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Chemotherapy Use Is a Significant Predictor for Sexual Dysfunction in Women with Gynecologic Cancer

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Abstract

Objectives: Sexual dysfunction is a significant survivorship issue in women with gynecologic cancer. We examined the association between chemotherapy and impaired sexual functioning. **Methods:** A cross sectional study of women with gynecologic cancer was conducted with a 181-item survey of validated instruments. A sub-analysis of women with chemotherapy treatment was performed to examine factors associated with sexual function including age, menopause status, BMI, diagnosis, stage, surgery/radiation use, active disease status, number of regimens, and number of cycles. Sexual dysfunction was measured by change in the Female Sexual Function Index (FSFI) score from pre-treatment with a significant decline in sexual function determined to be a 5.6 point decrease using a Reliable Change Index Statistic (RCIS). Standard statistical tools were employed. **Results:** A total of 107 (63%) of the women in the larger study had received chemotherapy as part of their treatment and were included in the sub-study. Women undergoing chemotherapy were more likely to experience sexual dysfunction post-treatment (51% vs. 26%; OR 2.9, 95% CI 1.5 - 5.7). In bivariate analyses, sexual dysfunction following chemotherapy was associated with age < 50 (80% vs. 42%; OR 5.6, 95% CI 1.9 - 16.6), premenopausal (30.8% vs. 12.7%, OR 3.1, 95% CI 1.1 - 8.2) cervical cancer (25.5% vs. 10.0%, OR 3.1, 95% CI 1.0 - 9.4), and low (I/II) stage (51.1% vs. 24.5%; OR 3.2, 95% CI 1.4 - 7.7). **Conclusions:** Women treated with chemotherapy for gynecologic cancer are at a significant risk of impaired sexual function. Women with cervical cancer, early stage disease, those who are premenopausal, and those younger than age 50 are at the highest risk.

Keywords

Chemotherapy, Sexual Health, Survivorship

1. Introduction

Sexual dysfunction is a significant survivorship issue in women with gynecologic cancer. Approximately 100,000 women were newly diagnosed with a gynecologic malignancy in 2015 [1]. As we improve our ability to recognize and treat these cancers, more and more women are surviving long after their initial diagnosis. As survival trends continue to improve, attention to quality of life outcomes has become increasingly important. Sexual well-being has been shown to be strongly linked to overall life satisfaction [2]. Unfortunately, a malignancy of the female pelvic organs inherently and fundamentally affects a woman's sexuality.

Sexual dysfunction in women can be characterized by either difficulties with sexual interest and arousal or genito-pelvic pain associated with penetration [3]. It is estimated that over 90% of women diagnosed with a gynecologic malignancy will exhibit some degrees of sexual dysfunction following their diagnosis [4]. Multiple modalities that are used to treat these diseases may have a detrimental effect on sexual function. We explored the association between chemotherapy and impaired sexual functioning.

In this study, we sought to examine not only whether or not there was an impact of chemotherapy on sexual function, but also what characteristics of patients, diagnoses, and chemotherapies put patients at high risk for sexual dysfunction. The purpose of this detailed analysis of the impact of specific factors related to chemotherapy on female sexual function is to help providers better identify members of their patient population that are particularly vulnerable to sexual dysfunction.

2. Methods

Institutional review board approval was obtained through the Colorado Multiple Institutional Review Board (COMIRB). This study represents a sub-analysis of a prospective cross-sectional study undertaken in a cancer center in a regional academic hospital. The study population included women diagnosed with a biopsy proven gynecologic cancer between the ages of 18 - 89 years of age that had completed at least an initial treatment regimen for their malignancy. Women with either initial diagnosis or cancer recurrence between September 2009 and December 2014 were offered enrollment. Inclusion criteria for study participants was defined as women between the ages of 18 - 89 diagnosed with a histologically confirmed gynecologic cancer, including recurrent disease if initial treatment had been completed within the last five years. Exclusion criteria were those women who did not fulfill inclusion criteria, those who were illiterate, and those who spoke only languages other than English or Spanish.

This retrospective sub-analysis specifically focused the sexual function components of the larger study as measured by administering a validated instrument called the Female Sexual Function Index (FSFI). FSFI is a self reported 19-item survey evaluating aspects of sexual function, including desire, arousal, lubrication, satisfaction, orgasm and pain, over the course of the 4 weeks preceding administration of the survey. The FSFI is validated for both pre- and post-meno-

pausal women [5]. Sexual dysfunction was defined as a decrease of 5.6 points on FSFI from the pre-treatment score as calculated using a Reliable Change Index Statistic (RCIS). The survey instrument was available and validated in both English and Spanish.

A retrospective chart review was performed by a team of medically trained researchers that conducted a detailed review of individual charts. Specific definitions for each variable collected were distributed to each research assistant prior to initiation of data collection. Data abstracted included diagnosis, disease status, and multiple specific details regarding chemotherapeutic treatment received. Diagnoses of gynecologic malignancy were confirmed with histology. Disease status was recorded as either primary or recurrent. Specific chemotherapeutic agent, number of regimens, and number of cycles were collected. The dosage and duration of each individual chemotherapeutic was administered according to standardized regimens as defined by the NCCN according to cancer histology.

The primary outcome was a decrease in the FSFI score of at least 5.6 points, thus indicating sexual dysfunction. Statistical analysis was performed with IBM SPSS statistics version 21. Statistical significance was estimated with chi-square tests for dichotomous and categorical variables and Student's t-tests were used to compare continuous variables. Multivariable analyses were used to determine factors that were independently associated with sexual dysfunction. Variables significant in bivariate analyses were included in the multivariable model. For all tests, a p value of <0.05 was considered statistically significant.

3. Results

A total of 107 (63%) of the women in the larger study received chemotherapy as part of their treatment and were included in the sub-study. The population treated was composed almost exclusively of Caucasian women with either private or government insurance (Medicaid/Medicare). In terms of patient characteristics, sexual dysfunction following chemotherapy was associated with age less than 50 years (80% vs. 42%; OR 5.6, 95% CI 1.9 - 16.6) in bivariate analysis. Obesity as defined by a BMI greater than 30 was not associated with increased sexual dysfunction. Pre-menopausal status was also significantly associated with increased risk of sexual dysfunction in bivariate analysis (30.8% vs. 12.7%; OR 3.05, 95% CI 1.14 - 9.18) (**Table 1**).

Disease characteristics that were shown to increase risk of sexual dysfunction included diagnosis of cervical cancer (25.5% vs. 10.0%; OR 3.1, 95% CI 1.0 - 9.4) and low stage (I/II) (51.1% vs. 24.5%; OR 3.2, 95% CI 1.4 - 7.7). Neither uterine/endometrial nor ovarian malignancies were independently associated with decreased sexual function scores in bivariate analyses. There were fewer than 10 patients with reported vulvar, vaginal or other disease sites. Neither active disease nor recurrent disease was predictive of sexual dysfunction.

Women undergoing chemotherapy were more likely to experience sexual dysfunction post-treatment (51% vs. 26%; OR 2.9, 95% CI 1.5 - 5.7). Specific chemotherapy factors including agent, number of regimens, and number of cycles

Table 1. Factors affecting sexual dysfunction in gynecologic cancer patients receiving chemotherapy.

Variable	Sexual dysfunction n = 52	No sexual dysfunction n = 55	OR (95% CI)
Patient factors			
Pre menopausal	30.8%	12.7%	3.05 (1.14 - 9.18)
Age < 50	30.8%	12.7%	5.10 (1.85 - 14.10)
BMI > 30	28%	24.5%	1.20 (0.50 - 2.89)
Disease factors[°]			
Primary disease	72.2%	55.6%	2.18 (0.88 - 5.41)
Active disease	50.0%	51.0%	0.96 (0.43 - 2.13)
Low stage (I/II)	48.0%	22.6%	3.22 (1.35 - 7.65)
Recurrent disease	26.8%	44.4%	1.0
Disease site			
Cervical cancer	25.0%	9.1%	4.49 (1.26 - 16.0)
Ovarian cancer	51.9%	47.3%	1.79 (0.72 - 4.45)
Uterine cancer	21.2%	34.5%	1.0
Treatment factors			
Chemotherapy	74.3%	25.7%	2.42 (1.24 - 4.69)
Chemo + surgery	44.0%	34.0%	0.11 (0.01 - 2.30)
Chemo + radiation	55.0%	45.0%	0.17 (0.01 - 4.03)
Chemo + surgery + radiation	59.0%	41.0%	0.20 (0.01 - 4.07)
Chemotherapy details[§]			
Carboplatinum	69.2%	72.7%	0.84 (0.37 - 1.95)
Cisplatin	46.2%	32.7%	1.76 (0.80 - 1.95)
Paclitaxel	69.2%	72.7%	0.84 (0.37 - 1.95)
>6 cycles chemotherapy	33.3%	36.4%	0.58 (0.25 - 1.34)
>1 chemotherapy regimen	25.5%	39.6%	0.52 (0.23 - 1.20)

[°]Remaining diagnoses including vulvar, vaginal, and other were represented in fewer than 10 patients surveyed. [§]Chemotherapies including pegylated liposomal doxorubicin, topotecan, and gemcitabine, bevacizumab were used to treat fewer than10 patients surveyed.

were not predictors of sexual dysfunction in bivariate analysis. Other treatment factors including history of surgical management or radiotherapy were analyzed and also not found to be independent predictors of sexual dysfunction.

In summary, significant factors correlated with decreased sexual function in bivariate analysis include age less than 50, pre-menopausal status, and a diagnosis of cervical cancer. In multivariate analysis, only age less than 50 remained independently predictive of sexual dysfunction (OR 6.4; 95% CI 2.17 - 18.86).

4. Discussion

Women treated with chemotherapy for gynecologic cancer are at significant risk for impaired sexual function. Our study found that women less than age 50 were at particular risk for developing sexual dysfunction after treatment with chemotherapy. Additional identified risk factors include pre-menopausal status and a diagnosis of cervical cancer.

It is well established that women treated for malignancy are at high risk for sexual dysfunction [6] [7]. This study sought to improve our capacity to identify patients most at risk for sexual impairment following chemotherapy for gynecologic malignancy. While we anticipated a "dose-response" relationship, there was no association between increased number of cycles or regimens and increased risk for sexual dysfunction. Additionally, it has been shown that chemotherapeutics that have a pronounced effect on physical appearance, such as alopecia following taxane treatment, are associated with a higher degree of sexual dysfunction in breast cancer [8]; however, we do not find that any particular agent correlates with an increased degree of sexual dysfunction in women diagnosed with a gynecologic malignancy.

It is integral to survivorship care that quality of life issues such as sexual function is addressed as an important component of holistic cancer treatment. A large prospective study investigating physician-patient discussions regarding sexuality in an outpatient gynecology setting found that only 3% of patients initiated a conversation regarding difficulties with sexual performance [9]. Although mechanisms to prevent and address sexual dysfunction in the clinical setting exceed the scope of this paper, it is important that providers maintain an awareness of those patients at particularly high risk. Our findings are consistent with other studies, which have found that younger women diagnosed with a malignancy are at particularly vulnerable to negative quality of life outcomes [10] [11]. Furthermore, evidence shows that even patients remote from treatment could benefit from continued support in regards to their emotional and psychological needs, and that women who have received chemotherapy are more likely to have unmet survivorship needs than women that have received other forms of treatment [12].

Strengths of this study included that it was conducted amongst a specific population at a single institution, which enabled us to analyze treatment course and outcomes with a rare degree of detail. The survey design allows women to answer what might be uncomfortable questions for them in a protected and private manner. Weaknesses included that the initial cross-sectional survey design was inherently subject to both recall and selection bias. Additionally, the relatively small sample size does result in a better statistical powering of the study. There was very little variation in demographic representation, with almost all women in our study being white and insured; so, the data might not extrapolate to women of differing ethnicities or socioeconomic backgrounds.

Overall, the purpose of this study was to elucidate factors surrounding the use of chemotherapy to treat gynecologic malignancies in order to better predict, pre-

vent, and identify sexual dysfunction in these patients. Chemotherapy, regardless of number of cycles, type of agent, or number of regimens, is a risk factor for compromised sexual function. Patients under age 50 are particularly at risk for developing these sequelae of chemotherapeutic treatment. Sexual function is an important factor in overall quality of life, and it is integral that gynecologic oncology providers consider this in the survivorship care which they provide to their patients.

Conflict

The authors report no conflict of interest.

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