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Body mass index and sexual function in women with gynaecological cancer

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Abstract

Objectives: To investigate the association between body mass index (BMI) and sexual functioning in gynaecologic cancer patients. To determine the association between socio-economic deprivation and sexual functioning.

Methods: This is a prospective cohort study on women undergoing surgery for suspected or proven gynaecological cancer between September 2014 and February 2016 in the Royal Cornwall Hospital Trust. Patients were invited to participate by completing the Female Sexual Function Index (FSFI) at three time points: preoperative, 3 months postoperative, and 1 year postoperative. A semiparametric model of the FSFI score was used to establish the association between BMI and sexual functioning.

Results: A total of 257 patients were approached of which 166 patients were included. Fifty-two patients (33.8%) were overweight (BMI, 25-29.9 kg/m^2), 44 (28.6%) were obese (BMI, 30-39.9 kg/m^2), and a further 20 (13.0%) morbidly obese (BMI $\geq$ 40 kg/m^2). Overweight and obese women reported improved sexual functioning compared with normal-weight women in endometrial, ovarian, and vulvar cancers. Among cervical cancer, worse sexual functioning was seen in women with an increased BMI; however, this was not significant. Younger age was associated with improved sexual function, and sexual functioning was better postoperatively for all patients compared with preoperatively. There was no evidence of relationship between deprivation and sexual functioning in gynaecological cancer patients.

Conclusion: Higher BMI is associated with improved sexual functioning in endometrial, ovarian, and vulvar cancer; however, this was not seen in cervical cancer patients. There is no evidence of correlation between deprivation and sexual functioning.

KEYWORDS

body mass index, Cancer, gynaecology, oncology, physiological, quality of life, sexual dysfunction, social class

1 | BACKGROUND

Gynaecological cancer accounts for 15.2% of female cancer diagnoses annually, with an estimated total of over 1.3 million new cases and 600 000 deaths worldwide in 2018.[1] The availability of improved diagnostics and more efficacious therapies has led to an increased number of survivors. The diagnosis and treatment of gynaecological cancers are associated with major physical and psychological stress

for women and negatively influence their quality of life.[2,3] In addition, gynaecological cancer and its treatment directly influence a woman's reproductive organ and sexual functioning.[4]

Sexual functioning is an important yet underreported part of a woman's quality of life. Previous studies have shown that women often experience serious disruptions in sexual function after treatment for gynaecological cancer.[5-7] This can cause women to feel less interested in sexual relations, with negative impact on their relationship with partners.[8] Therefore, the detection and treatment of sexual problems in women with gynaecological cancer are important, but are still met with reluctance by clinicians.[8]

Together with the rise in prevalence of obesity in the general population[9] and the increased risk of cancer associated with obesity, a significant proportion of women with gynaecological cancer are obese.[10] In 2016, 40% of adult women worldwide were overweight (body mass index [BMI], 25-29.9), with a further 15% being obese (BMI $\geq$ 30).[11] There is a strong relationship between obesity and low socio-economic status (SES) in developed countries.[12,13] In addition, socio-economic deprivation has been shown to be associated with an increase in both the incidence and survival of gynaecological cancers.[14] A lower socio-economic status has also been independently associated with poorer quality of life in gynaecologic cancer patients after treatment.[15]

An emerging body of evidence indicates that obesity negatively impacts the quality of life throughout the cancer care pathway.[16] However, the association between BMI and sexual functioning in gynaecological cancer patients remains unclear.

The aim of this study is to determine the association between BMI and sexual functioning in women undergoing treatment for gynaecological cancer. In addition, we plan to assess the association between socio-economic deprivation and sexual functioning.

2 | METHODS

This is a prospective cohort study in the Royal Cornwall Hospital Trust in Truro, United Kingdom (UK), on women undergoing surgical treatment for gynaecological cancer. Women were eligible for participation if they had a suspected or proven primary gynaecological cancer, including endometrial, ovarian, vulvar, and cervical cancer, and were receiving surgery as part of their treatment. Exclusion criteria were less than 18 years of age, receiving treatment in the palliative setting, concurrent cancer, or inability to give informed consent.

The recruitment period was from September 2014 until February 2016 with a follow-up period of 12 months. Ethical approval was obtained through the NRES Ethical Committee South West Cornwall and Plymouth 14/SW/0136, and the study had full Trust approval.

Patients were approached to participate and complete the questionnaires during routine clinical visits. The questionnaires were collected preoperatively for all patients and at 3 months postoperative and 1 year postoperative visits for cancer patients. The questionnaires were only available in English and had to be completed on paper, and written informed consent was obtained prior to administration of the questionnaires.

Patient characteristics including height and weight, comorbidities, smoking status, and marital status were collected during clinical visits. Demographics such as age, postcode, and ethnicity were collected from medical records. The patients' postcode was used to identify the geographical location of residence, so that it could be assigned a deprivation risk using the English Indices of Multiple Deprivation (IMD) 2015,[17] which are published by the UK Department for Communities and Local Government and measure a spectrum of deprivation.

The Female Sexual Function Index (FSFI) was used to assess sexual functioning, which has been validated in the general population,[18] in cancer patients, and cancer survivors.[19,20] FSFI is a 19-item self-report questionnaire covering specific domains relevant to female sexuality including desire, arousal, lubrication, orgasm, satisfaction, and pain. Overall domain scores vary between the interval 2-36, with a higher score indicating higher sexual functioning. The previously validated cut-off value of 26.55 was used to diagnose female sexual dysfunction (FSD), where a score below 26.55 indicates sexual dysfunction.[21]

2.1 | Statistical methods

With a background incidence of 40% of sexual dysfunction in the general female population[22] and 63% in gynaecological cancer patients,[23] we performed a sample size calculation (α = 0.05 and power of 80%). The sample size was calculated to be 146 patients.

Continuous outcomes were presented as medians and interquartile ranges, and categorical data were presented as frequencies and proportions. To avoid discarding data due to missing entries, we adopted a simple imputation scheme for BMI and IMD. For IMD, the missing observations were replaced with the median over the whole data set. For BMI, if one entry was missing, it was replaced with the median of the other two entries. However, if two entries were missing, they were replaced with the one observed entry. If all three BMI entries were missing, BMI was calculated as the median over the complete data set.

For the FSFI scores, no imputation strategy has been applied, but a principled approach was used, which allows inference without discarding data and without imputation. The FSFI scores are represented as intervals[24]; a completely unobserved score will be represented as the interval 2-36. There was no difference between the 3- and 12-month postoperative data for FSFI; therefore, to reduce the complexity of the model, we used a binary factor "pre-op/post-op." The patients with final histology "benign" only answered the preoperative questionnaire; therefore, they were excluded from further analysis at 3 and 12 months postoperative.

The association between BMI and the FSFI outcomes was assessed using semiparametric regression analysis, while correcting for confounders such as age and treatment modality. A multistage bootstrap procedure was implemented to take into account potential intrasubject correlations. Data were analysed by using R3.4.3 and the icenReg library.[24]

3 | RESULTS

A total number of 257 patients were approached, of which 170 patients consented, resulting in a recruitment rate of 66%. Four patients dropped out of the study that resulted in a total study population of 166 women with FSFI data of 498 observations; see Figure 1.

3.1 | Baseline characteristics

The demographics and baseline characteristics of the study cohort are presented in Table 1. For the overall cohort, age at diagnosis ranged from 28 to 86 years, with a median age of 62.0 (interquartile range, 18). BMI ranged from 19.3 to 51.0, with a median of 28.8 (interquartile range, 8.8). For 127 patients, the final histology was cancer (76%); for 39 patients, the final histology was benign. The majority of patients who had a cancer diagnosis were diagnosed with endometrial cancer (EC, N = 58, 46%), followed by ovarian (OC, N = 47, 37%), vulvar (VC, N = 13, 10%), and cervical cancer (CC, N = 9, 7%). Most patients presented with stage 1 disease (64%), followed by stage 3 (22%), stage 2 (5%), and stage 4 (5%). The entire population is Caucasian (98% White British/Cornish, 2% any other White background).

3.2 | FSFI and BMI

In endometrial, ovarian, and vulvar cancer patients, low values of BMI were associated with low FSFI scores, whereas high values of BMI were associated with higher scores (Table 2). However, in cervical cancer patients, high BMI was inversely associated with FSFI.

3.3 | FSFI, age, and cancer type

There was a relationship between FSFI scores and age at diagnosis, with older women experiencing lower scores and younger women experiencing higher scores. However, for older women, there are not many observed scores (Table 2). Cervical cancer patients were younger (median age, 33), with a lower BMI and higher IMD than patients affected by other cancer types. They also have higher average FSFI scores (median score, 20; Table 2). Vulvar cancer patients on the other hand had consistently low FSFI scores and were older of age (median age, 75).

The cumulative distribution of FSFI scores using the Turnbull non-parametric estimates,[24] stratified by cancer type, showed that vulval and cervix cancer are associated with extreme scores. The distribution of FSFI scores for the group of women with final histology benign (measured preoperatively only) is similar to the FSFI scores for women with endometrial and ovarian cancer (see Figure S1).

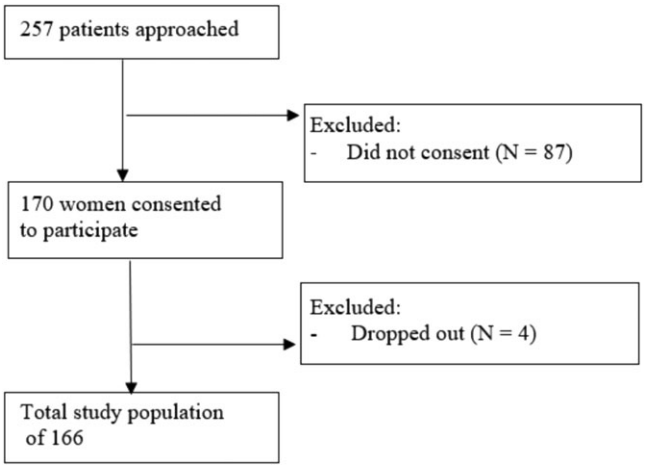

FIGURE 1 Flow chart of recruitment

TABLE 1 Study characteristics

Variable	Value
No. of patients	166
Median age, y	62.0
Median BMI	28.8
BMI groups	
<25	38 (22.9%)
25-30	52 (31.3%)
30-40	44 (26.5%)
>40	20 (12.0%)
Unknown	12 (7.2%)
Ethnicity	
White British/Cornish	162 (97.6%)
Any other white background	4 (2.4%)
Smoking	
Yes	8 (4.8%)
No	73 (44.0%)
Ex-smoker	10 (6.0%)
Unknown	75 (45.2%)
Comorbidities	
None	24 (14.5%)
One	53 (31.9%)
Two or more	76 (45.8%)
Unknown	13 (7.8%)
Cancer type	
Endometrial	58 (34.9%)
Ovarian	47 (28.3%)
Benign	39 (23.5%)
Cervix	9 (5.4%)
Vulvar	13 (7.8%)
Stage	
I	81 (63.8%)
II	6 (4.7%)
III	28 (22.0%)
IV	6 (4.7%)
Unknown	6 (4.7%)
(Neo)adjuvant treatment	
No	107 (64.5%)
Yes	59 (35.5%)
Type (neo)adjuvant treatment	
Chemotherapy	40 (67.8%)
Radiotherapy	10 (16.9%)
Chemotherapy + radiotherapy	8 (13.6%)
Hormonal	1 (1.7%)
Recurrence	
Yes	18 (10.8%)
No	148 (89.2%)

3.4 | FSFI over time

The median FSFI score preoperatively and postoperatively with bootstrapped 95% confidence intervals (CI) suggests a difference in the score preoperatively and 3 and 12 months postoperatively, but no appreciable difference between the latter two. Cervical cancer

TABLE 2 Median and interquartile ranges

Cancer Type	BMI	IMD (Thousands)	Age at Diagnosis	FSFI Score	# Exact FSFI Scores
Cervix	23 [20, 28]	19.1 [11.9, 25.3]	33 [30.5, 64.3]	19.7 [4, 29.7]	19
Endometrial	31.3 [25.9, 37.1]	11.3 [8.8, 15.3]	64.4 [55.17, 71.46]	6.7 [5.1, 21.9]	52
Ovarian	28 [24, 30]	12.0 [10.3, 16.2]	61.5 [53.2, 70.8]	5.4 [3.6, 15.8]	48
Vulval	28.1 [26.7, 30.1]	13.8 [11.1, 18.5]	74.94 [71.9, 82.0]	5.8 [4.8, 7]	7

patients have the largest increase in the median FSFI score after surgery (from 10.3 to 19.7), followed by endometrial cancer patients (from 5.8 to 12); although in all cases, the confidence intervals are quite large due to the small number of exact FSFI scores (see Table S1).

3.5 | FSFI and socio-economic deprivation

There was no clear evidence of a relationship between IMD and FSFI (data not shown).

3.6 | Patient comments on FSFI

Interestingly, patients provided us with written comments on the FSFI form; these are presented in Data S1.

3.7 | Semiparametric regression analysis

The hazard ratios (HRs) for every variable are presented in Table 3 with the value larger than one corresponding to a reduction of the FSFI score and values smaller than one corresponding to an increase of the FSFI. The following independent variables, cancer type, BMI, IMD, preoperative/postoperative, and age, were analysed with FSFI. The results from the semiparametric Turnbull proportional hazards model[24] match qualitatively the patterns we have seen from the exploratory analysis. They confirm that age (HR, 1.02; CI, 1.01-1.04), "pre/post-op" time intervals (HR, 1.4; CI, 1.09-1.92), and vulvar cancer diagnosis (HR, 0.78; CI, 0.62-0.94) were significant associated with FSFI (Table 3).

4 | DISCUSSION

Quality of life is an important aspect of life for women diagnosed and treated for cancer. Gynaecological cancer affects women's reproductive organs, and it influences their sexual functioning; for younger women who lose their fertility, it can have an even more devastating effect. In addition, gynaecological cancer treatment directly affects the reproductive organs with pelvic radiation being associated with vaginal stenosis and fibrosis and surgery leading to removal of reproductive organs and mutilating scars. This can affect body image and lead to feeling of loss of femininity.[25] Furthermore, chemotherapy and/or surgery can induce a premature menopause with complaints of hot flushes, night sweats, genitourinary atrophy, insomnia, fatigue, and vaginal dryness.[26] Our study showed that nearly all women included had low FSFI scores (sexual dysfunction), which is in keeping with previous studies.[27]

When assessing the relationship between female sexual functioning and BMI following gynaecologic oncology procedures, our data suggest an association between BMI and FSFI scores, where a higher BMI is associated with better sexual functioning. This is especially seen in women with vulvar cancer, but there seems to be a similar trend for endometrial and ovarian cancer. However, for cervical cancer, high BMI was not associated with improved FSFI score, and indeed, a trend towards an inverse association was noted; nevertheless, this did not reach the significant level. An explanation may be that higher levels of BMI are associated with higher oestrogen levels, due to oestrogen production in adipose tissue.[28] This has a positive effect on vaginal moistening, which could explain why overweight women with vulvar cancer reported less sexual problems.[29]

The fact that high BMI was associated with better sexual functioning in women with vulvar, endometrial, and ovarian cancer and not in women with cervical cancer might be explained by the fact most women with cervical cancer were premenopausal, whereas the women in the other groups tended to be postmenopausal. Our results are in line with a study done by Oldenburg et al, which showed that higher BMI was inversely associated with sexual/vaginal problems in endometrial cancer.[29] However, Armbruster et al found no association between BMI and sexual function or sexual interest in endometrial cancer survivors at least 6 months after treatment.[30] A recent study by this team reported an association between physical inactivity and poorer sexual functioning in ovarian cancer survivors; however, no association between BMI and sexual dysfunction was found.[31] For vulvar and cervical cancer, the literature is scarce, and the link between BMI and sexual functioning is unclear. Therefore, further

TABLE 3 Hazard ratios with bootstrapped 95% CI

Parameter	Hazard Ratios
BMI	0.98 [0.94, 1.08]
Cancer type	
Cervix	0.147 [0.0120, 5.1]
Endometrial	1.07 [0.156, 18.9]
Ovarian	5.6 [0.64, 138]
Vulval	1494 [11.0, 1.82×10^6]
Cancer type * BMI interactions	
Cervix	1.05 [0.93, 1.14]
Endometrial	0.99 [0.91, 1.06]
Ovarian	0.95 [0.85, 1.02]
Vulval	0.78 [0.62, 0.94]
Pre-op	1.40 [1.09, 1.92]
Age at diagnosis	1.02 [1.01, 1.04]
IMD^2	1.00 [0.9997, 1.001]

research is needed to further investigate other factors that can influence sexual functioning including the impact of cancer diagnosis on relations and psychological morbidity.

Age is a known risk factor for sexual dysfunction in the general population[32]; furthermore, Gao et al showed age as a risk factor of sexual dysfunction in endometrial cancer survivors.[5] Our data suggest a relationship between sexual functioning and age at diagnosis, with older women experiencing lower scores and younger women experiencing higher scores. Older women were also less likely to complete the FSFI, and elderly women did show lower scores; however, they frequently reported not being sexually active but satisfied with their lack of sexual activity.

Remarkably, our study showed lower sexual functioning scores preoperatively compared with postoperatively (both at 3 months and 1 year); this may be due to pretreatment anxiety, depression, and anger that can influence relationships and sexuality.[33] The preoperative period represents a time of increased stress and anxiety while waiting for new or potential cancer diagnosis.[34] This can also explain why patients with a final benign diagnosis had low FSFI scores preoperatively in this study. After treatment, the observed FSFI may be secondary to the certainty of diagnosis and treatment success. Previous studies have shown improvement in sexual dysfunction over shorter follow-up period (up to 6 months); however, no studies have demonstrated changes over 1 year follow-up; therefore, further research is needed.[35]

The socio-economic status (SES) and deprivation (IMD) are important predictors of health and affect the survival from gynaecological cancers.[14] Since previous research showed a poorer quality of life in more deprived patients with gynaecologic cancer, we examined the association between sexual functioning and deprivation. However, we did not find an association between female sexual dysfunction and overall deprivation as measured by the Index of Multiple Deprivation.

This study offers new information on the relationship of BMI and sexual functioning in women who are treated for gynaecologic cancer. Our study suggests that age and BMI are associated with sexual functioning in gynaecological cancer patients, with overweight and obese patients reporting better sexual functioning in endometrial, ovarian, and vulvar cancer patients. This is one of the first studies to evaluate different aspects of sexuality and sexual functioning including arousal, satisfaction, orgasm, and pain preoperatively and with 1 year follow-up in association with BMI indices. The strengths of our study include the prospective cohort design with patient-reported data collected preoperative with subsequent follow-up for 1 year at two different intervals. A standardized, validated questionnaire was used, which is validated not only in the general population but for cancer patients as well.[19]

5 | CONCLUSION

High BMI is associated with improved sexual functioning in vulvar, ovarian, and endometrial cancer patients, but not in cervical cancer patients. However, there is no correlation between socio-economic deprivation and sexual functioning. Further research is needed to assess these associations in more detail.

Increasing awareness of the impact of a gynaecological cancer diagnosis on sexual functioning can improve care and counselling in the perioperative setting.

5.1 | Clinical implications

BMI has an impact on the psychosexual functioning of women with gynaecological cancer with higher BMI being associated with better sexual functioning. This is not the case for cervical cancer; therefore, clinicians will need to take measures in addressing any psychosexual issues during and after treatment. This is important in order to improve their quality of life.

5.2 | Study limitations

Limitations of this study are the relatively small study population and the limited number of fully observed scores making the analysis of the FSFI data a complex problem. In addition, this study possibly involved a somewhat select group of women—those who were willing to complete the questionnaire. Because we only have a small sample size of vulvar and cervical cancer patients, we were limited in our analysis. Sexuality remains a difficult but important topic that is reflected in the fact some patients who agreed to participate in the study did not fill out the sexual functioning questionnaires.

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CONFLICT OF INTEREST

We declare that the contents of this paper have not been published or considered for publication elsewhere. All authors made substantial contribution to conception and design, and/or acquisition of data and/or analysis and interpretation of data, participated in drafting the article or revising it critically for important intellectual content, and gave final approval of the version to be submitted and any revised version to be published. There is no financial support or relationship that may pose conflict of interest.

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SUPPORTING INFORMATION

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