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#### Sexual Health Issues in Women Treated for Carcinoma Breast and Carcinoma Cervix

Review Article

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#### **Abstract**

The most frequently treated cancer in women, include breast and genital malignancy; of which cervical and uterine cancer are commonest. Treatment of these cancer can cause adverse short term and long term effects on sexual health.

Sexual dysfunction is common in cancer survivors. Despite marked advances in the management of these malignancies, side effects of various treatment modalities utilized; surgery, radiation, chemotherapy and hormonal treatment can lead to sexual health issues in women. Although sexual dysfunction leads to immense distress, majority of the women who have undergone treatment for breast and cervical carcinoma are not evaluated or treated appropriately for sexual dysfunction. Sexual problems and menopause related symptoms can have a significant negative impact on quality of life. Research has shown that at least 50 percent of the women treated for cervical carcinoma develop sexual dysfunction after completion of treatment.

In this article we provide an overview of the various treatment modalities and associated sexual health issues afflicting women that compromise their quality of life.

#### Introduction

Gynecological cancers contribute significantly to the burden of malignancies among women, with approximately one million cases worldwide. In addition, it has been noted that the incidence of breast cancer has increased globally [1]. Breast carcinoma is the most frequently encountered malignancy in women. With the improvement in management strategies, increased number of women survive breast carcinoma. This leads to breast carcinoma survivors being the largest proportion of cancer survivors. In the United States, breast cancer survivors account for 41 percent of the cancer survivors [2].

One of the important issues faced by these cancer survivors are those of sexual dysfunction. In a study conducted by Kowalczyk, patient who underwent breast surgery were reported to have a negative impact on sexual function. Presence of a sexual partner, availability of a support system and anxiety are found to be predictors of sexual function in breast cancer survivors [3]. Raggio

et al., assessed breast cancer survivors at a median of 7 years after detection with breast carcinoma. In this study, the survivors were evaluated for sexual dysfunction using female sexual function index (FSFI) and the female sexual distress scale-revised (FSDS-R). They found that complaints of sexual dysfunction were reported among 77 percent of the survivors based on the Female Sexual Function Index (FSFI) [4].

Attempts to improve sexual function in breast cancer survivors have been reported. Hummel et al evaluated the use of Internet based cognitive behavioral therapy on sexual function and relationship intimacy. It was concluded that Internet based cognitive behavioral therapy has salutary effects on sexual functioning, body image and menopausal symptoms in breast cancer survivors [5].

Among the gynecological cancers, commonest are cervical and uterine cancers. Cervical carcinoma is predominantly seen in low and middle income countries. 85 percent of the cases occur in the developing countries. Among these cases, seventy percent are de-

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tected in Stage III or higher due to lack of awareness and proper screening. This leads to increased mortality rates. However with advances in treatment, mortality rates in breast and cervical cancer have decreased, leading to increased survival and increase in morbidity [6, 7]. It is paramount that healthcare providers discuss sexual health issues after cancer treatment.

#### **Breast Carcinoma: Sexual Issues**

Breast cancer is treated by a combination of surgery, chemotherapy, radiation and hormonal treatment. All these modalities have various impacts on sexual health issues among women. The importance of sexual health in cancer survivors was demonstrated by a survey conducted by Livestrong in 2010. Out of more than three thousand patients included, 24 % were breast cancer survivors. Post treatment sexual function and satisfaction were ranked third among the most frequently reported concerns [9]. Sexual concerns result in significant emotional distress including sadness, depression, issues related to personal appearances, stigma and negatively impacts on personal relationship.

Surgical management of breast cancer entails surgery of either part or the entire breast and axilla, which may be either unilateral or bilateral. On assessing the impact of surgery and the type of surgery performed for breast carcinoma, it was noted that women undergoing mastectomy reported greater disruption in their lives, lower scores in term of body image. When mastectomy was compared to conservative surgery, it was reported that women undergoing mastectomy had significantly greater problems associated with sexual health. There was improvement in certain parameters over time but sexual function remained compromised [10]. The role of breast reconstructive surgery in maintaining sexual health is a subject of discussion. Although some studies suggest performing reconstructive surgery results in improved sexual function, other studies offer less promising results [11-13].

Chemotherapy is utilised in treatment of breast carcinoma in a large number of patients. In women who have not attained menopause, chemotherapy can lead to ovarian failure and early onset of menopause. This leads to hypoestrogenism causing loss of libido and other sexual dysfunction. Vulvo-vaginal atrophy is one of the commonest side effects of hypoestrogenism. Chemotherapy inherently can lead to a negative impact on global physical function, decreased interest, arousal and desire [14]. Radiotherapy is utilised in the treatment of breast carcinoma based on the treatment protocols and the pathological features of the tumour. Radiation results in locoregional adverse effects like breast pain, upper limb discomfort and lymphedema. All these are associated with a negative impact on sexual function. However exact impact of radiation alone on sexual health is difficult to determine as it is always associated with combination of surgery and chemotherapy as treatment modality [15-18].

Endocrine therapy is another important modality for treatment of breast cancer. Tamoxifen is utilized in pre menopausal women. For post menopausal women, aromatase inhibitors are prescribed as endocrine therapy to reduce cancer recurrence. Hormonal therapy may adversely impact sexual health. It was noted that 30-40 percent of women treated with tamoxifen and almost half of the patients treated with aromatase inhibitors reported sexual health issues. Increased dyspareunia and vaginal dryness are noted

with the use of aromatase inhibitors as compared to tamoxifen. Furthermore, use of aromatase inhibitors is associated with increased risk of lichen sclerosus leading to severe itching, thinning of the perineal skin which causes bruising and tearing of the skin [19, 20].

Sexual health is often an ill addressed medical issue. Despite proven sexual health issues, less than half the women who are treated for breast cancer receive any medical attention for the same. This could be due to a combination of multiple factors such as reluctance of women to discuss and seek treatment for the sexual problems along with the possible lack of background and knowledge of sexual health issues among the primary treating physician. Halley et al., put forth possible barriers for appropriate management of sexual dysfunction.

- Sexual function was considered in terms of a physical domain and not a global issue.
- Patients were not sure as to where to seek appropriate treatment.
- Lack of services [21].

#### **Cervical Cancer**

Compared to any malignancy, issues of long-term psychological, social adaptation and quality of life are highest with cervical cancer survivors. It is associated with high proportion of long term survivors and involves a gender specific organ affecting sexuality and sexual functioning. This constitutes an important dimension of quality of life. According to the SEER data there has been a decline in the incidence of cervical carcinoma in developed countries like USA. Majority of the new cases and deaths related to cervical carcinoma (approximately 85% and 90%, respectively) occur in low-resource countries [22-23]. Cervical carcinoma is usually detected at an age where women are at the peak of their sexual activity and family building [24]. The most common sexual health issues noted in cervical carcinoma survivors include decreased elasticity and atrophy of vagina, decreased lubrication, loss of vaginal sensation, reduced arousal and sexual desire, dyspareunia and vaginal bleeding [25-27].

Surgical management of cervical cancer includes conization, simple hysterectomy and radical hysterectomy with lymphadenectomy based on the tumour characteristics and clinical stage. Radical hysterectomy results in a negative impact on sexual health which adversely impacts quality of life. Short term complications include shortening of vagina, dyspareunia, orgasmic problems, genital numbness and sexual dissatisfaction. Long term effects include reduction in sexual desire, lymphedema, decreased lubrication and persistent numbness [28-31]. Nerve sparing surgery has been proposed to reduce the morbidity associated with radical surgery. When compared to the conventional surgery, nerve sparing surgeries are not only associated with better bowel and bladder function but also improvement in sexual dysfunction [32]. Studies compared the extent of surgery on sexual dysfunction. On comparing radical hysterectomy to more conservative treatment options like cervical conization, it was noted that women who had undergone radical hysterectomy reported worse sexual functions across all FSFI parameters [33]. Studies comparing radical hysterectomy with radical trachelectomy, revealed no difference in sexual health issues among women undergoing either of the procedure [34].

In cases of advanced cervical carcinoma multi modal therapy in the form of External beam radiotherapy (EBRT) and vaginal brachytherapy (VBT) with or without concurrent chemotherapy is utilised for treatment. Radiation is associated with an adverse impact on sexual health by causing vaginal stenosis and fibrosis, shortening of the vagina, atrophy of vaginal tissue, dyspareunia [35-39]. When radiation is combined with surgery, sexual dysfunction is worse as compared to those women who undergo treatment by surgery only [28, 40]. In a retrospective study Frumovitz et al assessed sexual function among cervical cancer survivors with a long term follow up of seven years. They reported that radiotherapy had a negative impact on sexual function. Patients treated by radiotherapy reported a greater difficulty to be sexually aroused, decreased vaginal lubrication and decreased sexual satisfaction. Similar findings of statistically significant sexual dysfunction following treatment by radiation when compared to surgery were reported by Bermark et al and Jensen et al., [40-42] Radiation therapy also had adverse impact on bowel and bladder function. Women treated by radiation therapy reported incontinence and cystitis which affected self confidence and indirectly had a negative impact on the sexual health of women [43].

Women treated for cervical cancer experience sexual dysfunction after either surgery or radiotherapy. Complication secondary to vaginal morbidity and bowel and bladder dysfunction following surgery result in sexual health issues. These complications can be reduced with less radical, nerve sparing procedures. Radiation therapy used as either a primary form of treatment or adjuvant treatment after surgery, results in a higher degree of sexual dysfunction and morbidity [43].

#### Assessment of Sexual Dysfunction

In a survey of gynecologic oncologists conducted by Wiggins et al, it was found that less than half the clinicians obtained details regarding sexual history. Another obstacle in the management of sexual dysfunction is that of lack of proper methodology to screen and detect the problem. Hurdles in appropriate management of sexual dysfunctionare noted with both, the clinician as well as patients [44].

#### **Problems with Clinicians**

- Lack of knowledge and understanding of safe, viable options for treatment.
- Time consuming
- Need to establish baseline sexual function [45].

#### Patient related Issues: [46]

- Concerns of being dismissed
- Fear of physician being uncomfortable
- Feeling of lack of treatment options
- Cultural hindrance
- Ignorance

#### Various tools to assess sexual function: [49]

• The European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Cervix Module 24

- Female Sexual Function Index (FSFI)- Most frequently utilised tool to assess sexual dysfunction and has good reliability
- Leiden Questionnaire
- Late Effects Normal Tissues (LENT)-Subjective, Objective, Management, Analytic (SOMA)- Jointly developed by EORTC and RTOG. It has both subjective and objective elements utilised to assess the impact of radiotherapy

# Management of female sexual health issues in treated case of carcinoma breast and carcinoma cervix

Women treated for breast carcinoma and cervical carcinoma have various sexual health issue, needing a multidimensional approach to manage these issues. The treatment plan addresses the underlying issues which can be secondary to the disease pathology, treatment induced or psychological (anxiety and depression). Management of sexual health issue entails open communication, education and medical understanding [48].

#### Female Sexual Interest/ Arousal Disorder

Patient is reported to have reduced sexual interest if any 3 of the following are manifested [49]

- · Decrease in interest in sexual activity
- Reduction in sexual thoughts
- Nonreceptive to a partner's initiation.
- Decreased sexual pleasure in 75-100% of her encounters
- Reduced arousal to any sexual cues
- Decreased genital/ non genital sensations

Sexual desire can be impacted adversely by various psychological factors like stress, negative body perception, trauma, depression and anxiety. Hence psychotherapy is successfully used to treat problems arising in terms of sexual desire. Cognitive behaviour therapy has been utilised for management of sexual dysfunction in cervical cancer survivors. Treatment was associated with improvement in desire, arousal, orgasm, satisfaction and overall improvement of FSFI score. It had no effect on pain, but did improve genital arousal and reduced distress [50, 51].

Flibanserin, a post synaptic serotonin receptor modulator was approved by US FDA for the management of hypoactive sexual desire disorder. Studies have revealed that treatment with flibanserin was associated with significant improvement in sexual desire and distress. Commonest side effects include dizziness, somnolence, nausea and fatigue. Flibanserin is contraindicated with the use of alcohol as it may cause severe hypotension and syncope [52, 53].

#### Female orgasmic disorder

Behavioural techniques involving graded stimulation of the genitals leads to increased arousal and orgasm. They have shown to be successful in almost 90 percent of the cases [54]. A combined approach involving both cognitive and behavioural interventions is recommended.

Medical management using various medications has been attempted, the drugs usually utilised are antidepressants. Among these paroxetine has the worst profile of adverse effects. Other SSRI including fluoxetine, sertraline or fluvoxamine may be used. Bupropion is another medication that can be considered for managing sexual dysfunction. In addition to antidepressant, one of the off label use of testosterone is utilising its libido enhancing effects. However in view of lack of studies, it is not recommended for use [55, 56].

## Dyspareunia/penetration disorder

Treatment of gynaecologic malignancies is associated with dyspareunia. This may occur following treatment due to shortening, stenosis, decreased lubrication and atrophy of the vagina. Restoring vaginal lubrication, normalising the pH, vaginal dilatation and pelvic floor therapy contribute to alleviate the symptoms.

Non hormonal treatment options include vaginal moisturizers and lubricants. These may be utilised several times to improve tissue quality, discomfort and to reduce dryness.

Various products are available which can be utilised as vaginal moisturisers [57].

#### Polycarbophil based: [58-60]

- They result in hydration of the underlying cells and cause maturation of vaginal epithelium.
- They results in reduction of bacterial vaginosis.
- Studies revealed improvement in dyspareunia and irritation comparable to the use of vaginal oestrogen. Vaginal oestrogen was superior to this compound for improvement in vaginal dryness.

#### Hyaluronic acid based: [61, 62]

- A glycosaminoglycan that leads to water retention and lubrication.
- It decreases vaginal pH, causes a decrease in vaginal symptoms, atrophy and dryness.

#### Hyaluronic acid, vitamin A, and vitamin E suppository: [63]

• Effective in reducing vaginal dryness and dyspareunia.

## Vaginal Lubricants

Lubricants result in temporary reduction in dryness, vaginal pain, mucosal tears and irritation. A large number of products are available over the counter. Water or silicone based products are preferred over petroleum based lubricants. Petroleum based lubricants are associated with unpleasant odour, vaginal infections. On the other hand water and silicone based lubricants not only have a better adverse effect profile, they are easily washed away by soap and water. For better efficacy lubricants must be applied by both partners [57].

# Low dose oestrogen therapy

Low dose oestrogen therapy is efficacious in management of adverse genitourinary effects following menopause. Low dose oestrogen can be used in the form of cream, tablets and rings which improves symptoms due to vaginal atrophy without marked increase in serum oestrogen. However there are reports of in-

creased risks of stroke, breast cancer and coronary heart disease as per the Women's Health Initiative report with the use of estrogen. Estrogen therapy is contraindicated in survivors of hormone dependant cancer. Hence initiation of therapy must be done after discussing the risk to benefit ratio. Estrogen be considered for women surviving non hormone receptor positive cancer in whom other options of treatment have failed [64-66].

#### Non hormonal treatment

Ospemifene is the only FDA approved non estrogenic medication for the management of moderate to severe dyspareunia due to vulvo-vaginal atrophy. It is a selective estrogen receptor modulator, which needs further evaluation for cancer survivors. Lignocaine has been used in breast cancer survivors for treatment of severe dyspareunia. When applied to vulvar vestibular tissue before penetration, it reduces distress and improves comfort. Further studies are needed to determine its application in gynaecologic cancers [67-69].

#### Vaginal dilators

Vaginal dilators are used in the prevention of vaginal stenosis secondary to pelvic radiotherapy. Although recommended, data supporting the use of dilators is conflicting and adherence is poor. They are beneficial in the management of dyspareunia and the vaginal morbidity secondary to the treatment and lack of estrogen [57, 70-72].

#### Pelvic floor muscle exercise

Strengthening pelvic floor musculature is an important aspect in sexual function. Patients who were managed with pelvic floor physical therapy have reported decrease in pain during intercourse, more pain free encounters and improvement in sexual function [73, 74].

#### Conclusion

Cancer survivors experience sexual dysfunction to a varying degree either secondary to the disease pathology or the treatment. Although an important aspect which impacts the quality of life of cancer survivors, it's a domain not adequately assessed or addressed. Furthermore, sexual dysfunction and poor quality of life can be easily addressed by simple measures.

Sexual health needs better understanding, addressal during medical evaluation after treatment completion. When needed, professionals specialising in this domain must be involved. In countries with low resource settings, management of sexual health issues is restricted by cultural and social factors. However these problems are frequent in cancer survivors and negatively impact the life of survivors. Hence its imperative to address this issue.

Further research and study is needed to understand the sexual health issues, identify risk factors, and determine treatment options.

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