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The relationship between anxiety and vaginal-related sexual health in postmenopausal breast cancer survivors on aromatase inhibitors therapies: a cross sectional study

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Abstract

Purpose—Sexual health problems and anxiety are disruptive symptoms in breast cancer survivors; however, little is known about these symptoms in postmenopausal breast cancer survivors on aromatase inhibitors therapies. This study aimed to determine the relationship between anxiety and vaginal-related sexual health problems in this population.

Methods—We analyzed cross-sectional data from a cohort study of postmenopausal women breast cancer survivors receiving aromatase inhibitors. Vaginal-related sexual health problems were assessed with the Breast Cancer Prevention Trial Symptom Checklist. Anxiety was assessed with the anxiety subscale of the Hospital Anxiety and Depression Scale. We used multivariable logistic regression to evaluate relationship between anxiety and vaginal-related sexual health adjusted for clinical and sociodemographic variables.

Results—Among 974 patients, 305 (31.3%) reported anxiety and 403 (41.4%) had vaginal-related sexual health problems. Compared to those without anxiety, patients with borderline and clinically abnormal anxiety reported higher rates of vaginal-related sexual health problems (36.8% vs. 49% and 55.7% respectively, $p < 0.001$). In multivariate analyses adjusted for clinical and sociodemographic factors, abnormal anxiety was associated with a higher rate of vaginal-related sexual health problems, with adjusted odds ratios of 1.69 (95% CI 1.06–2.70, $p = 0.03$). Vaginal-

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Declarations

Conflict of interest The authors declare the following financial relationships: JJM reports grants received on behalf of Memorial Sloan Kettering Cancer Center from Tibet CheeZheng Tibetan Medicine Co. Ltd. and from Zhongke Health International LLC outside the submitted work. Other authors have no relevant financial or non-financial interests to disclose.

Ethics approval This research was reviewed and approved by the Institutional Review Board of the University of Pennsylvania and the ACC Clinical Trials Scientific Review and Monitoring Committee.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish The authors affirm that human research participants provided informed consent for publication.

related sexual health problems were more frequent among patients who were under 65 years of age, received Taxane-based chemotherapy, reported depression, and were married/living with a partner ($p < 0.05$).

Conclusion—Among postmenopausal breast cancer survivors on aromatase inhibitors therapies, anxiety was significantly associated with vaginal-related sexual health problems. As treatments for sexual health problems are limited, results suggest that psychosocial interventions for anxiety could potentially be adapted to simultaneously address sexual health needs.

Keywords

Anxiety; Sexual health; Vaginal-related sexual health problems; Breast cancer; Breast cancer survivors; Postmenopausal; Aromatase inhibitors

Introduction

Sexual health problems, such as vaginal dryness and pain with intercourse, are common yet under-diagnosed and under-treated symptoms that diminish breast cancer survivors' quality of life and wellbeing [1–5]. Breast cancer survivors are at a greater risk of vaginal-related sexual health problems than the general population due treatment-induced hormonal changes commonly seen with adjuvant aromatase inhibitor (AI) therapies [2, 3, 6]. This issue is particularly important for women with hormone receptor-positive tumors who receive endocrine treatments [7, 8] as a standardized care [9], and for those with chemotherapy-induced premature menopause [7, 10]. Despite the high prevalence in this patient population, little research has explored clinical or sociodemographic correlates of sexual health problems, which could help illuminate survivors' needs and potential interventions [11].

Anxiety is another common symptom among breast cancer survivors. Limited research suggests that anxiety and sexual health problems frequently co-occur in this population [5, 12–19]. For example, in a study of 167 breast cancer survivors (mean age 60.8; 97.1% female), half of patients with anxiety and/or depression (72.4%) also reported sexual disorders (35.9%) [19]. Similarly, in a cohort of 360 sexually active young female breast cancer survivors (age 22–50), greater severity of sexual health problems was associated with poorer mental health [20]. However, to our knowledge, no studies have examined the relationship between anxiety and vaginal-related sexual health problems in postmenopausal breast cancer survivors on AI.

To address this critical knowledge gap, we aimed to determine the relationship between anxiety and vaginal-related sexual health problems in a large sample of postmenopausal breast cancer survivors on AI therapies. We further aimed to identify other clinical and sociodemographic factors potentially associated with vaginal-related sexual health problems. Our findings illuminate the clinical needs of this large, growing population and contribute new knowledge to inform screening, as well as symptom management interventions.

Methods

Study design and population

We analyzed cross-sectional data from the Wellness After Breast Cancer (WABC) study, which focused on overall symptom burden and its effects on clinical outcomes in 1072 postmenopausal breast cancer survivors on AI therapy [21]. Participants were recruited from the Abramson Cancer Center (ACC) of the University of Pennsylvania (Philadelphia, PA) between November 2011 and April 2015. Patients were eligible if they were: (1) English speaking; (2) postmenopausal women with a stage 0 to III hormone receptor-positive breast cancer; (3) users of a third-generation AI; and (4) had finished chemotherapy, radiotherapy, and/or surgery at least 1 month prior to study enrollment. The Institutional Review Board of the University of Pennsylvania and the ACC Clinical Trials Scientific Review and Monitoring Committee approved the study. Details about the study protocol are described elsewhere [21].

The current study is a secondary analysis of WABC data. We included all participants who answered at least 1 of 2 sexual health problems questions (i.e., vaginal dryness and/or pain with intercourse), resulting in a sample of 974 participants (Table 1).

Vaginal-related sexual health problems (primary outcome)

The primary outcome was vaginal-related sexual health problems as measured by the vaginal problems subscale on the Breast Cancer Prevention Trial (BCPT) Symptom Checklist [22]. The BCPT is a valid and reliable measure commonly used in women with breast cancer (Cronbach's coefficient for the vaginal problems subscale is 0.79) [22]. Patients use a 5-point Likert scale (0 = not at all; 1 = slightly; 2 = moderately; 3 = quite a bit; 4 = extremely) to rate the extent to which they were bothered by each of two symptoms: vaginal dryness and pain with intercourse during the prior 4 weeks. Participants rating either symptom as a 2 or higher were classified as having vaginal-related sexual health problems. Both symptoms are common indicators of sexual health in breast cancer survivors [11, 23].

Anxiety (primary exposure)

The primary exposure was anxiety as measured by the Hospital Anxiety and Depression Scale (HADS)—Anxiety subscale [24]. This 14-item widely used instrument measures symptoms of anxiety and depression on two 7-item subscales, HADS Anxiety and HADS Depression [25, 26] (Cronbach's alpha 0.87 and 0.81 respectively [27]). Items are scored on a 4-point scale ranging between 0 and 3 and summed for each subscale. Score cutoffs are 0–7 (normal), 8–10 (borderline), and ≥ 11 (clinically abnormal) [24].

Covariates

We included sociodemographic (age, race, ethnicity, education level, and marital status), and clinical data (cancer stage, years since diagnosis, cancer treatment type, and type of aromatase inhibitors treatment and years of aromatase inhibitors use, BMI, depression) as covariates.

Statistical analysis

Descriptive statistics were calculated as frequencies and percentages. We used Chi-square tests to assess the relationship between sexual health problems and anxiety, and other clinical and sociodemographic variables. Depression variable was dichotomized into "No, HADS < 8" and "Yes, HADS ≥ 8) versus the original 3-items: "No, HADS < 8", "Borderline, HADS, 8–10", and "Abnormal, HADS ≥ 11" because of small number of participants had abnormal depression. Bivariate analyses examined whether anxiety and sociodemographic and clinical characteristics were associated with the primary outcome. Variables associated with the primary outcome at the p value < 0.10 in bivariate analyses were included in multivariable logistic regression analyses. Results are presented as adjusted odds ratios (AOR) for multivariate logistic regression analyses with 95% confidence intervals (CI). All statistical analyses were conducted using STATA (Windows version 12.0, StataCorp LLC, College Station, TX, USA).

Results

Patient characteristics

Among the 974 participants in the study, the mean age was 62.3 (SD 9.5) years. The majority were white (83.8%), non-Hispanic or Latino (97.5%), with college education or above (81.2%), and married or living with a partner (64.8%). Additional patient characteristics are presented in Table 1.

Prevalence of anxiety and vaginal-related sexual health problems

Of 974 study participants, 190 (19.5%) reported borderline anxiety and 115 (11.8%) reported abnormal anxiety. In total, 403 (41.4%) participants reported vaginal-related sexual health problems, with vaginal dryness experienced by 380 (39.0%) and pain with intercourse by 271 (29.1%) participants. Table 1 summarizes the prevalence of vaginal-related sexual health problems among different sub-groups of patients based on sociodemographic and clinical characteristics.

The relationship between anxiety and vaginal-related sexual health problems

Among 190 participants with borderline anxiety, 93 (64%) also reported vaginal-related sexual health problems, and among 115 participants with abnormal anxiety, 64 (55.7%) reported vaginal-related sexual health problems. Compared to those without anxiety, patients with borderline and clinically abnormal anxiety reported higher rates of sexual health problems (36.8% vs. 49% and 55.7% respectively, $p < 0.001$). Bivariate analyses (Table 2), indicated that higher anxiety scores were associated with vaginal-related sexual health problems, indicating that patients with greater severity of anxiety were more likely to report vaginal-related sexual health problems. In our final logistic regression model (Table 2), vaginal-related sexual health problems were significantly associated with more severe symptoms of anxiety (AOR = 1.69, 95% CI 1.06–2.70) adjusting for other sociodemographic and clinical variables.

Sociodemographic and clinical factors associated with vaginal-related sexual health problems

In addition to anxiety, several other sociodemographic and clinical factors were associated with vaginal-related sexual health problems (Table 2). Compared to patients 65 years and older, sexual health problems were significantly associated with younger age groups: 52–64 (AOR = 2.11, 95% CI 1.39–3.20) and 51 and younger (AOR = 1.80, 95% CI 1.04–3.09). Vaginal-related sexual health problems were also more likely to be reported by patients who had undergone Taxane-based chemotherapy (AOR = 1.47, 95% CI 1.09–1.98), reported depression (AOR = 1.80, 95% CI 1.13–2.87), and were married or living with a partner (AOR = 1.80, 95% CI 1.32–2.45). Non-white and overweight and obese (BMI of 30 or above) participants were less likely to report vaginal-related sexual health problems (AOR = 0.65, 95% CI 0.43–0.98, and AOR = 0.62, 95% CI 0.44–0.87 respectively). Older age (> 70 years), education level, and normal BMI had no significant associations with vaginal-related sexual health problems.

Discussion

In the analysis of 974 postmenopausal breast cancer survivors receiving AI, we identified that clinically abnormal anxiety and vaginal-related sexual health problems were prevalent and characterized by an association that remained statistically significant after adjusting for covariates. We also identified several other co-variables such as receipt of Taxane-based chemotherapy, younger age (< 64 years), depression and marital status that were associated with vaginal-related sexual health problems. These findings establish the association between anxiety and vaginal-related sexual health problems in postmenopausal breast cancer survivors that warrants further research. Moreover, cancer-related sexual health problems should be further researched and managed recognizing the multifactorial and bio-psychosocial nature.

The prevalence of vaginal-related sexual health problems in our study population was high (over 41%), which is consistent with findings of other epidemiologic studies of long-term breast cancer survivors [28, 29]. However, previous studies relied on smaller sample sizes (i.e., 83, and 134, respectively) and did not focus on postmenopausal breast cancer survivors on AI. As hormonal treatment including AIs is an essential treatment component of breast cancer treatment and survivorship care for women with hormone receptor positive breast cancer, our findings highlight the clinical importance of screening for sexual health problems in this population. The American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline recommends that primary care physicians assess and manage sexual health among female adult breast cancer survivors [30]. This includes screening for signs and symptoms of sexual dysfunction, problems with sexual intimacy, and other contributing factors, and counseling patients regarding treatment options. However, these are low level evidence recommendations, and more research on how best to screen, diagnose, and manage sexual health problems in this population are urgently needed.

Our study demonstrated a significant dose–response relationship between anxiety and vaginal-related sexual health problems in postmenopausal breast cancer survivors on AI.

Although anxiety is a major factor in the etiology of sexual health in the general and breast cancer populations [31–34], the relationship between the two symptoms in postmenopausal breast cancer survivors has seldom been explored [35, 36]. To our knowledge, our study is the largest to examine the association between anxiety and vaginal-related in postmenopausal breast cancer survivors on AI. The relationship between anxiety and vaginal-related sexual health is likely to be bidirectional. First, since anxiety is known to impact perceptions of pain in cancer patients [37, 38], it may increase perception of vaginal dryness and pain with intercourse [33, 34]. Second, increased vaginal-related sexual health problems (e.g., pain with intercourse and vaginal dryness) may also cause elevated levels of anxiety concerning sexual performance or relationship issues, leading to sexual avoidance and lowering quality of life. As there are many more evidence-based interventions for anxiety symptoms rather than sexual health, our finding raises the possibility that addressing anxiety may impact perception and experience of sexual health problems that warrant further research.

We also identified several clinical and sociodemographic risk factors for vaginal-related sexual health problems that convey this issue has multi-factorial etiology and fits into the bio-psycho-social framework of symptom distress. For example, estrogen withdraw to be an important factor in sexual health. In our study, we found that receipt of Taxane-based chemotherapy, lower (< 25) BMI and younger age (< 64 years) are significantly associated with sexual health problems which it is likely due to the drastic decrease in estrogen levels [39, 40]. In addition, we found that patients who reported borderline or worse depression were almost twice more likely to experience vaginal-related sexual health problems, which may be partially due to the adverse effects of antidepressant medication, but also due to stress, trauma, and other psychological burdens that often accompany a breast cancer diagnosis. We also found that vaginal-related sexual health problems are significantly associated with younger age (< 64 years) and marital status, which may be because younger and married/living with partner patients are more likely to be sexually active than those who are older or single. This finding, however, may also be related to reporting bias among different populations [37, 38, 41, 42]. Our study results suggest that incorporating multiple risk factors can aid in more precise diagnosis of sexual health problems and further emphasize the need to identify modifiable risk factors in the development of complex interventions to address this important clinical problem.

Our findings should be considered in light of several limitations. This study is a single-site study with mostly white, stage 0–III, postmenopausal breast cancer survivors receiving AI therapy, and thus not representative of other racial/ethnic groups or survivors with advanced disease. We were unable to test for causality or the temporal relationship through the cross-sectional design of the study. In addition, our data derived from a survey that relied on patient-reported outcomes, which present the inherent risk of recall bias. Furthermore, the 4-week recall period for vaginal-related symptoms as measured by the BCPT Symptoms Checklist may be too long for some patients and too short for patients who have not engaged in sexual activity in the past 4 weeks. There is also a possibility of a social desirability bias in the analyzed sample, since not all participants answered all vaginal-related items. The primary outcome was measured only as vaginal dryness and pain with intercourse and therefore does not capture other important sexual health problems (e.g., loss of sensation,

lack of arousal, sexual activity, or function); however, this measure is a validated instrument. In addition, we did not control for common medications which may affect sexual health, such as high blood pressure medications, benzodiazepines or antidepressants.

Despite these limitations, to our knowledge, our study is the largest study to examine the relationship between anxiety and vaginal-related sexual health problems, in postmenopausal breast cancer survivors on AI. We identified a significant association between anxiety and vaginal-related sexual health after adjusting for covariates. Furthermore, our findings suggest future clinical care and research should consider the interconnection among biological, psychological, and socio-environmental factors affecting sexual health in order to address the needs of this large and growing population of breast cancer survivors.

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Data availability

The data of this study will be available from the corresponding author upon reasonable request.

Abbreviations

ACC	Abramson Cancer Center
AI	Aromatase inhibitor
AOR	Adjusted odds ratio
BCPT	Breast Cancer Prevention Trial Symptom Checklist
BMI	Body mass index
95% CI	95% Confidence interval
HADS	Hospital Anxiety and Depression Scale
WABC	Wellness After Breast Cancer

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Table 1

Participant characteristics

Characteristics	Overall	Vaginal-related sexual health problems*		Vaginal dryness		Pain with intercourse	
	N (%)	*n* (%)	*p*-value**	*n* (%)	*p*-value**	*n* (%)	*p*-value**
Total	974 (100)	403 (41.4)		380 (39.0)		271 (29.1)	
Anxiety			< 0.001		< 0.001		< 0.001
No (HADS < 8)	669 (68.7)	246 (36.8)		231 (34.5)		163 (25.2)	
Borderline (HADS 8–10)	190 (19.5)	93 (49.0)		89 (46.8)		66 (36.9)	
Abnormal (HADS ≥ 11)	115 (11.8)	64 (55.7)		60 (52.2)		42 (39.6)	
Age (years)			< 0.001		< 0.001		< 0.001
> 70	182 (18.7)	44 (24.2)		40 (22.0)		15 (8.7)	
65–70	221 (22.7)	85 (38.5)		82 (37.1)		49 (23.4)	
52–64	452 (46.4)	215 (47.6)		201 (44.5)		153 (35.3)	
< 51	119 (12.2)	59 (49.6)		57 (47.9)		54 (46.2)	
Race			< 0.001		< 0.001		< 0.001
White	816 (83.8)	360 (44.1)		399 (41.5)		248 (31.8)	
Non-White	158 (16.2)	43 (27.2)		41 (26.0)		23 (15.1)	
Ethnicity			0.001		0.001		0.003
Hispanic or Latino	24 (2.5)	18 (75.0)		17 (70.8)		13 (56.5)	
Not Hispanic or Latino	950 (97.5)	385 (40.5)		363 (38.2)		258 (28.4)	
Education level			0.02		0.02		0.04
High school or less	183 (18.8)	62 (33.9)		57 (31.2)		40 (22.7)	
College or above	790 (81.2)	340 (43.0)		322 (40.8)		230 (30.5)	
Marital status			< 0.001		< 0.001		< 0.001
Married, living w/partner	627 (64.8)	300 (47.9)		280 (44.7)		219 (36.1)	
Single, divorced, separated, widowed	340 (35.2)	101 (29.7)		99 (29.1)		50 (15.7)	
BMI			< 0.001		< 0.001		< 0.001
< 25	380 (39.0)	180 (47.4)		171 (45)		136 (37.1)	
25–30	287 (29.5)	123 (42.9)		117 (40.8)		77 (28.6)	
> 30	307 (31.5)	100 (32.6)		92 (30)		58 (19.7)	
Cancer stage			0.89		0.94		0.92

Characteristics	Overall	Vaginal-related sexual health problems*		Vaginal dryness		Pain with intercourse	
	N (%)	*n* (%)	*p*-value**	*n* (%)	*p*-value**	*n* (%)	*p*-value**
0 and I	494 (51.3)	202 (40.9)		194 (39.3)		137 (29.2)	
II	344 (35.7)	143 (41.6)		132 (38.4)		95 (28.5)	
III	125 (13.0)	54 (43.2)		50 (40.0)		36 (30.5)	
Years since diagnosis			0.73		0.73		0.67
> 5 years	176 (18.1)	69 (39.2)		64 (36.4)		48 (28.4)	
2–5 years	372 (38.2)	159 (42.7)		147 (39.5)		109 (30.8)	
< 2 years	426 (43.7)	175 (41.1)		169 (39.7)		114 (27.9)	
Chemotherapy			< 0.001		0.004		< 0.001
No chemo	455 (46.7)	159 (35.0)		153 (33.6)		95 (22.0)	
Chemo without Taxane	97 (10.0)	42 (43.3)		39 (40.2)		27 (29.0)	
Chemo with Taxane	422 (43.3)	202 (47.9)		188 (44.6)		149 (36.6)	
Radiation			0.42		0.37		0.73
No	272 (27.9)	107 (39.3)		100 (36.8)		75 (28.3)	
Yes	702 (72.1)	296 (42.2)		280 (39.9)		196 (29.4)	
Current AI			0.51		0.56		0.83
Anastrozole (Arimidex)	778 (80.3)	328 (42.2)		308 (39.6)		219 (29.6)	
Exemestane (Exemestane)	58 (6.0)	21 (36.2)		19 (32.8)		16 (28.6)	
Letrozole (Femara)	133 (13.7)	51 (38.4)		50 (37.6)		35 (26.9)	
Years of AI use			0.96		0.84		0.68
> 3 years	242 (24.9)	99 (40.9)		91 (37.6)		62 (26.8)	
1–3 years	498 (51.1)	207 (41.6)		195 (39.2)		141 (29.8)	
< 1 year	234 (24.0)	97 (41.5)	0.001	94 (40.2)	0.001	68 (30.1)	0.02
Depression							
No (HADS < 8)	859 (88.2)	339 (39.5)		319 (37.1)		230 (27.9)	
Yes (HADS ≥ 8)	115 (11.8)	64 (55.7)		61 (53.0)		41 (39.1)	

Not all cell values add up due to missing data

*Vaginal-related Sexual Health Problems are defined as vaginal dryness and pain with intercourse

**_p_-values were based on Chi square tests; _p_-value < 0.05 is statistically significant

Table 2

Bivariate and multivariate logistic regression

	Bivariate logistic regression			Multivariate logistic regression		
	OR	**95% CI**	***p*-value**	**AOR**	**95% CI**	***p*-value**
Anxiety						
No (< 8)	–			–		
Borderline (8–10)	1.65	1.19–2.28	0.003	1.36	0.96–1.94	0.08
Abnormal (≥ 11)	2.16	1.45–3.22	< 0.001	1.69	1.06–2.70	0.03
Age						
> 70	–			–		
65–70	1.96	1.27–3.03	< 0.001	1.52	0.96–2.40	0.07
52–64	2.84	1.93–4.19	< 0.001	2.11	1.39–3.20	< 0.001
< 51	3.08	1.88–5.06	< 0.001	1.80	1.04–3.09	0.03
Race						
White	–			–		
Non-white	0.47	0.32–0.69	< 0.001	0.65	0.43–0.98	0.04
Ethnicity						
Hispanic or Latino	–			–		
Not Hispanic or Latino	0.23	0.09–0.58	0.002	0.25	0.09–0.65	0.005
Education level						
High school or less	–			–		
College or above	1.47	1.05–2.07	0.02	1.15	0.80–1.66	0.46
Marital status						
Single, divorced, separated, widowed	–			–		
Married, living w/partner	2.17	1.64–2.87	< 0.001	1.80	1.32–2.45	< 0.001
BMI						
< 25	–			–		
25–30	0.83	0.61–1.13	0.25	0.91	0.66–1.26	0.58
> 30	0.54	0.39–0.73	< 0.001	0.62	0.44–0.87	0.01
Chemotherapy						
No chemo	–			–		

	Bivariate logistic regression			Multivariate logistic regression		
	OR	**95% CI**	***p*-value**	**AOR**	**95% CI**	***p*-value**
Chemo without Taxane	1.42	0.91–2.22	0.12	1.11	0.69–1.79	0.66
Chemo with Taxane	1.71	1.30–2.24	< 0.001	1.47	1.09–1.98	0.01
Depression						
No (< 8)	–			–		
Yes (HADS_dep ≥ 8)	1.92	1.30–2.85	0.001	1.80	1.13–2.87	0.01

OR odds ratio, *CI* confidence interval, *AOR* adjusted odds ratio

p-value < 0.05 is statistically significant