satisfaction. Other biopsychosocial aspects should also be considered, such as body image impairment, relationship issues, or mental health status.

4.7. Clinical Implications. Finally, the wide-ranging nature of the factors, which affect the sexuality of these patients, makes a comprehensive approach necessary in order to guarantee pleasurable sexual experiences. For that reason, in the ongoing RCT, both study groups are receiving a multidisciplinary approach (moisturizers, lubricants, pelvic floor muscle relaxation, vibrator, and sexual counseling). We expect to extend these sexual baseline data at the end of the RCT and to report the specific role of laser therapy on it.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon request.

Ethical Approval

This paper adheres to the law of data protection and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The Ethics Committee Board of Hospital Clinic of Barcelona approved this study (HCB/2019/0786).

Consent

Informed consent was obtained from all individual participants included in the study. The patients gave written informed consent to use its data.

Conflicts of Interest

C. Castelo-Branco declares the following conflicts of interest: Pharmacological Advisory Board, Theramex, Pierre-Fabre Iberia; Pharmacological Speaker, Lacer, Theramex, Shionogi; Medical Society Board, European Society of Gynecology (treasurer). The other authors declare no conflicts of interest.

Authors' Contributions

Sònia Anglès-Acedo was responsible for conceptualization, methodology, investigation, resources, data curation, writing the original draft, writing, reviewing, and editing the manuscript, and supervision. Eduard Mension was responsible for conceptualization, methodology, formal analysis, investigation, resources, data curation, and supervision. Laura Ribera-Torres was responsible for investigation, resources, data curation, and writing, reviewing, and editing the manuscript. Sílvia Gómez Carballo was responsible for resources and data curation. Isabel Matas was responsible for resources and data curation. Marta Tortajada was responsible for resources and data curation. Inmaculada Alonso was responsible for conceptualization, methodology, investigation, resources, supervision, project administration, and funding acquisition. Camil Castelo-Branco was responsible for conceptualization, methodology, investigation, writing, reviewing, and editing the manuscript, supervision, project administration, and funding acquisition. Sònia Anglès-Acedo and Eduard Mension have contributed equally to this work.

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Supplementary Materials

Data comparing women who accepted versus women who rejected specialized sexual assessment regarding baseline characteristics and basic sexual assessment were analysed on Appendices 1 2, respectively. (*Supplementary Materials*)

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