THE JOURNAL OF
SEXUAL MEDICINE

Aromatase Inhibitors Are Associated With Low Sexual Desire Causing Distress and Fecal Incontinence in Women: An Observational Study

Penelope J. Robinson, MBiostat,[1,*] Robin J. Bell, MB, BS, PhD, MPH, FAFPHM,[1,*] Marie K. Christakis, MD,[2] Stephanie R. Ivezic,[1] and Susan R. Davis, MB, BS, PhD, FRACP[1]

ABSTRACT

Background: Little is known of the impact of aromatase inhibitor (AI) therapy on sexual and pelvic floor function.

Aim: To document the prevalence of, and factors associated with, low desire, sexually related personal distress, hypoactive sexual desire dysfunction (HSDD), and pelvic floor dysfunction in women 10 years after breast cancer diagnosis.

Methods: This was a prospective, observational, community-based cohort study of Australian women with invasive breast cancer recruited within 12 months of diagnosis. 1,053 of the 1,305 who completed the initial 5 years of study follow-up agreed to be re-contacted, and 992 of these women alive 10 years after diagnosis were sent the study questionnaire.

Outcomes: The main outcome measure was HSDD determined by a score no higher than 5.0 on the desire domain of the Female Sexual Function Index (FSFI) plus a score of at least 11.0 on the Female Sexual Distress Scale—Revised (FSDS-R). Pelvic floor disorders, including urinary incontinence, fecal incontinence, and pelvic organ prolapse, were assessed using validated questionnaires. Multivariable logistic regression was used to assess factors associated with low desire, personal distress, and HSDD.

Results: 625 completed questionnaires were returned. The respondents' median age was 65.1 years (range = 36.4—95.5). Current AI use was reported by 10% and tamoxifen use was reported by 3.4%. 521 of the 608 women (85.7%; 95% CI = 82.9—88.5) who competed the FSFI desire domain had low sexual desire, and 246 of the 563 women (43.7%; 95% CI = 39.6—47.8%) who completed the FSDS-R had sexually related personal distress. 221 of the 559 women (39.5%; 95% CI = 35.5—43.6%) who completed the 2 questionnaires had HSDD. Current AI users were more likely to have HSDD than non-users (55.2% [95% CI = 42.2—68.1] vs 37.8% [95% CI = 33.5—42.0]; $P = .01$). HSDD was more prevalent in sexually active, current AI users (66.7%; 95% CI = 49.4—83.9) vs current non-users (43.6%; 95% CI = 37.0—50.2; $P = .02$). In a logistic regression model, HSDD was significantly associated with current AI use and inversely associated with age. Fecal incontinence was more prevalent in AI users than in current non-users (29.8% [95% CI = 17.8—41.8] vs 16.4% [95% CI = 13.2—19.6], respectively; $P = .01$).

Clinical Implications: It is important to address women's sexual health even many years after their breast cancer diagnosis.

Strengths and Limitations: Strengths include a representative sample, use of validated questionnaires, and few missing data. Limitations include sexual activity being a 4-week recall.

Conclusions: AI use is associated with HSDD and fecal incontinence in women who are 10 years after breast cancer diagnosis. **Robinson PJ, Bell RJ, Christakis MK, et al. Aromatase Inhibitors Are Associated With Low Sexual Desire Causing Distress and Fecal Incontinence in Women: An Observational Study. J Sex Med 2017;XX:XXX—XXX.**

Key Words: Aromatase Inhibitor; Hypoactive Sexual Desire Disorder; Breast Cancer; Fecal Incontinence

Received June 12, 2017. Accepted September 29, 2017.

[1]Women's Health Research Program, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia;

[2]Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

*Equivalent contribution.

https://doi.org/10.1016/j.jsxm.2017.09.018

INTRODUCTION

Breast cancer is the most common cancer in women.[1] In developed countries breast cancer is mostly diagnosed in postmenopausal women and approximately 75% of these women have hormone receptor positive (HR^+) disease.[2] Clinical guidelines recommend that postmenopausal women with HR^+ breast cancer be treated with an aromatase inhibitor (AI) as primary therapy for 5 years or after 2 to 3 years of initial tamoxifen followed by an AI to achieve at least 5 years of oral adjuvant endocrine therapy.[3,4] Because 5 years of an AI after completion of 5 years of tamoxifen increases disease-free survival, many women continue taking an AI up to 10 years after diagnosis.[5] Also, women commonly switch between endocrine therapies during their years of treatment, often as a consequence of side effects.[6]

More than 90% of women receiving adjuvant endocrine therapy for breast cancer report menopausal vasomotor symptoms and have lower quality-of-life scores than community controls.[7–9] AI therapy results in profound estrogen depletion.[10] Compared with tamoxifen, AI therapy has been associated with significantly higher rates of vaginal dryness (16.3% with AI vs 8.4% with tamoxifen) and dyspareunia (17.8% with AI vs 7.5% with tamoxifen).[10]

Small studies, which have mostly used convenience sampling, have suggested sexual dysfunction after breast cancer and cancer treatment is common.[11–13] The Bupa Health Foundation Health and Wellbeing after Breast Cancer Study (Bupa Study) was a longitudinal study of 1,683 Australian women recruited within 12 months of their first diagnosis of invasive breast cancer and followed annually for another 5 years. The aim of the Bupa Study was to document the physical and psychological health of women after breast cancer diagnosis.[2] Although 80% of the partnered women younger than 70 years in the Bupa Study reported satisfaction with their sexual function before their diagnosis, by 2 years after diagnosis 70% of these women reported sexual problems.[14] Women taking an AI were more likely to report sexual concerns, but sexual function was not assessed using validated questionnaires.[14]

In addition to estrogen being essential for vulvovaginal health, there is biological plausibility that estrogen deficiency contributes to the development of pelvic floor dysfunction (PFD), including urinary incontinence (UI), fecal incontinence (FI), and pelvic organ prolapse (POP).[15,16] Whether the profound estrogen depletion achieved with AI therapy is associated with an increased likelihood of PFD is uncertain. Furthermore, the extent to which women experience low sexual desire associated with personal distress several years after a diagnosis of breast cancer and whether this is exacerbated by AI therapy are not known.

Most women who participated in the Bupa Study agreed to be re-contacted for further research when they completed their 5th follow-up questionnaire. This has provided a unique opportunity to investigate the sexual well-being and prevalence of PFD in this well-characterized cohort and to determine whether symptom prevalence differed between current users of an AI and current non-AI users an average of 10 years after diagnosis.

METHODS

Participants

The Bupa Study was a prospective cohort study conducted in the Australian state of Victoria, which documented the physical, psychological, and socioeconomic consequences of treatment of breast cancer in the first 6 years after diagnosis. Women in the study were recruited within the first year of their diagnosis with invasive breast cancer, from June 2004 to December 2006, at which time they completed the "enrollment questionnaire." They were subsequently followed annually for 5 years and completed a study questionnaire in each of these years called follow-up questionnaires 1 to 5 (FQ1–5). Recruitment was mainly (78%) through the Victorian Cancer Registry with the remainder of participants volunteering directly to the Monash University Women's Health Program in response to advertisements about the study.[2] We previously reported that the women in this cohort were representative of all women newly diagnosed with invasive breast cancer in Victoria in age, tumor size at diagnosis, and location of residence.[2]

1,053 of the 1,305 women who completed FQ5, on average 5.8 years (95% CI = 5.2–6.4) after diagnosis, had agreed to be re-contacted and 60 of these women had since died and 1 was lost to follow-up. The remaining 992 were invited to participate in the present cross-sectional study, approximately 10 years after the initial diagnosis, and at this stage to complete the 10th follow-up questionnaire (FQ10).

This research was approved by the ethics committee of the Cancer Council of Victoria and the Monash University Human Research Ethics Committee. All participants provided written informed consent and could withdraw at any time.

Study Process

Study participants were posted a questionnaire labeled with their existing Bupa Study identification number. Completed questionnaires were returned in a reply prepaid envelope. Participants were asked to provide permission to be re-contacted for essential data clarification. Women were re-contacted only to check essential data points. Participants were not contacted if the only data missing were from the sexual function questionnaires.

The FQ10 requested information that included gynecologic surgery (hysterectomy and bilateral oophorectomy) and what, if any, adjuvant endocrine therapy (tamoxifen and AIs anastrazole, letrozole, and exemestane) they were currently taking or had ever taken. We asked about current weight, parity, breast cancer recurrence, or development of a new breast cancer. We also asked about the number of children and their current partnership status.