

Assessment of long-term sexual function of cervical cancer survivors after treatment: A cross-sectional study

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Abstract

Objectives: This study aimed to investigate the long-term sexual function of patients with cervical cancer who underwent treatment and to explore influential factors.

Methods: This retrospective cross-sectional study was conducted at Peking University First Hospital in (Beijing, China). A total of 207 patients, who were diagnosed with Stage IA-IIA cervical cancer and had undergone surgical treatment (some patients had also been treated with adjuvant radiotherapy and chemotherapy) between January 2010 and August 2020, completed questionnaires via telephone. The median time since diagnosis was 54 (range, 13–138) months. Sexual function was assessed using the validated short form of Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12). The multivariate logistic regression analysis was performed to determine factors influencing sexual function after treatment.

Results: The mean preoperative PISQ-12 score was 39.42 ± 3.922 , and the mean postoperative PISQ-12 score was 32.60 ± 6.592 , indicating a significant decrease in postoperative PISQ-12 score compared with pre-operation ($p < 0.001$). In total, 49.8% of the patients had sexual dysfunction after treatment. According to the results of the multivariate logistic regression analysis, longer follow-up (months), ovariectomy, lack of hormone replacement therapy after ovariectomy and adjuvant radiotherapy were significantly associated with sexual dysfunction after treatment ($p < 0.05$). There was no significant correlation among surgical method, tumor stage, adjuvant chemotherapy, and sexual dysfunction after treatment.

Conclusions: The sexual function of cervical cancer survivors significantly decreased after treatment, which was related to the length of follow-up, ovariectomy, and adjuvant radiotherapy. Hormone replacement therapy after ovariectomy can help patients to improve their sexual function.

Key words: adjuvant radiotherapy, cervical cancer, hysterectomy, long-term sexual function, PISQ-12.

INTRODUCTION

Cervical cancer (CC) is one of the most common malignant tumors in women. According to the statistics presented by the National Cancer Center of China, there were about 98 900 CC patients in China in 2015.¹ In 2018, it was reported that CC ranked fourth in incidence among malignant tumors of the female reproductive system worldwide, seriously

threatening women's health.² With the advances of CC screening, CC patients showed a trend of becoming younger over the rising proportion of early-stage CC, and early-stage CC patients can survive for a long time after standard treatment. Given the high 5-year survival rate of CC patients, CC survivors' quality of life is worthy of further investigation, and the sexual function is an important component of the quality of life.³

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At present, surgery is the main therapeutic approach for early-stage CC, and adjuvant radiotherapy and chemotherapy are used according to patients' clinical conditions. Patients may receive multiple treatment modalities, accompanied with long-term influences on sexual function, and numerous studies have shown that there is a correlation between CC treatment and changes in sexual function.⁴⁻⁶ A large number of studies have reported that CC survivors mainly suffer from sexual discomfort, vaginal shortening, decreased vaginal elasticity, pelvic nerve damage, vaginal dryness, dyspareunia, insertion pain, vaginal bleeding, and decreased sexual interest compared with healthy controls.^{4,5,7} In addition, sexual dysfunction may also negatively affect the relationship between CC patients and their spouses, leading to emotional alienation and marital problems.^{4,6,8,9}

In previous studies, the short-term sexual function of CC survivors has been extensively discussed, while further attention needs to be paid to long-term follow-up of those survivors. The present study aimed to evaluate the long-term sexual function of CC survivors after cancer therapy (follow-up time, 13–138 months), and to investigate the possible effects of multiple treatment modalities and demographic variables on the sexual function of CC survivors using the validated short form of Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12).

MATERIAL AND METHODS

Study population

A total of 207 CC (Stage IA-IIA) survivors who underwent surgical treatment in the Peking University First Hospital (Beijing, China) between January 2010 and August 2020 were enrolled in the present observational, cross-sectional study. The median time since diagnosis was 54 (range, 13–138) months. Inclusion criteria were as follows: (1) patients with CC Stage IA-IIA; (2) patients aged 18–70 years old and were sexually active before being influenced by CC; (3) patients who were fully aware of the disease and symptoms. Exclusion criteria were as follows: (1) patients with CC stage > IIA; (2) patients with metastatic carcinoma from colorectal cancer after colostomy or enterectomy; (3) patients with tumor recurrence or complicated with other malignant tumors; (4) mental diseases (sequelae of cerebrovascular diseases, anxiety, depression, cognitive impairment, etc.); and (5) a history of anorectal

disorders, such as fecal incontinence, inflammatory bowel disease or gastrointestinal motility disorders.

Ethics approval

The study was approved by the Ethics Committee of the Peking University First Hospital, China (No. 2021-388, November 15, 2021).

Procedures

First, researchers identified patients who met the eligibility criteria, contacted them by phone, explained the objectives of the study, and obtained consent from patients. Those patients who refused were excluded from the study. Second, patients were interviewed to obtain the preoperative and postoperative PISQ-12 scores and patients' demographic data, in which the PISQ-12 questionnaire was completed by the interviewer. Third, patients' medical records were reviewed and clinical and demographic data were extracted by the interviewer.

Questionnaire design

The PISQ-12 questionnaire was used to evaluate patients' sexual function before surgery and during the last 6 months. The PISQ is a generalizable sexual function questionnaire that was originally developed, to evaluate three major domains of behavioral-emotive, physical, and partner-related. The PISQ-12 is a 12-item form designed to assess sexual function in women with urinary incontinence or pelvic organ prolapse.¹⁰ The total score of the PISQ-12 questionnaire ranges from 0 to 48. The higher the score is, the better the quality of sexual life is. A Chinese version of the PISQ-12 (CV-PISQ-12) score ≥ 32.5 was suggested as a normal sexual function.¹¹

Statistical analysis

The statistical analysis was performed using the SPSS 23.0 software (IBM Corp., Armonk, NY, USA). Descriptive and frequency analyses were used to summarize patients' demographic and clinical characteristics. Count data were presented as frequency (n [%]); the measurement data were expressed as mean \pm standard deviation (SD) or median (interquartile range [IQR]) according to whether they were normally distributed. The paired t -test was utilized for analyzing normally distributed data, and the Wilcoxon signed-rank test was used to analyze abnormally distributed data. The multivariate logistic regression analysis was employed to analyze patients' demographic and clinical characteristics to assess their influences on

CC survivors' sexual function after surgical treatment, in which age (years), BMI, PISQ-12 score (preoperative), parity and follow-up (months) were analyzed as continuous variables. $p < 0.05$ was considered statistically significant.

RESULTS

The research team identified 668 female patients with CC who met the eligibility criteria. A total of 331 patients were enrolled, of whom 207 (62.53%) respondents completed the PISQ-12 questionnaire (Figure 1).

The patients' demographic and clinical characteristics are presented in Table 1. The patients' mean age was 49.58 ± 8.439 (range, 31–72) years old. The majority of the patients (87%) were diagnosed with the International Federation of Gynecology and Obstetrics (FIGO) Stage I, and only 27 (13%) patients were diagnosed with FIGO Stage IIA. Besides, 107 (51.7%) patients underwent laparoscopy, and the remaining 100 (47.8%) patients received laparotomy; 99 (47.8%) patients' ovaries were removed. Only 7 (7.1%) patients received hormone replacement therapy (HRT) after ovariectomy. Based on the presence of relevant risk factors, 82 (39.2%) patients underwent adjuvant chemotherapy, and 43 (20.8%) patients received adjuvant radiotherapy postoperatively. Chemotherapy combining paclitaxel-platinum (protocol TP) was performed for 72% of patients, 25.6% of them received chemotherapy combining bleomycin-ifosfamide-platinum (protocol BIP) and 2 patients

received unknown chemotherapy. Among patients receiving adjuvant radiotherapy, 34 (79.1%) patients received external beam radiation therapy (EBRT) alone, 3 (7.0%) patients received intracavitary brachytherapy (ICBT) alone, with combination EBRT and ICBT given to only 6 (14%) patients.

The postoperative PISQ-12 score was significantly reduced compared with pre-operation ($p < 0.001$). In

TABLE 1 Demographics and clinical characteristics of patients

Characteristic	No. of patients (%), median (IQR) or mean \pm SD
Age (year), mean \pm SD	49.58 \pm 8.439
BMI (kg/m ²), median (IQR)	23.8751 (22.0386–26.1719)
Parity, median (IQR)	1 (1–2)
Mode of delivery, Freq (%)	
Vaginal	161 (77.8%)
Cesarean section	39 (18.8%)
Nullipara	7 (3.4%)
FIGO tumor stage, Freq (%)	
Ia	73 (35.3%)
Ib	107 (51.7%)
IIa	27 (13%)
Follow-up (months), median (IQR)	54 (31–79)
Operation mode, Freq (%)	
Abdominal	100 (47.8%)
Laparoscopic	107 (51.7%)
Ovariectomy, Freq (%)	
Yes	99 (47.8%)
No	108 (52.2%)
With adjuvant chemotherapy, Freq (%)	82 (39.2%)
TP	59 (72.0%)
BIP	21 (25.6%)
Unknown	2 (2.4%)
Without adjuvant chemotherapy	125 (60.8%)
With adjuvant radiotherapy, Freq (%)	43 (20.8%)
EBRT	34 (79.1%)
ICBT	3 (7.0%)
EBRT + ICBT	6 (14.0%)
Without adjuvant radiotherapy	164 (79.2%)

Note: Data are presented as the means \pm standard deviations or numbers (%). and Abbreviations: BIP, bleomycin-ifosfamide-cisplatin; BMI, body mass index; EBRT, external beam radiation therapy; FIGO, International Federation of Gynecology and Obstetrics; ICBT, intracavitary brachytherapy; IQR, interquartile range; SD, standard deviation; TP, paclitaxel-platinum.

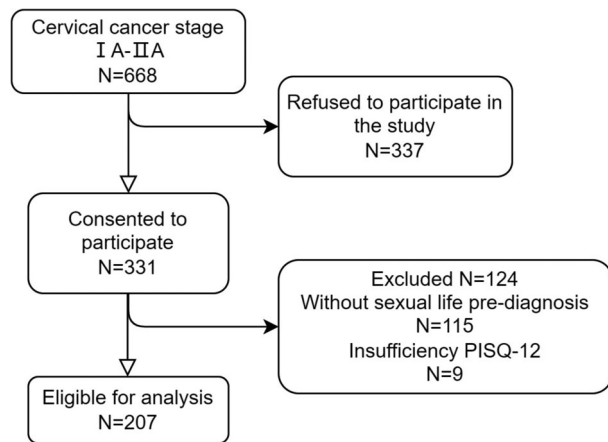


FIGURE 1 Graphical representation of patient recruitment and response via telephone follow-up

the PISQ-12 domain analysis, the scores of the three major domains all significantly decreased ($p < 0.001$). Meanwhile, 49.8% (103/207) of patients reported posttreatment sexual dysfunction. The preoperative and postoperative PISQ-12 scores were compared in Table 2.

Several risk factors that influenced postoperative PISQ-12 scores of CC patients were assessed using univariate analysis (Table 3). The results of univariate analysis showed that age, FIGO tumor stage, follow-up time (months), preoperative PISQ-12 score, ovariectomy, laparoscopy, and adjuvant therapy (chemotherapy/radiotherapy) were significantly correlated with

postoperative sexual dysfunction. Different radiation regimens have different effects on patients' postoperative sexual function ($p < 0.05$). Besides, body mass index (BMI), parity, and mode of delivery had no significant correlation with postoperative sexual dysfunction.

In the present study, a multivariable logistic regression model was established to examine the influences of different independent variables on the sexual dysfunction in patients with cervical cancer after treatment (Table 4). According to the results of the multivariate logistic regression analysis, follow-up (months), ovariectomy, and adjuvant radiotherapy were significantly associated with postoperative

TABLE 2 Comparison of preoperative and postoperative PISQ-12 scores ($n = 207$)

	Preoperative score	Postoperative score	<i>p</i>
Total PISQ-12 score	39.42 ± 3.922	32.60 ± 6.592	<0.001
Behavioral-emotive score	10.67 ± 3.039	6.56 ± 3.762	<0.001
Physical score	15.26 ± 1.336	14.54 ± 1.985	<0.001
Partner-related score	13.49 ± 1.119	11.51 ± 2.275	<0.001

Table 3 Risk factors for CC patients' PISQ-12 scores (postoperative) according to univariate analyses

Variable	OR	95% CI	<i>p</i>
Age (years)	1.066	1.029, 1.105	0.000
BMI	0.979	0.905, 1.060	0.604
Parity	0.869	0.580, 1.301	0.495
Mode of delivery			0.529
Nullipara	Ref		
Vaginal	0.986	0.490, 1.985	0.969
Cesarean section	2.595	0.489, 13.767	0.263
FIGO tumor stage			0.005
Ia	Ref		
Ib	0.417	0.169, 1.025	0.057
IIa	1.145	0.489, 2.683	0.755
Follow-up (m)	1.023	1.013, 1.032	0.000
PISQ-12 score (preoperative)	0.866	0.802, 0.935	0.000
Laparoscopic	0.485	0.279, 0.845	0.011
Ovariectomy	2.975	1.689, 5.239	0.000
No	Ref		
Yes			
Without HRT	0.680	0.126, 3.669	0.654
With HRT	3.345	1.868, 5.990	0.000
With adjuvant chemotherapy	2.123	1.203, 3.746	0.009
With adjuvant radiotherapy			0.016
No	Ref		
EBRT	3.730	1.639, 8.489	0.002
ICBT	2.686	0.239, 30.213	0.424
EBRT + ICBT	NA		

Abbreviations: BMI, body mass index; CI, confidence interval; EBRT, external beam radiation therapy; FIGO, International Federation of Gynecology and Obstetrics; HRT, hormone replacement therapy; ICBT, intracavitary brachytherapy; OR, odds ratio. and NA, Since all six patients who received EBRT + ICBT presented with postoperative sexual dysfunction, the corresponding specific OR, 95% CI and *p* values were not available.

TABLE 4 Multivariate logistic regression model evaluating the influence of different variables on sexual dysfunction (cutoff score of PISQ-12 is 32.5)

Variable	Logistic regression	
	OR and 95% CI	<i>p</i>
Age (years)	0.984 (0.927, 1.044)	0.594
FIGO tumor stage		0.129
IA	Ref	
IB	11.950 (0.853, 4.458)	0.113
IIA	0.927 (0.252, 3.414)	0.909
PISQ-12 score (preoperative)	0.931 (0.839, 1.033)	0.178
Follow-up (months)	1.021 (1.007, 1.035)	0.003
Laparoscopic Ovariectomy	0.894 (0.435, 1.838)	0.761
No	Ref	0.031
Yes		
Without HRT	0.896 (0.108, 7.436)	0.919
With HRT	3.602 (1.337, 9.707)	0.011
Adjuvant radiotherapy	5.000 (1.879, 13.306)	0.001
Adjuvant chemotherapy	0.610 (0.261, 1.425)	0.254

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics; HRT, hormone replacement therapy.

sexual dysfunction. Among them, adjuvant radiotherapy was the most important influential factor, leading to the poor postoperative sexual function (odds ratio [OR]: 5.000, 95% confidence interval [CI]: 1.879–13.30, $p < 0.01$). Patients with hormone HRT after ovariectomy had similar postoperative sexual function with nonovariectomized patients (OR: 0.896; 95% CI: 0.108–7.43, $p > 0.05$) while patients without HRT after ovariectomy were more likely to have postoperative sexual dysfunction (OR: 3.602, 95%CI: 1.337–9.70, $p < 0.05$). Additionally, it was revealed that CC patients were more likely to be dissatisfied with their sexual life when the duration of follow-up was prolonged (OR: 1.02, 95%CI: 1.007–1.035, $p < 0.05$).

DISCUSSION

According to the latest international guidelines,^{12,13} surgical treatment is the first option for early-stage CC patients, where cervical conization, total simple hysterectomy, modified radical hysterectomy or radical hysterectomy may be selected according to the stage of disease and the severity of CC. For patients with Stage IA1 disease who do not need to fertility preservation, extra-fascial hysterectomy is commonly

recommended for those patients without LVSI. If LVSI is present, then modified radical hysterectomy with sentinel lymph node (SLN) mapping/pelvic lymph node dissection (PLND) is recommended. For patients with Stage IA2-IB2 and partial IB3-IIA disease, the recommended surgical option is radical hysterectomy and bilateral PLND. In addition, patients with corresponding high-risk or medium-risk factors were given postoperative supplementary radiotherapy or adjuvant chemoradiotherapy according to the estimated prognosis. However, the above-mentioned treatments may have negative effects on the sexual function.^{4,5} Previous studies^{14,15} have suggested that patients with CC experience worse sexual function compared to control group of healthy women.

In the present study, PISQ-12 scores of early-stage CC survivors were significantly reduced after treatment compared with pretreatment ($p < 0.001$), which was similar to previously reported findings. Corrêa et al.¹⁵ reported a case-control evaluation of 37 patients with CC after treatment and found that the cancer group exhibited more vaginal stenosis or shortening and sexual dysfunction compared with the control group. Pieterse et al.¹⁴ evaluated the problems with miction, defecation, and sexuality after the radical hysterectomy of 94 CC survivors in Stage I-IIA throughout 24 months of follow-up. The patients' sexual function was significantly negatively influenced compared with both healthy controls and their situation before the treatment. The negative consequences included less lubrication, a narrow and short vagina, senseless areas around the labia, dyspareunia, and sexual dissatisfaction. Previous studies have mainly concentrated on the short-term sexual function of CC patients after treatment, while our study assessed the long-term sexual function of CC patients (follow-up period was 13–138 months).

The present study revealed that with the increase of follow-up time, CC patients were more likely to develop postoperative sexual dysfunction, which could be associated with the increase of patients' age, especially when they gradually stepped into menopause, resulting in significantly reduction of estrogen secretion. Ovary is an important organ for secretion of female sex hormones. Ovariectomy significantly decreases estrogen secretion, and it may negatively influence health of the vagina, causing sudden, strong, and long-term symptoms, including hot flashes, vaginal dryness, vaginal atrophy, dyspareunia, mood swings, irritability, and an overall decline in quality of life. The present study found that

postoperative sexual function was significantly impaired in patients undergoing ovariectomy without HRT (OR: 3.602, 95% CI: 1.337–9.70, $p < 0.05$), which was consistent with the result of previous studies,¹⁶ and patients with HRT after ovariectomy had better postoperative sexual function. Therefore, the conservation of ovary and appropriate use of estrogen replacement therapy are important factors influencing CC survivors' quality of life. Radiation therapy can adversely affect sexual function by causing vaginal fibrosis, decreased elasticity, vaginal narrowing, vaginal atrophy, insufficient vaginal lubrication, shortened vaginal length during intercourse, and even pelvic fibrosis. Additionally, radiotherapy can lead to ovarian failure, resulting in symptoms, such as early menopause, hyposexuality, and bleeding after sex.⁵ In the current study, it was revealed that radiotherapy was an important independent risk factor for postoperative sexual dysfunction (OR: 5.000, 95% CI: 1.879–13.30, $p < 0.01$), which was consistent with the previously reported finding.^{17–19} Pelvic floor muscle exercises (PFME), vaginal lubrication, and vaginal dilation can assist patients to improve their sexual function.^{20–22}

Sexual dysfunction is a common clinical challenge among CC survivors in China, and a great number of patients strongly desire to obtain further information on how to manage sexual problems, while no adequate attention has been paid to sexual function on behalf of healthcare providers, impairing the diagnosis and treatment of sexual disorders.^{8,23,24} In China, only a small proportion of cervical cancer patients receive HRT after medically induced menopause caused by ovariectomy, the present study's confirmation of HRT's effectiveness has important clinical implications for healthcare providers. Given that sex is a taboo subject, some participants are reluctant to ask for help. In Chinese clinical settings without routine sexual behavior assessment, early assessment of postoperative sexual function and psychosocial adjustment should be involved in routine nursing practice, and the comprehensive sexual health assessment should be routinely performed.^{25,26} Culturally competent healthcare service delivery can improve health outcomes, increase the efficiency of clinical staff, and enhance patient satisfaction.^{23,27} Besides, healthcare professionals should receive more formal training on sexual dysfunction, provide patient-centered open communication, and develop psychosocial interventions.^{28,29}

Regarding the main advantages of the present study, its sample size was larger than other relevant studies, and validated standardized questionnaires

were used. Moreover, confounding factors were controlled through multivariate logistic regression analysis, suggesting a more accurate direction for future studies. There were also some limitations in the present study. First, as a retrospective cross-sectional study, we can only assess some relevant factors influencing sexual function, while causal relationship cannot be proved between these factors and sexual dysfunction. The lack of comparison with healthy female controls is also a limitation to consider. Second, there was a possibility of high attrition and response bias due to the utilization of questionnaires. Third, the investigation of preoperative PISQ-12 scores was conducted within 13–138 months after diagnosis rather than before radical hysterectomy, which might cause recall bias, and ideally baseline function should be achieved preoperatively. Finally, some patients who agreed to participate in the survey responded reluctantly or ambiguously to the questionnaire, possibly due to feeling of shyness or uncomfortableness when they answered questions related to sexual function. Despite these limitations, the results of this study have important implications for healthcare providers aiming to provide optimal clinical care.

The risk factors related to sexual function of CC patients undergoing treatment are worthy of additional investigation. In the future research, it will be essential to conduct a prospective controlled study on the factors influencing postoperative sexual function, and the effects of clinical psychological comprehensive intervention on CC patients' sexual function should be further assessed. Moreover, to avoid recall bias, sexual function assessment should be routinely performed before CC treatment. In addition, in order to achieve a sufficiently robust prospective study within a reasonable time frame, further efforts should be dedicated to carry out a multicenter study and to integrate sexual health assessment procedures into clinical care standards.

In summary, the present study revealed that sexual function was significantly negatively influenced in CC survivors who underwent treatment. Radiotherapy was found as the most important influential factor, while the duration of follow-up, ovariectomy and HRT after ovariectomy were also of great importance. Healthcare providers should pay further attention to the sexual health education and consultation of patients and their families, and present necessary sexual life guidance, psychological support, and auxiliary treatment to enhance the sexual function of patients, so as to improve their quality of life.

AUTHOR CONTRIBUTIONS

Ye Lu, Hui-Zhong Wang, Rui-Ju He: conception and design. **Hui-Zhong Wang:** data analysis. All authors contributed to data collection and drafting the article, and approved the final version to be published.

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CONFLICT OF INTEREST

The authors declare no conflict of interests for this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to the privacy of research participants.

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