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Sexual function following hysterectomy for endometrial cancer: A five-year follow up investigation

Lindsey Buckingham *, Ashley Haggerty, Ashley Graul, Mark Morgan, Robert Burger, Emily Ko, Uduak Andy, Robert Giuntoli

University of Pennsylvania Health System, 3400 Civic Center Blvd, Third Floor, West Pavilion, Philadelphia 19104, PA, USA

HIGHLIGHTS

- We showed stable sexual function in endometrial cancer patients over a 5 year period.
- Sexual function was comparable between endometrial cancer patients and urogynecology controls.
- Sexual function in survivorship is an important topic that requires further study.

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ABSTRACT

Objectives. We sought to determine a baseline and five-year follow up sexual function score in women undergoing hysterectomy for endometrial cancer.

Methods. A cross-section of endometrial cancer patients receiving care from 2006 to 2010 was identified. Patients were surveyed during academic year 2011 using the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ). Respondents were re-surveyed in 2016. The PISQ was also administered at a single time point to a control group of urogynecology patients. Statistical analyses were conducted using STATA software, version 13.1.

Results. 129 endometrial cancer and 63 matched urogynecology patients responded to an initial survey and sufficiently answered the PISQ. There was no statistical difference in BMI, race, diabetes, or smoking history between groups. In 2011, 62.5% of endometrial cancer patients versus 72.6% of urogynecology patients reported sexual activity ($p = 0.166$). Median PISQ score for these groups was 33 [IQR 29–38] and 32 [IQR 28–37] respectively ($p = 0.472$). Twenty-nine (22%) endometrial cancer patients sufficiently answered the initial and 5-year follow up PISQ to be included in follow up analysis. Median PISQ score at five years was not significantly different from baseline: 31 [IQR 27–39] versus 33 [IQR 31–38] ($p = 0.299$). With multivariable modeling, no demographic or clinical characteristics of endometrial cancer patients were independently associated with sexual function (p = NS).

Conclusions. Sexual function for endometrial cancer patients was not significantly different from women treated for benign disease. Sexual function also remained stable for endometrial cancer patients regardless of time from initial treatment. Further prospective studies are needed to better characterize sexual function in endometrial cancer survivors.

1. Introduction

In the United States, endometrial cancer is the most common gynecologic malignancy and accounts for approximately 15% of hysterectomies annually [1,2]. The majority of endometrial cancer patients are diagnosed at an early stage and are most often cured of their disease. Although often focused on survival outcomes, more recent research has attempted to better understand and mitigate the impact of endometrial cancer treatment on quality of life.

The impact of surgery for gynecologic cancer on patient sexual function remains poorly elucidated. Although probably best studied for cervical cancer [3,4], prospective data on the long-term effects of hysterectomy on sexual function in endometrial cancer patients is lacking [5–7]. Available literature presents inconsistent results. While some

* Corresponding author at: 3400 Civic Center Blvd, Third floor, West Philadelphia 19104, PA, USA.
E-mail address: Lindsey.buckingham@uphs.upenn.edu (L. Buckingham).

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groups report consistent and persistent impairment of sexual function [7–10], others demonstrate either no harm or improved function after initial decline [5,11–16].

The primary objective of this study was to determine baseline and five year follow up sexual function in post hysterectomy endometrial cancer patients. The secondary objective was to compare baseline sexual function of these endometrial cancer patients to a matched population of post hysterectomy patients with benign (urogynecologic) disease.

2. Methods

This prospective study was carried out at two hospitals within the University of Pennsylvania Health System (UPHS) and was approved by the University of Pennsylvania IRB. Study subjects consisted of endometrial cancer patients undergoing hysterectomy within UPHS between 2006 and 2010. These patients were identified and offered participation in the form of a mailed survey. Informed consent was included in the survey packet. The initial survey was completed during the 2011 academic year, and was repeated in 2016. Respondents with non-endometrioid histologies were excluded from analysis. The same survey was administered to a control group of UPHS post hysterectomy urogynecology patients at a single time point. Inclusion criteria for the urogynecology cohort included mild prolapse (defined as grade 0–1) and history of a hysterectomy.

Subjects were surveyed on multiple aspects of survivorship and quality of life. This study was restricted to subjects' answers to a short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ). The PISQ is a generalizable sexual function questionnaire that was originally developed to evaluate 3 areas of sexual function: behavioral/emotive, physical, and partner-related. The long form consists of 31 questions and was validated to measure both sexual function and desire [17]. A shortened, 12-question version of the original PISQ (PISQ-12) was adapted and validated several years later [18]. Each item in the survey is scored on a Likert scale of 0–4. Total PISQ score is calculated by totaling scores of all items. For positive questions 0 = never and 4 = always. Reverse scoring was used for negative questions wherein 0 = always and 4 = never. Maximum score is 48, and a higher PISQ score correlates to better sexual function. Scores for the PISQ-12 are only valid if 10 or more questions are answered. Study subjects omitting greater than 2 items on the survey were excluded from analysis.

Patient charts were reviewed by designated investigators and clinical and demographics data were abstracted. The primary outcome was analyzed using Wilcoxon signed rank test for paired *t*-test of data that was not normally distributed. Bivariable analyses of demographics characteristics were performed to identify potential confounders. Descriptive statistics were performed using non-parametric tests.

3. Results

3.1. Comparison groups

During academic year 2011, 490 surveys were mailed to endometrial cancer patients who had undergone hysterectomy between 2006 and 2010. 208/490 (42%) of surveys were returned, and 129/208 (62%) of respondents sufficiently completed the PISQ for inclusion. 208 follow-up surveys were mailed in 2016 and 78 patients returned the survey. 41/78 (53%) met inclusion criteria, however, only 29 had sufficiently answered the initial PISQ survey. This left 29/129 (22%) matched pairs for analysis (Fig. 1). Time from cancer diagnosis to the initial survey ranged from 0 to 6 years (median 2) and time to follow up survey ranged from 4 to 10 years (median 6). One hundred twenty four urogynecology patients met prolapse grade and surgical criteria, though only 63/124 (51%) sufficiently answered the PISQ to be included in analysis.

3.2. Demographics

Mean ages were significantly different, 63 (SD ± 11) years and 57 (SD ± 11) years for the endometrial cancer baseline cohort and urogynecology controls respectively ($p = 0.0003$). A majority of subjects in both groups were white. However, a significantly higher percentage of the urogynecology group was black (30.2%), compared to the endometrial cancer group (10%) ($p = 0.001$). Median body mass index (BMI) was not significantly different: 30 [IQR 24–35] for endometrial cancer baseline and 28 [IQR 23–33] for urogynecology ($p = 0.40$). Mean number of births were 1.8 (SD ± 1.4) and 2.1 (SD ± 1.3) for endometrial cancer patients and urogynecology patients respectively ($p = 0.10$). History of smoking was not significantly different between the two groups: ($p = 0.531$). Oral hormone replacement therapy (OHRT) use was reported in 11% (7/63) of urogynecology patients and 4% (5/129) of baseline endometrial cancer patients ($p = 0.04$). Depression was reported by 5% (3/63) of urogynecology and 23% (30/129) of baseline endometrial cancer patients ($p = 0.003$) (Table 1). The baseline endometrial cancer cohort was compared to a subset of endometrial cancer patients who completed surveys both at baseline and 5 years (matched pairs) and no statistically significant differences were found in any of the measured demographics (data not shown).

3.3. Staging and adjuvant treatment

The majority of patients in the baseline endometrial cancer group were stage I at diagnosis: 68% (88/129) were Ia and 16% (20/129) were Ib. The remaining patients included 5/129 (3.9%) stage II, 12/129 (9.3%) stage III, and 4/129 (3.1%) stage IV (Table 2).

Approximately 46% (59/129) of the baseline cohort received adjuvant therapy. Among patients receiving adjuvant therapy, the majority 26/129 (20%) received radiation alone. Vaginal brachytherapy was the predominant treatment modality (20/26), with combination vaginal brachytherapy and external beam radiation given to only 4/26 patients. Of the remaining 2 patients, 1 received EBRT alone and the final received unknown radiation (Table 2).

Combination radiation and chemotherapy was administered to 17/129 (13%) of patients. The majority (9/17) receiving combination therapy had stage 3 disease. Of the remaining recipients, 6/17 received sensitizing chemotherapy with vaginal brachytherapy (4/6) or external beam (2/6) radiation (Table 2).

Chemotherapy alone was administered to only 13/129 patients (10%). Six patients with stage I disease had clear cell or serous histologies, 5 patients had stage III and IV disease, and the remaining 2 received chemotherapy at recurrence (Table 2).

3.4. Sexual function

In each analyzed group, greater than 60% of participants reported being sexually active in the 6 months prior to survey. Sexual activity in the baseline endometrial cancer group was not significantly different from urogynecology controls ($p = 0.166$). Median baseline sexual function (PISQ score) was not significantly different between baseline endometrial cancer patients and urogynecology patients: 33 [IQR 29–38] versus 32 [IQR 28–37] ($p = 0.472$) (Fig. 2). Median PISQ score for matched pairs at baseline was 31[IQR 27–39] while median five-year follow up score was 33 [IQR 31–38] ($p = 0.299$) (Fig. 3). When stratified by time from diagnosis to survey, five-year follow up data failed to show a significant difference in median PISQ score between baseline and follow up survey regardless of survey timing relative to initial treatment ($p = 0.78$) (Fig. 4). Furthermore, no difference was found in median PISQ for patients receiving hysterectomy alone or hysterectomy with adjuvant therapy 33 [IQR 28–39] and 33 [IQR 29–38] respectively ($p = 0.992$).

Scores from the PISQ questionnaire were analyzed by item in order to elucidate specific differences in function. As expected, significant

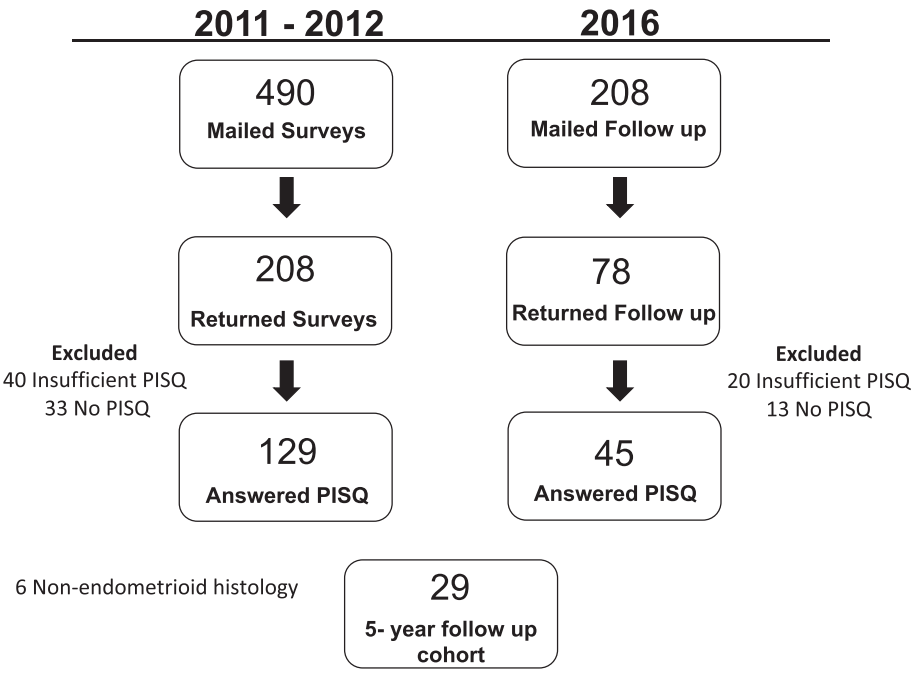

Fig. 1. Graphical representation of patient recruitment and response via mailed survey.

differences were found between baseline endometrial cancer patients and urogynecology patients on items that assessed continence. Within the matched pairs cohort, a significant difference was found for the item assessing intensity of orgasm as compared to "past". At baseline, median score was 1 (less intense), while at 5-year follow up median score improved to 2 (same intensity) ($p = 0.0007$). Data not shown.

4. Discussion

The short and long term effects of endometrial cancer diagnosis and treatment on sexual function are poorly characterized. We obtained a postoperative and 5-year follow up sexual function survey in a cohort of women who underwent hysterectomy for uterine cancer. We found no statistically significant change in overall sexual function at 5 years follow up. Some follow up surveys were completed up to 10 years from initial treatment and demonstrated stable sexual function over time. Baseline PISQ scores for the endometrial cancer and urogynecology cohorts (which served as a baseline control) were similar. These scores were comparable despite a higher incidence of depression in the endometrial cancer patient cohort, suggesting that the impact of diagnosis and treatment of endometrial cancer are similar to the impact of the diagnosis and treatment of a benign disease such as prolapse.

Literature on sexual function in gynecologic oncology patients is limited [8,19] and the majority is focused on cervical cancer survivors. In contrast to endometrial cancer patients who are treated primarily with hysterectomy, many cervical cancer patients receive radiation as primary therapy. Therefore despite similar survivals, different

Table 1
Demographics data for baseline endometrial cancer and urogynecology cohorts. Significant differences were found in age, race, and rates of depression and incontinence.

	Urogynecology (n = 63)	EC baseline (n = 129)	p value
Age, mean + SD	57 ± 11.1	63 ± 11.2	0.0003
BMI, median [IQR]	28.2 [22.5–32.9]	29.6 [23.6–34.9]	0.459
Race, Freq (%)			0.001
White	39 (61.8)	107 (83)	
Black	19 (30.2)	12 (10)	
Other	1 (1.6)	6 (4.7)	
Unknown	6 (6.4)	3 (2.3)	
Parity, mean + SD	2.1 ± 1.3	1.8 ± 1.4	0.103
Smoking, Freq (%)			
No	38 (60.3)	77 (59.7)	0.531
Yes	25 (39.7)	52 (40.3)	
Oral HRT			0.062
No	56 (88.9)	124 (96)	
Yes	7 (11.1)	5 (4)	
Depression			0.003
No	51 (94.4)	99 (76.7)	
Yes	3 (5.6)	30 (23.3)	
Urine incontinence			0.0000
No	34 (54)	102 (81.6)	
Yes	29 (46)	23 (18.4)	
Fecal incontinence			0.000
No	38 (65.5)	120 (96.8)	
Yes	20 (34.5)	4 (3.2)	
PISQ total score, median [IQR]	32 [28–37]	33 [29–38]	0.472

Table 2
Stage and adjuvant therapy data for EC baseline and matched pairs cohorts. No significant differences were found between the groups.

	EC baseline (n = 129)	EC matched pairs (n = 29)	p value
Stage Freq (%)			0.843
Ia	88 (68)	17 (58.6)	
Ib	20 (15.5)	7 (24.1)	
II	5 (3.9)	1 (3.5)	
III	12 (9.3)	3 (10.3)	
IV	4 (3.1)	1 (3.5)	
No adjuvant	70 (54)	11 (38)	0.215
Chemotherapy	(n = 16)	(n = 4)	0.909
Chemo alone	11 (8.5)	2 (7)	
At recurrence	2 (1.6)	0	
Other cancer	3 (2.3)	2 (7)	
Radiation	(n = 26)	(n = 6)	0.081
Vaginal brachytherapy	20 (16)	4 (14)	
External beam	1 (0.8)	0	
Combination	4 (3)	2 (7)	
Unknown	1 (0.8)	0	
Chemotherapy + radiation	(n = 17)	(n = 9)	0.133
Vaginal brachytherapy	5 (4)	5 (17)	
External beam	5 (4)	2 (7)	
Combination	7 (5)	2 (7)	

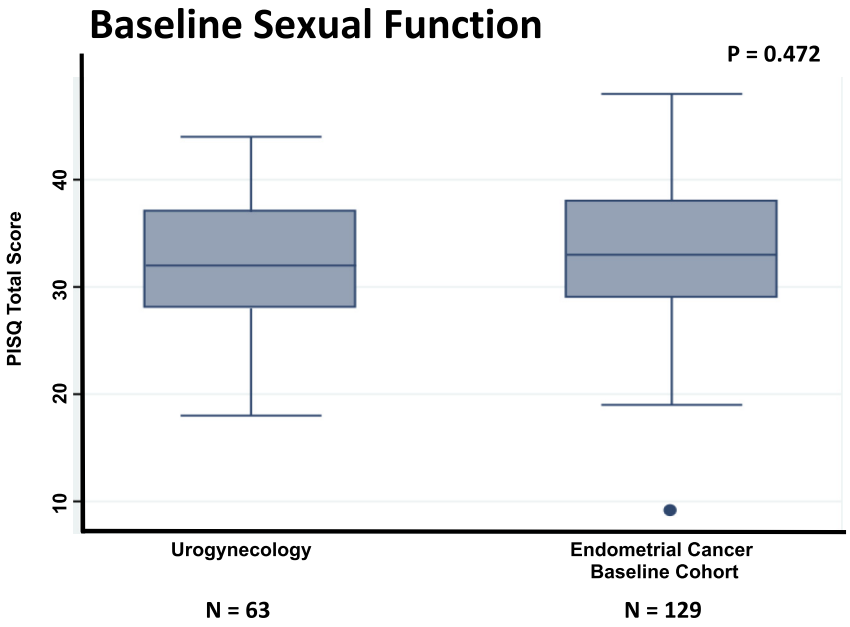

Fig. 2. Median and IQR of PISQ scores for EC baseline cohort vs urogynecology controls.

treatment regimens make comparison between these groups difficult [3,4,19]. Forty six percent of the baseline endometrial cancer cohort received some form of adjuvant therapy. Although many patients received vaginal brachytherapy alone, some received both chemotherapy and radiation. We observed no significant differences in function when compared to controls. In contrast, a recent review of the literature regarding sexual function after treatment for cervical cancer found that patients receiving adjuvant therapy reported higher rates of sexual dysfunction [3].

Reports of the effects of endometrial cancer treatment on sexual function are mixed. Some studies have reported worse sexual function after hysterectomy for endometrial cancer, however measures of sexual function were not standardized and frequently extrapolated from quality of life surveys [7–10,20]. Nout et al. showed sexual function scores below age-matched norms for endometrial cancer patients participating in the PORTEC-2 trial [20]. Aerts et al. reported worse sexual function in endometrial cancer patients when compared to women undergoing benign hysterectomy, though function was stable over time [13]. In a 2017 study, Gao et al. reported poor sexual function and low rates of intercourse in 118 Chinese women surveyed after surgery for endometrial cancer [21]. Conversely, several larger studies have shown sexual function to be stable or return to baseline over time [5,12–16,22]. Often, the largest studies pool gynecologic cancer types for comparison [6,16,23]. Various instruments are utilized in order to assess sexual function and few studies have long term follow up. A subanalysis of the LAP-2 study by Carter et al. used quality of life surveys

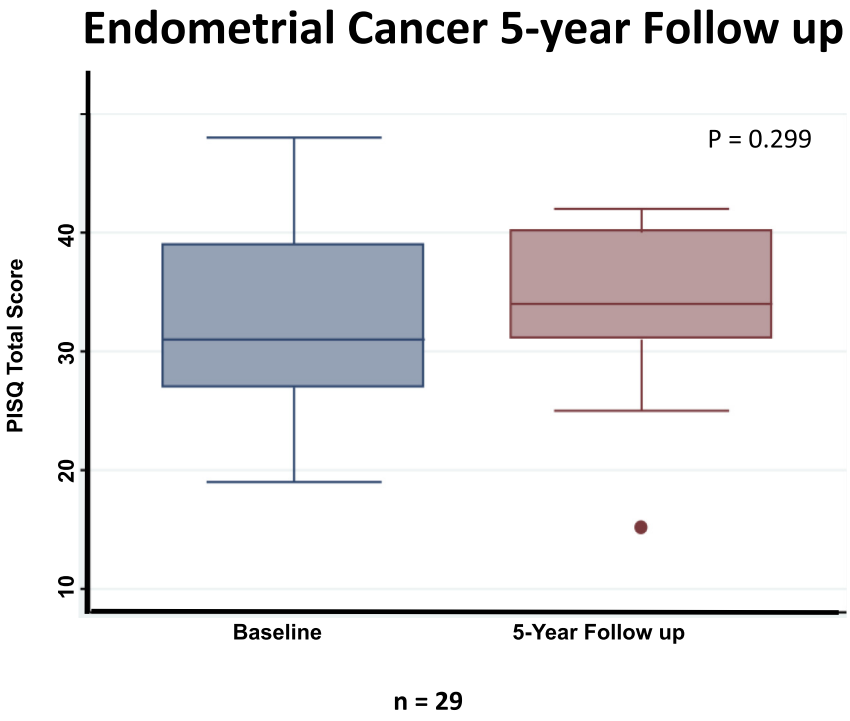

Fig. 3. Median and IQR for initial and follow up PISQ scores in endometrial cancer patients. Graphical representation of "EC matched pairs" cohort.

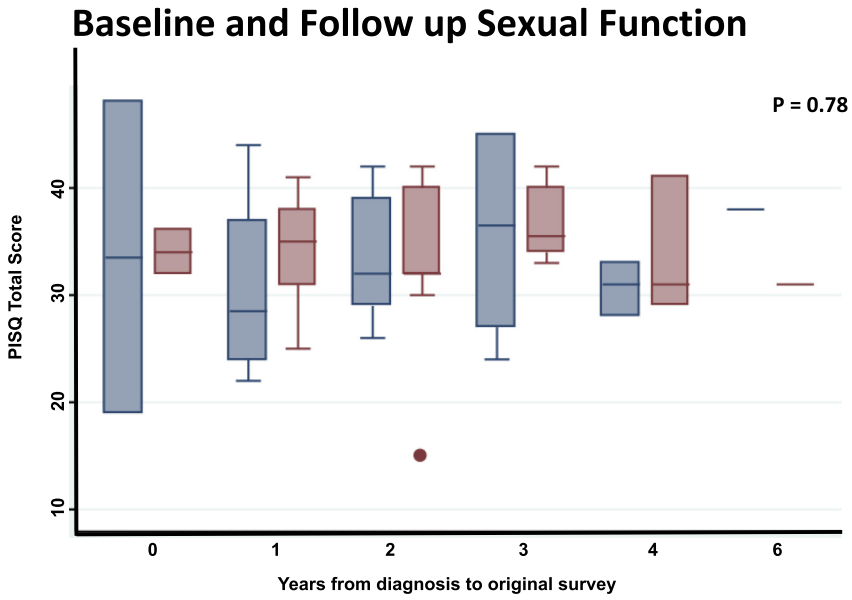

Fig. 4. Median and IQR for sexual function stratified by year from diagnosis. X-axis is survey year as related to diagnosis. Blue boxes represent initial survey administration, pink boxes represent follow up survey at 5 years from initial survey.

to evaluate sexual function showing an initial decline in sexual function, with scores returning to baseline levels at six months [5]. More recently, Ferguson and colleagues compared quality of life and sexual function scores in women undergoing minimally invasive versus open procedures for endometrial cancer. They found no statistically significant difference in sexual function between the two groups post-surgery, and each cohort's sexual function remained stable over 24 weeks. Of note, the mean score met criteria for sexual dysfunction [22]. Rowlands et al. used a national database of endometrial cancer patients in Australia to look at sexual function at 3 and 5-years post treatment. While more than 1/3 of patients (36%) scored near maximum sexual well-being using a validated sexual function questionnaire, no baseline data or control group were available for comparison [12]. Perhaps the longest interval follow up was published by Nout et al. who re-surveyed nearly 250 of the original PORTEC-1 subjects in 2011. Median time from surgery and treatment was 13 years. While the group showed no difference in sexual function between external beam radiation therapy and hysterectomy alone, sexual function scores for all subjects were low. Weaknesses of the trial include low percentage of sexual activity (24% of subjects) and use of multiple subscales taken from quality of life instruments to measure sexual function [11]. Our prospective study successfully captured data at two time points 5 years apart, and in some cases included patients who were more than 10 years from treatment. Similar to Ferrandina and Aerts, we showed that sexual function was similar to baseline even several years after surgery and adjuvant treatment [13,15]. Unlike the PORTEC-1 trial, we found that sexual function scores were not low overall and were comparable to benign controls [11].

Our investigation has several strengths. Although higher PISQ scores are associated with better sexual function, there is no consensus on the score associated with "normal" function. A matched control group served as point of reference for the PISQ score and demonstrated similar scores. By employing a non-cancer-specific instrument, we were able to adequately survey both cancer survivors and healthy controls. While the median age of the endometrial cancer cohort was 6 years older than the urogynecology cohort, the majority of patients in both groups were post-menopausal, making the difference less likely to be clinically significant. Lastly, our investigation used a validated sexual function questionnaire to obtain baseline and 5 year follow up data on sexual well-being in our patient population.

Our study has several limitations. As with any research utilizing surveys, there was a high attrition rate and potential for responder bias. Also, the PISQ survey was one of several surveys that patients were asked to answer simultaneously. Up to 50% of respondents failed to fill out the full PISQ survey at each time point. This could be due to responder fatigue or discomfort with answering questions about sexual health. Overall enrollment may not have been sufficiently powered to detect differences in the follow up group. The original survey was administered to patients postoperatively within 5 years of diagnosis rather than prior to hysterectomy. Ideally, baseline sexual function should be obtained prior to surgery.

Maximizing quality of life including sexual function in cancer patients, especially those with overall excellent survivorship such as endometrial carcinoma, must remain a priority. Our study suggests that endometrial cancer patients after hysterectomy enjoy baseline sexual function that is similar to benign counterparts and that this function is durable over many years. Further studies including prospective engagement of larger numbers of patients and employing cancer-specific validated survey instruments are needed.

Conflicts of interest

The authors report no conflict of interest.

CRediT authorship contribution statement

Lindsey Buckingham: Writing - original draft, Data curation. **Ashley Haggerty:** Data curation, Writing - review & editing. **Ashley Graul:** Data curation, Formal analysis. **Mark Morgan:** Writing - review & editing. **Robert Burger:** Writing - review & editing. **Emily Ko:** Formal analysis, Writing - original draft, Writing - review & editing. **Uduak Andy:** Data curation, Investigation. **Robert Giuntoli:** Conceptualization, Writing - original draft, Writing - review & editing.

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References

[1] J.D. Wright, et al., Nationwide trends in the performance of inpatient hysterectomy in the United States, Obstet. Gynecol. 122 (2 Pt 1) (2013) 233–241.
[2] S.L. Cohen, A.F. Vitonis, J.I. Einarsson, Updated hysterectomy surveillance and factors associated with minimally invasive hysterectomy, JSLS 18 (3) (2014).
[3] S. Ye, et al., A systematic review of quality of life and sexual function of patients with cervical cancer after treatment, Int. J. Gynecol. Cancer 24 (7) (2014) 1146–1157.
[4] I.D. White, The assessment and management of sexual difficulties after treatment of cervical and endometrial malignancies, Clin. Oncol. (R. Coll. Radiol.) 20 (6) (2008) 488–496.
[5] J. Carter, et al., Sexual function of patients with endometrial cancer enrolled in the Gynecologic Oncology Group LAP2 Study, Int. J. Gynecol. Cancer 22 (9) (2012) 1624–1633.
[6] W.A. Kylstra, et al., Sexual outcomes following treatment for early stage gynecological cancer: a prospective multicenter study, Int. J. Gynecol. Cancer 9 (5) (1999) 387–395.
[7] I. Juraskova, et al., Quantity vs. quality: an exploration of the predictors of posttreatment sexual adjustment for women affected by early stage cervical and endometrial cancer, J. Sex. Med. 9 (11) (2012) 2952–2960.
[8] S.R. Guntupalli, et al., Sexual and marital dysfunction in women with gynecologic cancer, Int. J. Gynecol. Cancer 27 (3) (2017) 603–607.
[9] S. Damast, et al., Sexual functioning among endometrial cancer patients treated with adjuvant high-dose-rate intra-vaginal radiation therapy, Int. J. Radiat. Oncol. Biol. Phys. 84 (2) (2012) e187–e193.
[10] N. Onujiogu, et al., Survivors of endometrial cancer: who is at risk for sexual dysfunction? Gynecol. Oncol. 123 (2) (2011) 356–359.
[11] R.A. Nout, et al., Long-term outcome and quality of life of patients with endometrial carcinoma treated with or without pelvic radiotherapy in the post operative radiation therapy in endometrial carcinoma 1 (PORTEC-1) trial, J. Clin. Oncol. 29 (13) (2011) 1692–1700.
[12] I.J. Rowlands, et al., Predictors of sexual well-being after endometrial cancer: results of a national self-report survey, Support Care Cancer 22 (10) (2014) 2715–2723.
[13] L. Aerts, et al., Sexual functioning in women after surgical treatment for endometrial cancer: a prospective controlled study, J. Sex. Med. 12 (1) (2015) 198–209.
[14] M. Becker, et al., Quality of life and sexual functioning in endometrial cancer survivors, Gynecol. Oncol. 121 (1) (2011) 169–173.
[15] G. Ferrandina, et al., Evaluation of quality of life and emotional distress in endometrial cancer patients: a 2-year prospective, longitudinal study, Gynecol. Oncol. 133 (3) (2014) 518–525.
[16] I. Juraskova, et al., Sexual adjustment following early stage cervical and endometrial cancer: prospective controlled multi-centre study, Psychooncology 22 (1) (2013) 153–159.
[17] R.G. Rogers, et al., A new instrument to measure sexual function in women with urinary incontinence or pelvic organ prolapse, Am. J. Obstet. Gynecol. 184 (4) (2001) 552–558.
[18] R.G. Rogers, et al., A short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12), Int. Urogynecol. J. Pelvic Floor Dysfunct. 14 (3) (2003) 164–168 (discussion 168).
[19] J. Carter, et al., The physical consequences of gynecologic cancer surgery and their impact on sexual, emotional, and quality of life issues, J. Sex. Med. 10 (Suppl. 1) (2013) 21–34.
[20] R.A. Nout, et al., Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data, Eur. J. Cancer 48 (11) (2012) 1638–1648.
[21] H. Gao, et al., Sexual function and quality of life among patients with endometrial cancer after surgery, Int. J. Gynecol. Cancer 27 (3) (2017) 608–612.
[22] S.E. Ferguson, et al., Prospective cohort study comparing quality of life and sexual health outcomes between women undergoing robotic, laparoscopic and open surgery for endometrial cancer, Gynecol. Oncol. 149 (3) (2018) 476–483.
[23] V. Goncalves, Long-term quality of life in gynecological cancer survivors, Curr. Opin. Obstet. Gynecol. 22 (1) (2010) 30–35.