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The effects of pre-operative menopausal status and hormone replacement therapy (HRT) on sexuality and quality of life after risk-reducing salpingo-oophorectomy

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ABSTRACT

Objectives: Investigate the effects of pre-operative menopausal status and HRT use on sexual outcomes following risk-reducing salpingo-oophorectomy (RRSO).
Study design: Cross-sectional study of 119 women who underwent RRSO between 2009 and 2014.
Main outcome measures: Data was collected via a questionnaire and serum test for testosterone and free androgen index (FAI). The questionnaire comprised demographic data and validated measures of sexual function, sexual distress, relationship satisfaction, body image, psychological stress, menopause quality of life and general quality of life.
Results: Rates of sexual issues were similar despite menopause status at operation. Women who were pre-menopausal at operation (mean age = 44years ± 5) had significantly higher rates of sexual distress ($p = 0.020$), dissatisfaction with sex life ($p = 0.011$) and bothersome sexual menopause symptoms ($p = 0.04$) than women who were post-menopausal (mean age = 55years ± 7). Pre-menopausal women reported higher psychological distress from surgery ($p = 0.005$) and poorer emotional ($p = 0.052$) wellbeing. HRT use reduced the rates of dyspareunia ($p = 0.027$) and the severity of sexual menopausal symptoms ($p = 0.030$). Androgen levels were not significantly associated with desire or arousal scores.
Conclusions: Regardless of menopausal status at operation, women experienced the same sexual issues at equivalent rates. However, pre-menopausal women reported higher sexual distress and dissatisfaction with sex life. Pre-menopausal women also had greater psychological distress and poorer emotional function.

1. Introduction

Ovarian cancer is a highly lethal malignancy, often diagnosed at a late stage, making it the fifth leading cause of cancer death among women in the United States [1]. The overall lifetime risk of developing ovarian cancer is 1.3% [1], however women with BRCA1, BRCA2 or Lynch Syndrome carry significantly higher lifetime risks of approximately 46%, 23% [2] and 13% respectively [3]. It is estimated that 13% of ovarian cancers are due to these germline mutations and other familial cancer syndromes [2]. In addition to these known genetic syndromes, the lifetime risk of ovarian cancer is also increased in those with a family history. The lifetime risk increases to 5% in women with one first-degree relative effected, and 7% if two relatives are effected [3].

At present, there is no effective screening test for ovarian cancer, and it is recommended that women at increased risk undergo risk-reducing salpingo-oophorectomy (RRSO) at age 40 or earlier, once child bearing is complete [4]. This operation often renders these women prematurely menopausal, with an associated increase in vasomotor symptoms and sexual issues [5–7]. Several studies have reported that hormone replacement therapy (HRT) does not entirely ameliorate these sexual symptoms [6–8], which have been

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linked to reduced satisfaction with the decision to undergo surgery [9].

Although current guidelines recommend that high risk women undergo RRSO at age 35–40, upon completion of child bearing [4], some who have this procedure may already be post-menopausal either due to chemotherapy for breast cancer, treatment with the GnRH agonist Goserelin, or choosing to delay surgery until after natural menopause. There is data to suggest that women experience similar menopausal and sexual symptoms after RRSO, regardless of their menopausal status at operation [6,7,10]. However, for women who are pre-menopausal this often means the abrupt onset of menopausal symptoms after surgery, while for women who are post-menopausal there may be no significant change [6]. The psychological and sexual effects of these symptoms following RRSO have not been extensively investigated.

Regardless of the menopausal status of a woman, bilateral oophorectomy results in a reduction in circulating testosterone, however this reduction is more marked in pre-menopausal women [11]. Lower circulating testosterone has been hypothesised as a cause of low sexual desire after bilateral oophorectomy and randomized-controlled trials have shown that testosterone replacement can improve sexual desire, frequency and satisfaction [12]. However, the relationship between androgen levels and sexuality after RRSO in women who were pre- or post-menopausal at the time of surgery is unknown. The primary aim of this study was to investigate the effects of pre-operative menopausal status and the post-operative use of HRT on sexuality and quality of life in women following RRSO. A secondary aim was to determine whether there was an association between circulating androgen levels and sexual outcomes in women after RRSO and, if so, whether there were differences between women who were pre-menopausal and post-menopausal at the time of surgery.

2. Methods

2.1. Study design

A cross-sectional study of women who had undergone RRSO was undertaken. Participants were asked to complete a comprehensive questionnaire and undergo testing for serum testosterone and free androgen index (FAI).

2.2. Setting

The study was conducted at the Department of Gynaecologic Oncology, St John of God Subiaco Hospital, which is a tertiary private hospital in Perth, Western Australia. This study was granted ethics approval by the St John of God Healthcare Human Research Ethics Committee (HREC) and the University of Notre Dame Fremantle HREC.

2.3. Participants

Potential participants were identified from the records of two consultant gynaecologic oncologists at St John of God Subiaco Hospital. Women were considered eligible to participate if they had undergone RRSO between January 1st 2009 and December 31st 2014 (6 months to 72 months previously). Patients were excluded if they had; a suspected gynaecologic malignancy, major psychiatric illness, intellectual impairment or limited English language skills. A total of 206 women were identified as eligible and were invited to participate by letter and study brochure, followed by a phone call to discuss participation. Women who were unable to be contacted by phone were sent a paper copy of the questionnaire. Recruitment was undertaken between 1st February and 30th June 2015. Consent to participate was implied by the women completing the questionnaire and presenting for the blood test.

2.4. Data sources

Data were collected via a comprehensive questionnaire, which included details regarding: previous hysterectomy, previous mastectomy, past history of cancer, current cancer treatment, previous and current hormone replacement use. The questionnaire also included the following 8 validated questionnaires: Female Sexual Function Index (FSFI) [13]; Sexual Activity Questionnaire (SAQ) [14]; Female Sexual Distress Scale Revised (FSDS-R)[15]; Relationship Assessment Scale (RAS) [16]; Body Image Self-Consciousness Scale (BISC) [17]; Menopause-specific quality of life questionnaire (MENQOL) [18]; Short Form Health Survey (SF-36) [19]; and Impact of Event Scale (IES) [20].

In addition to the questionnaire, participants were also asked to undergo serum testing for testosterone levels and free androgen index (FAI). Blood samples were collected in an SST tube and analysed on a Roche E6O2 Analyzer at St John of God Pathology. The laboratory normal ranges for testosterone (0.2–1.8 nmol/L) and FAI (0.5–4.0) were used to assign results as either “normal” or “low”.

2.5. Variables

Participants were assigned as either being “Pre-Menopausal” at the time of surgery or “Post-Menopausal”. Those who were regularly menstruating or younger women (<50 years) taking Tamoxifen, were considered “Pre-Menopausal”. Those who were no longer menstruating, either due to natural menopause or chemotherapy, were considered “Post-Menopausal”, as were women who were taking an aromatase inhibitor or the GnRH agonist Goserelin at the time of operation.

The hormone replacement therapy group was defined as women who were using estrogen tablets or patches at the time of completing the questionnaire. Those using topical vaginal estrogen were analysed as a separate group.

The 19-Likert item measure of female sexual function, the validated Female Sexual Function Index (FSFI) [13], was used to determine the diagnosis of Female Sexual Dysfunction (FSD) and Hypoactive Sexual Desire Disorder (HSDD). With an additional 0 category added to question 15, as recommended by Meyer-Bahlburg to allow for women not in a relationship, the FSFI total scores range from 1.6 to 36 [21]. A higher score in the FSFI indicates a higher level of sexual functioning. A cut-off score of 26.55 has been psychometrically validated to discriminate between sexually functional and dysfunctional women, with those scoring 26.55 or below being considered likely to have FSD [22]. The sub-score for desire has been evaluated in the diagnosis of Hypoactive Sexual Desire Disorder (HSDD), with those scoring 5 or less having a high likelihood of HSDD [23]. Sexual distress was determined using the cut-off of 11 or more on the Female Sexual Distress Scale-Revised to indicate high levels of sexual distress [15].

2.6. Bias

A potential source of bias in this study is non-response bias and attempts to minimize this included telephone and mail prompting. The potential of response bias was mitigated somewhat by the high participation rate (58%). Attempts to minimize the risk of information bias included the use of standardized and validated measures.