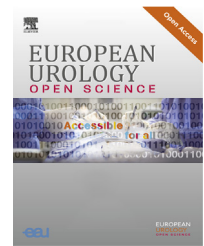


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## Urothelial Cancer

# Female Sexual Function After Radical Cystectomy: A Cross-sectional Study

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### Abstract

**Background and objective:** Radical cystectomy (RC) is the gold-standard treatment for muscle-invasive bladder cancer (MIBC). Approximately 25% of MIBC patients are women. In women, RC includes removal of the ovaries, uterus, and the anterior vaginal wall, during which nerve damage can occur, potentially impacting sexual function. Studies on sexual function among females following RC are sparse. Our aim was to investigate the impact of RC on female sexual function.

**Methods:** A cross-sectional registry study and a questionnaire survey were used. The Danish Cancer Registry was used to identify all female patients diagnosed with MIBC between 2015 and 2020 who were treated with RC and an ileal conduit. Comorbidity and complications data were obtained from the Danish National Patient Registry. The survey included European Organization for Research and Treatment of Cancer questionnaires on quality of life (EORTC-QLQ-C30) and sexual health (EORTC-SHQ-C22) and eight questions covering female sexual function.

**Key findings and limitations:** A total of 151 women completed the questionnaires, of whom 30 (21%) reported worries about resuming sexual activity after RC and 51 (34%) about resuming intercourse specifically. An altered perception of vaginal size was reported by 85 (56%) respondents. Prolonged time to experiencing orgasm was reported by 43 (51%) and anorgasmia by 23 (26%) of the sexually active women. Pain during and after penetration in  $\geq 50\%$  of attempts was reported by 29 (54%) and 23 (43%) respondents, respectively. There was moderate correlation between pain and sexual satisfaction ( $p < 0.001$ ).

**Conclusions and clinical implications:** RC can result in altered perception of vaginal size and pain on intercourse among female patients with bladder cancer, with potential effects on sexual satisfaction.

**Patient summary:** We assessed sexual outcomes for women after removal of the bladder for bladder cancer and carried out a survey among Danish women who underwent this treatment between 2015 and 2020. The majority of the women reported changes in sexual function, including pain during intercourse and altered perception of vaginal size.

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## 1. Introduction

Radical cystectomy (RC) is the golden standard when treating muscle-invasive bladder cancer (MIBC) [1]. Approximately 25% of all MIBC patients are women, for whom RC often includes removal of the ovaries and uterus [2]. The urethra and the anterior vaginal wall are also removed in women receiving an ileal conduit or continent cutaneous reservoir, but not in women receiving an orthotopic neobladder [3]. In Denmark, urinary diversion with an ileal conduit accounts for the majority of urinary diversions (90%) [4].

Extensive surgery in the pelvis can result in damage to autonomic and sensory nerves, with potential impacts on sexual function and desire and the ability to achieve orgasm [5]. Changes in vaginal dimensions can occur as a result of intraoperative vaginal reconstruction and can be potentially worsened by postoperative scarring [6]. In addition, removal of the ovaries results in an abrupt decrease in hormonal secretion, which may also impact sexual function [7]. One study showed a higher trend for impact on sexual function for women with an ileal conduit than for women receiving a pouch [8].

The use of patient-reported outcome measures (PROMs) in research has increased in recent years, especially in studies on quality of life (QoL), for which questionnaires often include sexual function. The specific questionnaires most often used for MIBC are the European Organization for Research and Treatment of Cancer (EORTC)-QLQ-BLM30 and Functional Assessment of Cancer Therapy (FACT)-BL instruments [9,10]. The sexual-specific questions in these questionnaires are limited in number and primarily focus on male impotence, female lubrication, and post-RC body image [11]. By focusing on only one symptom for each sex, other factors that may impact sexual health are not taken into consideration. By omitting, for example, orgasmic function and pain during intercourse, these questionnaires shed limited light on the real-life impact of RC on female sexual health. Another challenge with PROM research on sexual health is the lack of studies presenting results stratified by sex. This makes it difficult to differentiate the sex-specific impact of RC when questions are not sex-specific [12]. The literature covering female sexual function after RC is sparse [13]. The aim of our study was to examine and describe the impact of RC on female sexual function.

## 2. Patients and methods

### 2.1. Patient selection

We conducted a national cross-sectional registry study and a questionnaire survey. The Danish Cancer Registry was used to identify the study population. All female patients alive who were diagnosed with bladder cancer (BC)

between January 1, 2015 and December 31, 2020 and treated with RC and an ileal conduit were identified. Data on age, somatic and psychiatric comorbidities, and perioperative and postoperative complications were obtained from the Central Person Registry and the Danish National Patient Registry (DNPR). Details on treatment were obtained from the DNPR. TNM stage and histology were obtained from the Danish Cancer Registry. Exclusion criteria were a registered diagnosis of Alzheimer's disease or dementia in the DNPR or exemption from receipt of electronic mail according to the Danish national secure platform for digital communication (E-boks; <https://global.e-boks.com>). Along with a study invitation letter, the survey was distributed electronically on September 12, 2023 via SurveyXact (<https://rambollxact.com>). In cases with no response, a reminder was sent after 14 d. The option to reply to the survey was closed 1 mo after distribution.

### 2.2. Questionnaires

The survey consisted of two questionnaires, EORTC-QLQ-C30 [14] and EORTC-SHQ-C22 [15], chosen for their ability to measure QoL and sexual health, respectively, among cancer patients. The EORTC questionnaires are scored on a scale from 0 to 100. A high score for functional items represents good QoL, whereas a high score for symptom items represents a high level of symptomatology. We added questions covering female sexual health after RC and three questions on consulting health care professionals regarding sexual matters. Three of the questions (question 17–19) of The Female Sexual Function Index (FSFI) on pain [16], were modified to “after your surgery” instead of “over the past 4 weeks” to obtain answers from all the women who had attempted intercourse after RC. Specifically for this study, two questions on worries about resuming sexual activity, one question on altered perception of vaginal size, and one question on the impact of sexual problems on QoL were developed using the 4-point scoring scale of the EORTC questionnaires. Two questions on ability to achieve orgasm and time to orgasm were added, for which a 5-point Likert scale was used. One question on inability to achieve orgasm was added using the PRO Common Terminology Criteria for Adverse Events library of the National Cancer Institute (Q70) with a dichotomous (yes vs no) possibility modified with the option to reply “have not tried” instead of “prefer not to answer”. Before enrolment of the entire cohort, the questionnaire was tested in a pilot study involving six women who attended the post-RC follow-up program. The women were asked to complete the questionnaires and were interviewed afterwards about the content using a semi-structured approach (Supplementary Table 1).

### 2.3. Statistical analysis

All statistical analysis were conducted in R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) [17].

The EORTC questionnaires were scored according to guidelines [14,15], omitting missing data. Median scores and the interquartile range are presented for questionnaire data, as the data had a non-normal distribution. Frequencies and percentages are presented for the cohort characteristics. For correlations, a Wilcoxon signed-rank test and Spearman correlation were used to test for a relationship between a priori defined responses to the questionnaire. The test was used because of its ability to evaluate the strength and direction of a correlation between two nonparametric variables.

### 3. Results

We identified 388 female patients with BC who were treated with RC. A total of 99 women were excluded: 92 because of exemption from electronic mail receipt, and seven because they underwent RC as part of pelvic exenteration, for which the indication was not limited to BC. Thus, 289 women met the inclusion criteria, of whom 151 (52.2%) responded to the survey (Fig. 1).

The median age was 72 yr and the median age-adjusted Charlson comorbidity index was 4. The majority of the women had a body mass index  $>25$  kg/m<sup>2</sup> (61%) and a history of smoking (79%). A total of 66 (44%) had neoadjuvant chemotherapy and 54 (36%) underwent robot-assisted RC. The median time since surgery was 5 yr and the majority of the women (57%) had MIBC at the time of RC (Table 1).

**Table 1 – Characteristics of the 151 survey respondents**

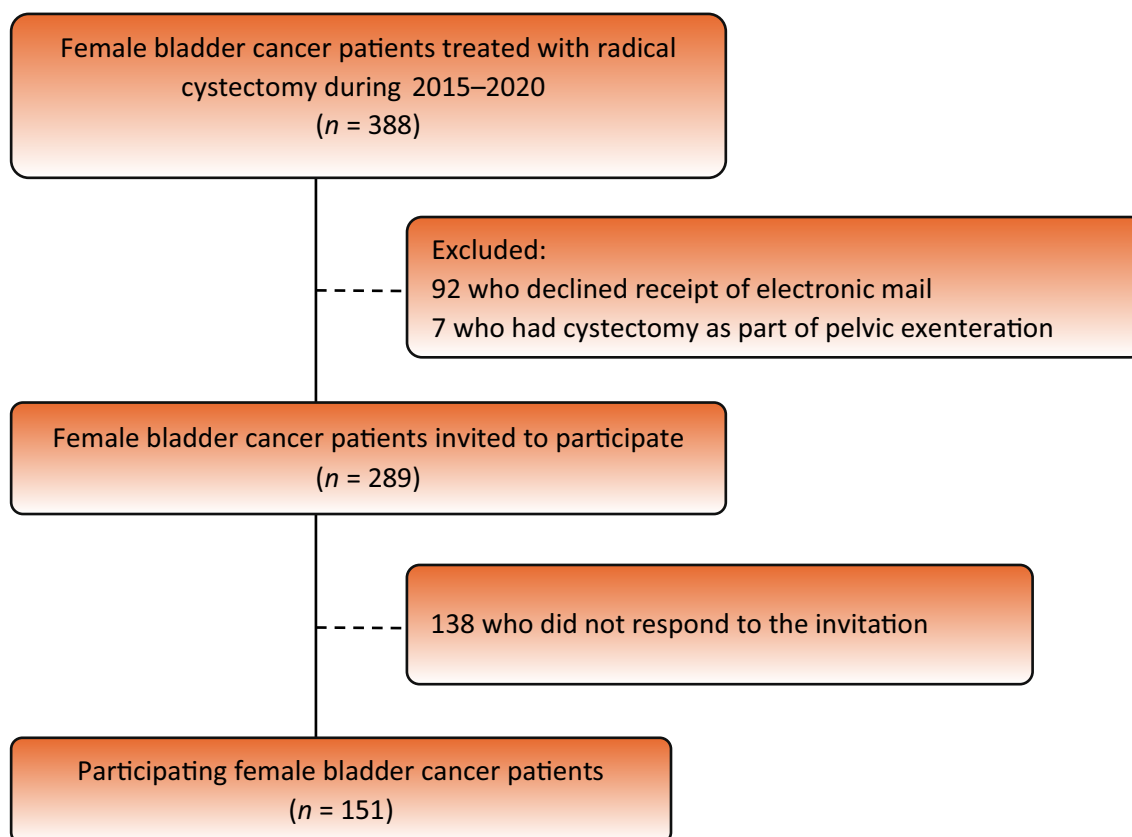
Parameter	Result
Median age, yr (Q1, Q3)	72 (65, 78)
Body mass index category, n (%)	
<25 kg/m <sup>2</sup>	59 (39)
25–30 kg/m <sup>2</sup>	65 (43)
>30 kg/m <sup>2</sup>	27 (18)
Smoking status, n (%)	
Never smoker	31 (21)
Former smoker	97 (64)
Current smoker	23 (15)
Median age-adjusted CCI (Q1, Q3)	4 (3, 4)
Neoadjuvant chemotherapy, n (%)	66 (44)
Robot-assisted RC, n (%)	104 (69)
Median time since RC, yr (Q1, Q3)	5 (4, 7)
TNM stage, n (%)	
≥T2	86 (57)
≥N1	10 (7)
≥M1	<5 (<5)

CCI = Charlson comorbidity index; Q1, Q3 = quartiles; RC = radical cystectomy.

None of the women were treated with radiotherapy before RC.

The 237 women who were excluded or did not respond were older, with a median age of 74 yr and 80 yr, respectively. [Supplementary Table 2](#) lists additional characteristics of the women who were excluded and those who did not respond.

One or more diagnoses of pelvic organ dysfunction after RC were registered for 20 women. Lymphoedema was registered for ten women (7%), vaginal hernia for 11 (<10%), and



**Fig. 1 – Flowchart of the patient inclusion process.**

vaginal stenosis and vaginal atrophy for fewer than five women (<5%) each. No other diagnoses related to the pelvic organs were registered.

Of the 151 women who responded, 34 (23%) were still sexually active, defined as having attempted intercourse at least once during the previous 6 mo. The reasons for sexual inactivity given by the 117 (77%) sexually inactive women are listed in [Table 2](#).

For the EORTC questionnaires, the rate of missing responses for items ranged from 0% to 3%. The median score for the Global Health Scale of the EORTC-QLQ-C30 was 75. The scores for functional scales are listed in [Table 3](#).

On the EORTC-SHQ-C22, the median score for the multi-item sexual satisfaction question was 44.4. The median score for the multi-item sexual pain question was 33.3. Only the sexually active women provided response to the single-item questions. The results are listed in [Table 4](#).

The semi-structured interviews after the pilot test did not lead to any changes to the supplementary questionnaire apart from the question on vaginal size, which was elaborated to include “as if the vagina seems shorter or narrower” to improve the understanding of what was asked.

**Table 2 – Sexual activity reported by the 151 survey respondents**

Parameter	Result
Sexually active, n (%)	34 (23)
Reason for sexual inactivity, n (%)	
Lack of desire	31 (27)
Pain	35 (30)
No partner	9 (8)
Unknown	42 (35)

**Table 3 – EORTC-QLQ-C30 scores reported by the 151 survey respondents**

Domain	Median score (Q1, Q3)
Global Health Scale	75 (58.3, 83.3)
Physical Functioning	86.7 (66.7, 100)
Role Functioning	100 (66.7, 100)
Emotional Functioning	91.7 (75, 100)
Cognitive Functioning	83.3 (83.3, 100)
Social Functioning	100 (66.7, 100)
Q1, Q3 = quartiles	

**Table 4 – EORTC-SHQ-C22 scores reported by the 151 survey respondents**

Question	Median score (Q1, Q3)
Multiple-item questions	
Sexual satisfaction	44.4 (33.3, 66.7)
Sexual pain	33.3 (0, 50)
Single-item question <sup>a</sup>	
Importance of sexual activity	33.3 (0, 33.3)
Decreased libido	33.3 (8.3, 66.7)
Incontinence	66.7 (0, 100)
Fatigue	0 (0, 0)
Treatment impact on sexual activity	33.3 (0, 33.3)
Partnership	33.3 (0, 33.3)
Body image	33.3 (33.3, 66.7)
Vaginal dryness	33.3 (0, 66.7)
Communication with professionals	66.7 (66.7, 100)
Q1, Q3 = quartiles.	
<sup>a</sup> Single-item questions were only scored by sexually active women (n = 34).	

For the RC-specific questionnaires, the rate of missing responses ranged between 0.7% and 7%. Thirty women (21%) reported that they were worried to a great extent about resuming sexual activity after RC, and 51 (34%) reported that they were worried to a great extent about resuming vaginal intercourse specifically. Altered perception of vaginal size after RC was reported as “a little” by 25 (17%), “quite a bit” by 27 (18%), and “very much” by 33 (22%) women. An ability to achieve orgasm before RC was reported by 137 women (90%). Prolonged time to achieve orgasm after RC was reported by 43 respondents (51%) and 62 (42%) had refrained from trying all together. Of the 85 women who had attempted to reach an orgasm, 23 (27%) reported anorgasmia after cystectomy. Vaginal intercourse at some point after RC was attempted by 54 respondents (35%). Pain during and after vaginal penetration in  $\geq 50\%$  of attempts was reported by 29 (54%) and 23 (43%) women, respectively. In a subgroup analysis for sexually active women, 16/34 (47%) experienced pain during vaginal penetration and 12/34 (35%) experienced pain after penetration in  $\geq 50\%$  of attempts. Among sexually inactive women who had attempted intercourse after RC, 13/20 (65%) experienced pain during vaginal penetration and 11/20 (55%) experienced pain after penetration in  $\geq 50\%$  of attempts. [Supplementary Table 3](#) lists the responses to the cystectomy-specific questions.

We found a weak correlation between reduced sexual satisfaction measured via the SHQ-C22 and the QLQ-C30 Global Health Scale. We also found moderate correlation between cystectomy-specific questions on pain in relation to intercourse and sexual satisfaction, weak correlation between orgasmic function and sexual satisfaction, and weak correlation between altered perception of vaginal size and pain in relation to intercourse ([Supplementary Table 4](#)).

A DNPR search revealed that none of the women were registered as having a diagnosis of sexual dysfunction after RC (ICD10 code DT983C or DT983D3). Of the 151 respondents, fewer than five were registered as having an appointment for sexual counseling. The pattern of answers to the RC-related questions showed the same tendency for the 20 women registered with pelvic organ dysfunction as for the remaining 131 women.

#### 4. Discussion

We found that 85 women (56%) experienced an altered perception of vaginal size to various degrees after RC. To the best of our knowledge, there are no studies describing this occurrence in a PROM setting [18], making comparison to other cohorts impossible. Although the women perceived an alteration in vaginal size, we cannot draw a conclusion on whether this causes a problem from our results. There might be a correlation between vaginal size and pain during intercourse, but no strong correlation was found when comparing covariates using Spearman’s method. This could potentially be attributed to the different approaches to vaginal reconstruction, specifically whether a rolling or clamping technique was applied [19,20]. Details regarding vaginal reconstruction are not recorded in Danish registries, so it was not possible to adjust for this variable.

Our subgroup analysis for sexually active women showed that 47% experienced pain during vaginal penetration and 35% experienced pain after penetration in  $\geq 50\%$  of attempts. This correlates well with findings in other studies that used FSFI scores [21,22]. We also found that pain was correlated with worse scores for the multi-item the EORTC-SHQ-C22 sexual satisfaction question. The proportion of women experiencing pain during intercourse was higher for the group that had attempted intercourse but were no longer sexually active when completing the questionnaire. Thus, pain might be a contributing factor in cessation of sexual activity after RC. Although pain during intercourse seems to be a problem for women following cystectomy, questions about pain during intercourse are limited in the BC-specific PROM questionnaires [9,23]. Thus, the growing interest in QoL and sexual dysfunction cannot rely only on EORTC or FACT questionnaires. Although treatment options do exist for pain during intercourse, further research into the true nature of the pain and possible options to prevent it for women undergoing cystectomy is warranted [7].

Vaginal dryness is the symptom most commonly asked about in the BC-specific questionnaires and is often the only female-specific question used to quantify sexual function, apart from feelings of femininity and altered body image [9,23,24]. In the present study, the median score for this question (EORTC-SHQ-C22, Q21) was low, suggesting that it was of less importance to the respondents. This symptom is often seen among elderly women with and without BC [25,26] and is thus not specific to treatment with RC. The rate of vaginal dryness among BC patients is between 15% and 42% [18,27]. Combined with the other noteworthy findings of this study, this raises the question of whether vaginal dryness alone should be used as a symptom that can provide an accurate picture of female sexuality and dysfunction. This highlights the need for more elaborate and varied questions investigating female sexual function to fully explore how vaginal dryness may correlate with effects such as pain during intercourse.

In the present study, 34 respondents (24%) were still sexually active and 54 (35%) had attempted intercourse after RC, which is similar to findings in other studies [21,28]. Reasons for sexual inactivity reported by the 20 women who had ceased sexual activity were equally distributed among those listed in Table 2. Of the responses to the question on whether the treatment had affected their sexual activity (EORTC-SHQ-C22, Q8), 14 (70%) were “quite a bit” or “very much”. Among the 96 sexually inactive women who had not attempted intercourse after RC, 39 (41%) replied “quite a bit” or “very much” to the same question. Thus, no specific reason for cessation of sexual activity can be identified. However, RC seems to have a profound impact on sexual activity in a large percentage of women and it can be assumed that it has some influence on the decision. This finding supports the need for more research into female sexual function after RC in order to fully understand the correlation.

One of the strengths of our study is its size: this is the largest study to date to examine female sexual function after RC [18]. Another is its ability to provide both PROM and

complete registry data from national registers of high validity [29]. However, the study has limitations, the first of which is its cross-sectional design, which has potential for recall bias considering the time since diagnosis when asked to recall conditions before surgery. This limits the ability to give an accurate description of preoperative and postoperative sexual function. Second, the response rate was only 52.2%. Nonresponders were older but otherwise comparable to responders. As increasing age has been associated with lower sexual activity [30], the level of sexual activity in our study may be overestimated, limiting the accuracy of the results. The rates for missing replies to the EORTC items were low (0–3%). This is consistent with the expected rate of 2%, which is likely to be higher for items addressing sexual issues according to guidelines [31]. Lastly, the absence of a correlation between specific questions and generic questionnaires may result from the question design for the study, which represents another limitation.

## 5. Conclusions

Female patients with BC should be informed that RC may result in altered perception of vaginal size and pain in relation to intercourse. These effects can potentially have a negative impact on sexual satisfaction, but further studies examining the correlation are warranted.

**Author contributions:** Rikke Vilsbøll Milling had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Milling, Jensen, Kingo.

*Acquisition of data:* Milling, Jensen.

*Analysis and interpretation of data:* Milling, Kingo.

*Drafting of the manuscript:* Milling.

*Critical revision of the manuscript for important intellectual content:* Seyer-Hansen, Graugaard-Jensen, Jensen, Kingo.

*Statistical analysis:* Milling.

*Obtaining funding:* Milling, Jensen.

*Administrative, technical, or material support:* Seyer-Hansen.

*Supervision:* Seyer-Hansen, Graugaard-Jensen, Jensen, Kingo.

*Other:* None.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.euros.2024.10.013>.



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