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Comparison of functional and oncological outcomes between uterus-sparing radical cystectomy and standard radical cystectomy in females: A retrospective study

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Purpose: This study aimed to compare the functional and oncological outcomes of females who underwent uterus-sparing radical cystectomy (USRC) and standard radical cystectomy (SRC).

Materials and Methods: Between February 2009 and December 2020, 90 female patients who underwent radical cystectomy with urinary diversion were included in this study, comprising the USRC and SRC groups. Functional outcomes were assessed in 63 patients who only underwent radical cystectomy with neobladder formation. Questionnaire scores, clean intermittent catheterization (CIC) rate, and urinary continence rate were analyzed. Oncological outcomes were assessed in 86 patients, regardless of the urinary diversion type. Overall survival (OS), cancer-specific survival (CSS), and recurrence-free survival (RFS) were compared.

Results: CIC rate was significantly lower in the USRC group than in the SRC group (14.7% vs. 48.0%; p=0.005). The continence rate was significantly higher in the USRC group than in the SRC group (85.3% vs. 40.0%; p=0.001). There were no significant differences in OS (p=0.890), CSS (p=0.700), or RFS (p=0.270) between the two groups. In multivariate analysis, uterine preservation did not significantly increase the hazard ratio (HR) of OS (HR, 0.62; 95% CI, 0.18–2.11; p=0.450), CSS (HR, 0.99; 95% CI, 0.22–4.40; p=0.990), or RFS (HR, 0.46; 95% CI, 0.19–1.11; p=0.840).

Conclusions: USRC resulted in higher continence rates and lower CIC rates than SRC without negatively affecting oncological outcomes. Hence, with thorough deliberation, USRC should be considered for females undergoing radical cystectomy.

Keywords: Bladder cancer; Cystectomy; Females; Hysterectomy; Uterus-sparing

INTRODUCTION

Bladder cancer is the 17th most common neoplasm in females, and the incidence is globally on the rise [1-3]. Radical cystectomy with urinary diversion is the recommended surgical treatment for muscle-invasive bladder cancer (MIBC) or high-risk-non-MIBC (NMIBC). Alternatively, for females with high risk of local recurrence due to the proximity of genital organs, the preferred method is standard radical cystectomy (SRC) involving *en bloc* resection of the bladder and

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adjacent pelvic organs, including the uterus [4-6]. However, uterine involvement in bladder cancer was only 0.3%–12.5% in previous studies, and routine hysterectomy during radical cystectomy has been questioned among urological surgeons [7-13]. Moreover, removal of the uterus can lead to functional complications, including hypercontinence, which requires clean intermittent catheterization (CIC), chronic urinary incontinence, infertility, and cessation of sexual life [9,12]. Therefore, there is substantial interest in uterus preservation during radical cystectomy to maintain urinary and sexual function [12,14,15]. In the present study, we compared the functional and oncological outcomes of radical cystectomy with or without uterus preservation to determine whether uterus-sparing radical cystectomy (USRC) can lead to superior functional outcomes without compromising oncological outcomes in females.

MATERIALS AND METHODS

1. Patient selection

This study was approved by Institutional Review Board of Seoul National University Hospital (IRB no. 2204-103-1316). Informed consent was waived due to the retrospective nature of study. We conducted a retrospective study of 90 females who underwent radical cystectomy with urinary diversion between February 2009 and December 2020. Patient data was retrospectively acquired by reviewing institutional electronic medical records, as well as the Seoul National University Prospectively Enrolled Registry for Urothelial Cancer [16]. Four patients were excluded from this study; three patients were excluded due to their histology, which does not fall into the major types of bladder cancer (urothelial cell carcinoma, squamous cell carcinoma, and adenocarcinoma), and the operation could not be completed in one patient due to severe intra-abdominal adhesions [17]. All surgeries were performed by three surgeons (predominantly by one surgeon, n=87, 96.7%). According to the surgical procedure, patients were categorized into two groups: USRC (radical cystectomy with uterus preservation, n=40) and SRC (radical cystectomy with preoperative hysterectomy or intraoperative hysterectomy, n=46). There were two types of urinary diversion: orthotopic ileal neobladder (n=63) and ileal conduit (n=23). Oncological analyses were conducted in all patients regardless of the urinary diversion type; however, functional analyses were only conducted in females who underwent radical cystectomy with continent urinary diversion (Fig. 1).

Females with MIBC or high-risk NMIBC who underwent radical cystectomy, with or without neoadjuvant chemotherapy and adjuvant chemotherapy, were included. All patients were diagnosed based on pathological results of transurethral resection or bladder biopsy. Preoperative imaging studies included computed tomography (CT) and pelvic magnetic resonance imaging (MRI). Currently, there are no official guidelines for USRC [12]. In this study, the patient who showed no uterine invasion on preoperative pelvic MRI met the criteria for preserving the uterus, regardless of

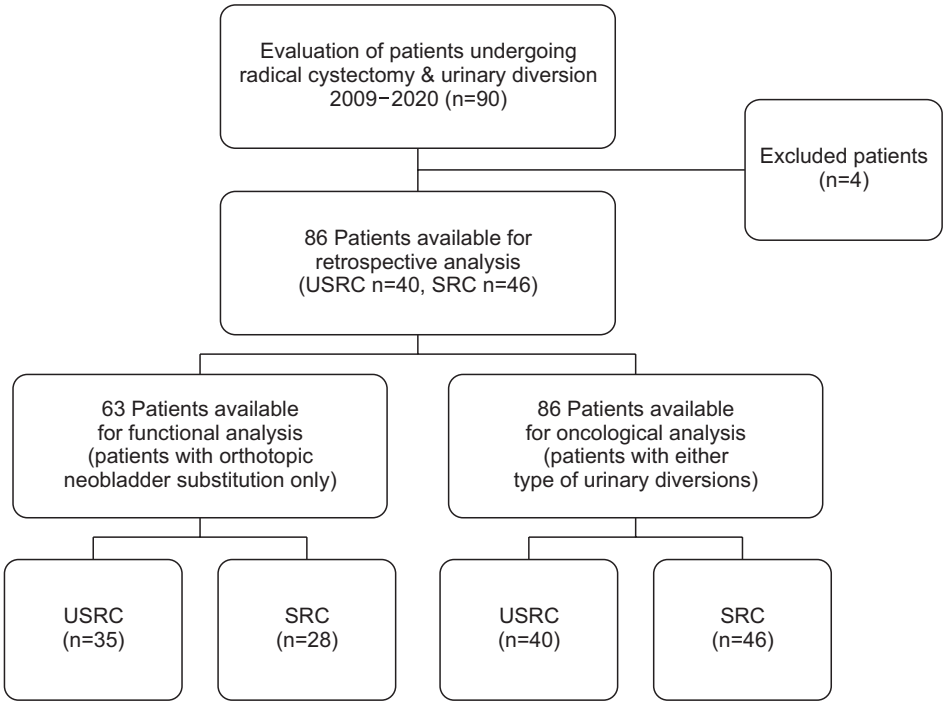

Fig. 1. Patient selection flowchart. USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy.

clinical T stage. In addition, the patients had a chance to discuss their preference for uterine preservation preoperatively with their doctors.

2. Follow-up

In an outpatient clinic, patients were evaluated at 3-month intervals within the first year following surgery and at 6-month intervals thereafter. Radiological examination was performed every 6 months to detect recurrence, and cystoscopy was only performed when the follow-up imaging study showed suspicious urethral recurrence. Moreover, to check the functional aspects of the patients who underwent continent urinary diversion, the need for CIC was determined on an individual basis, and the number of daily pad uses was checked. Uroflowmetry with bladder ultrasound scan was performed during every outpatient clinic visit, and urodynamic study (UDS) was performed 12-months postoperatively. CIC was indicated for patient with a residual urine volume greater than, or equal to, 100 milliliters, as assessed in either the bladder ultrasound scan or UDS. The Korean version of the Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index (FACT-VCI) questionnaire was administered to each patient to evaluate their quality of life both preoperatively and postoperatively.

3. Oncological outcomes

Oncological outcomes were assessed in 86 patients who underwent radical cystectomy regardless of the urinary diversion type (USRC, n=40; SRC, n=46). Recurrence was confirmed by biopsy or imaging. Overall survival (OS), cancer-specific survival (CSS), and recurrence-free survival (RFS) were compared between groups.

4. Functional outcomes

Functional outcomes were assessed in 63 patients who underwent radical cystectomy with orthotopic neobladder substitution only (USRC, n=35; SRC, n=28). Among 63 patients, 26 (USRC, n=14; SRC, n=12) who fully completed the FACT-VCI survey were included in the questionnaire analysis. Excluding the missing data, data from 59 patients (USRC, n=34; SRC, n=25) were assessed for CIC rate and daily pad use.

1) The Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index

The FACT-VCI is a questionnaire developed by Cookson and colleagues that can objectively assess life quality of patients who underwent radical cystectomy and urinary diversion has been validated [18,19]. The questionnaire is comprised of 27 items that are categorized into the physical, functional, emotional, and social/family well-being domains, along with 17 items that are especially related to urinary, sexual, and bowel functions [19]. Patients with higher scores have a better quality of life. FACT-VCI has been linguistically and psychometrically validated in the Korean language, and patients were asked to answer the Korean version of the FACT-VCI during the outpatient clinic visit [18,20]. The scores of the questionnaire before the surgery and within 12-month post-surgery were compared between the two groups.

2) Clean intermittent catheterization

Since incomplete emptying of the bladder is quite common among females who undergo orthotopic neobladder substitution, approximately 30% of females need CIC [4]. Therefore, the rates of CIC in the SRC and USRC groups at 12 months postoperatively were compared.

3) Urinary continence

Urinary continence was evaluated using the number of pads required per 24 hours. The severity of incontinence was categorized as follows: no pad was labeled as fully continent, pad=1 was labeled as socially continent, and pad>1 was considered incontinent [21,22]. Continence rates at 12 months postoperatively were analyzed.

5. Statistical analysis

A descriptive analysis was used to summarize the clinicopathological characteristics of the patients. The results are expressed in terms of number, median (interquartile range), and column percentages. An independent t-test was used for continuous variables, and a chi-squared test (or Fisher's exact test for cells less than five) was used for categorical variables. Univariate and multivariate Cox regressions were conducted to analyze variables associated with OS, CSS, and RFS, and the results are shown in terms of hazard ratios (HRs) and 95% confidence intervals (CIs). Kaplan–Meier analysis was performed to determine the 2-year survival rate for OS, CSS, and RFS. The mean preoperative and postoperative FACT-VCI total scores were calculated using the two-way analysis of variance (ANOVA). Statistical significance was set at a p-value <0.05. Statistical analyses were performed using the IBM Statistical Package for the Social Sciences version 25 (IBM Corp., Armonk, NY, USA) and MedCalc for Window version 19.4 (MedCalc Software bv, Ostend, Belgium).

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Table 1. Clinicopathological characteristics of patients

Parameter	Total (n=86)	USRC (n=40)	SRC (n=46)	p-value
Age (y)	69 (33–89)	69 (33–84)	69 (44–89)	0.910[a]
Follow-up period (mo)	23.7 (2.6–131.9)	25.9 (4.7–85.3)	18.8 (2.6–131.9)	0.090[a]
Body mass index (kg/cm^2)	23.6 (15.6–41.6)	24.5 (17.3–30.8)	22.4 (15.6–41.6)	0.160[a]
Types of surgery				0.050[b]
Open	60 (69.8)	32 (80.0)	28 (60.9)	
Robotic	26 (30.2)	8 (20.0)	18 (39.1)	
Types of urinary diversion				0.005[b]*
Neobladder	63 (73.3)	35 (87.5)	28 (60.9)	
Ileal conduit	23 (26.7)	5 (12.5)	18 (39.1)	
Preoperative clinical stage				0.330[b]
<T2	34 (39.5)	18 (45.0)	16 (34.8)	
≥T2	52 (60.5)	22 (55.0)	30 (65.2)	
Pathologic stage				0.210[b]
<T2	41 (47.7)	22 (55.0)	19 (41.3)	
≥T2	45 (52.3)	18 (45.0)	27 (58.7)	
Histological types				0.330[b]
Urothelial carcinoma	72 (83.7)	36 (90.0)	36 (78.3)	
Squamous carcinoma	11 (12.8)	3 (7.5)	8 (17.4)	
Adenocarcinoma	3 (3.5)	1 (2.5)	2 (4.3)	
Clinical T stage				0.101[b]
T0/Ta/Tis	5 (5.8)	4 (10.0)	1 (2.2)	
T1	29 (33.7)	14 (35.0)	15 (32.6)	
T2	37 (43.0)	19 (47.5)	18 (39.1)	
T3	11 (12.8)	3 (7.5)	8 (17.4)	
T4	4 (4.7)	0 (0.0)	4 (8.7)	
Pathologic T stage				
Urothelial carcinoma	72 (83.7)	36 (90.0)	36 (78.3)	0.620[b]
T0/Tis/Ta	16 (22.2)	11 (30.6)	5 (13.9)	
T1	13 (18.1)	7 (19.4)	6 (16.7)	
T2	8 (11.1)	4 (11.1)	4 (11.1)	
T3	16 (22.2)	7 (19.4)	9 (25.0)	
T4	2 (2.8)	1 (2.8)	1 (2.8)	
ypT0/ ypTis/ ypTa	8 (11.1)	4 (11.1)	4 (11.1)	
ypT2	1 (1.4)	0 (0.0)	1 (2.8)	
ypT3	6 (8.3)	2 (5.6)	4 (11.1)	
ypT4	2 (2.8)	0 (0.0)	2 (5.6)	
Squamous cell carcinoma	11 (12.8)	3 (7.5)	8 (17.4)	0.400[b]
T0/Tis/Ta	2 (18.2)	0 (0.0)	2 (25.0)	
T1	2 (18.2)	0 (0.0)	2 (25.0)	
T2	2 (18.2)	1 (33.3)	1 (12.5)	
T3	3 (27.3)	1 (33.3)	2 (25.0)	
ypT2	1 (9.1)	1 (33.3)	0 (0.0)	
ypT4	1 (9.1)	0 (0.0)	1 (12.5)	
Adenocarcinoma	3 (3.5)	1 (2.5)	2 (4.3)	0.390[b]
T2	1 (33.3)	0 (0.0)	1 (50.0)	
T3	2 (66.7)	1 (100.0)	1 (50.0)	
Pathologic lymph node stage				0.190[b]
N0	75 (87.2)	33 (82.5)	42 (91.3)	
N+	11 (12.8)	7 (17.5)	4 (8.7)	

Table 1. Continued

Parameter	Total (n=86)	USRC (n=40)	SRC (n=46)	p-value
Positive surgical margin				0.280[b]
No	76 (88.4)	34 (85.0)	42 (91.3)	
Yes	10 (11.6)	6 (15.0)	4 (8.7)	
Neoadjuvant chemotherapy				0.340[b]
No	67 (77.9)	33 (82.5)	34 (73.9)	
Yes	19 (22.1)	7 (17.5)	12 (26.1)	
Adjuvant chemotherapy				0.120[b]
No	69 (80.2)	35 (87.5)	34 (73.9)	
Yes	17 (19.8)	5 (12.5)	12 (26.1)	
Recurrence				0.800[b]
No	59 (68.6)	28 (70.0)	31 (67.4)	
Yes	27 (31.4)	12 (30.0)	15 (32.6)	

Values are presented as median (interquartile range) or number (%).
USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy; yp, neoadjuvant chemotherapy.
[a]:Independent t-test was used to analyze continuous variables.
[b]:Chi-squared (or Fisher's exact test for cells less than five) for categorical variables.
*Statistically significant p-value <0.05.

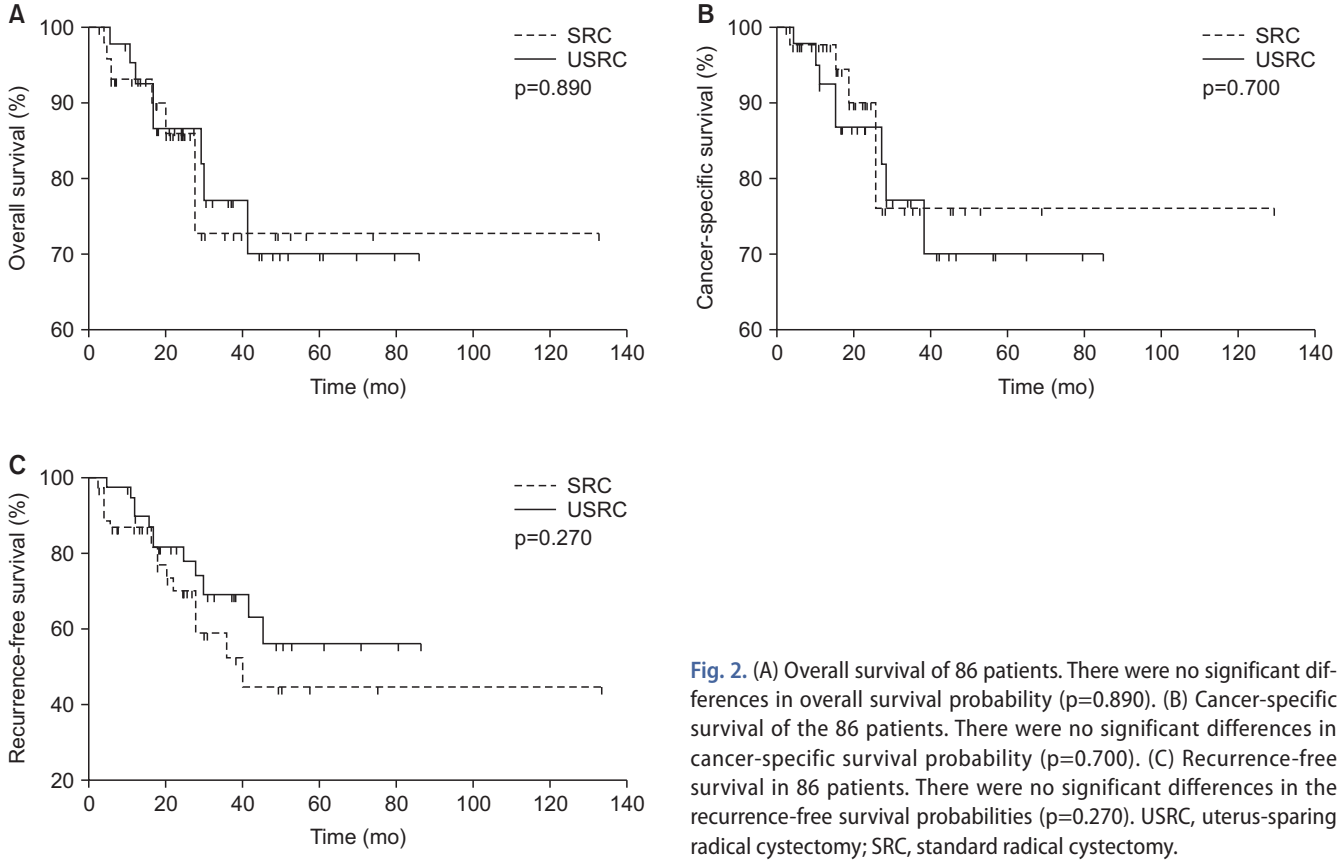

Fig. 2. (A) Overall survival of 86 patients. There were no significant differences in overall survival probability (p=0.890). (B) Cancer-specific survival of the 86 patients. There were no significant differences in cancer-specific survival probability (p=0.700). (C) Recurrence-free survival in 86 patients. There were no significant differences in the recurrence-free survival probabilities (p=0.270). USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy.

RESULTS

Eighty-six patients were enrolled for the final analysis (urothelial cell carcinoma, n=72; squamous cell carcinoma, n=11; and adenocarcinoma, n=3). Nineteen patients received neoadjuvant chemotherapy, and 17 patients received adjuvant chemotherapy. Among the 86 patients, 40 (46.5%) underwent USRC and 46 (53.5%) underwent SRC alone. There were no statistically significant differences in the clinical and pathological T stage between the USRC and SRC

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groups. There was no significant difference between the two groups in terms of pathological lymph node stage and surgical margin positivity. The median follow-up period was 23.7 months; the USRC group had a longer median follow-up period than the SRC group, but the difference was not statistically significant. The USRC group had a higher open surgery rate than the SRC group (80.0% vs. 60.9%, p=0.050). Orthotopic neobladder substitution was performed at a higher rate in the USRC group than in the SRC group (87.5 vs. 60.9%, p=0.005). Patient demographics are summarized in Table 1.

1. Oncological outcomes

In the USRC group, eight of the 40 patients (20.0%) died at a median follow-up of 25.9 months from metastasis. In the SRC group, seven of the 46 patients (15.2%) died at a median follow-up of 18.8 months, 5 from metastatic disease and two from other causes. Twelve (30.0%) patients in the USRC group and 15 (32.6%) patients in the SRC group experienced recurrence. Among the 12 patients with recurrence in the USRC group, only one patient showed recurrence in the uterus (8.3%). OS, CSS, and RFS probabilities following USRC and SRC were obtained via Kaplan–Meier survival curves. The 2-year OS, CSS, and RFS rates were 82.0%, 81.9%, and 78.0%, respectively, in the USRC group; The 2-year OS, CSS, and RFS rates were 85.9%, 83.0%, and 64.7%, respectively, for SRC group. There were no significant differences in OS (p=0.890), CSS (p=0.700), or RFS (p=0.270) between the two groups (Fig. 2).

Confounding factors that might influence patient prognosis were adjusted using multivariate cox regression analysis. It was found that uterine preservation did not significantly increase the HR of OS (HR, 0.62; 95% CI, 0.18–2.11; p=0.450), CSS (HR, 0.99; 95% CI, 0.22–4.40; p=0.990), or RFS (HR, 0.46; 95% CI, 0.19–1.11; p=0.840) after adjusting for several parameters shown in Tables 2–4.

2. Functional outcomes

The mean preoperative and postoperative (within 12 months) FACT-VCI total scores were compared between the USRC and SRC groups. The average preoperative scores for the USRC and SRC groups were 104.8 and 100.9, respectively. The postoperative average scores for the USRC and SRC groups were 96.72 and 99.69, respectively (Fig. 3). Although

Table 2. Univariate and multivariate Cox regression analyses of variables associated with overall survival

Prognostic factor	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (continuous variable)	1.02	0.96–1.07	0.560	1.03	0.97–1.09	0.390
Preservation						
Standard radical cystectomy		Referent			Referent	
Uterus-sparing radical cystectomy	0.93	0.34–2.58	0.890	0.62	0.18–2.11	0.450
Preoperative clinical stage						
<T2		Referent			Referent	
≥T2	3.23	0.91–11.48	0.070	2.25	0.60–8.50	0.230
Pathologic stage						
<T2		Referent			Referent	
≥T2	6.17	1.69–22.43	0.006*	6.14	1.53–24.55	0.010*
Lymph node positive						
Negative		Referent			Referent	
Positive	2.16	0.61–7.66	0.240	2.61	0.60–11.26	0.200
Surgical margin positive						
Negative		Referent			Referent	
Positive	2.34	0.75–7.45	0.140	3.06	0.84–11.13	0.910
Neoadjuvant chemotherapy						
No		Referent			Referent	
Yes	2.12	0.66–6.82	0.210	1.94	0.52–7.26	0.320
Adjuvant chemotherapy						
No		Referent			Referent	
Yes	1.20	0.38–3.78	0.760	0.52	0.13–2.02	0.340

HR, hazard ratio; CI, confidence interval.
*Statistically significant p-value <0.05.

Table 3. Univariate and multivariate Cox regression analyses of variables associated with cancer-specific survival

Prognostic factor	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (continuous variable)	1.02	0.96–1.08	0.510	1.03	0.97–1.10	0.370
Preservation						
Standard radical cystectomy		Referent			Referent	
Uterus-sparing radical cystectomy	1.25	0.41–3.85	0.690	0.99	0.22–4.40	0.990
Preoperative clinical stage						
<T2		Referent			Referent	
≥T2	2.74	0.75–10.00	0.130	1.86	0.46–7.29	0.370
Pathologic stage						
<T2		Referent			Referent	
≥T2	9.20	1.99–42.46	0.004*	8.88	1.80–43.86	0.007*
Lymph node positive						
Negative		Referent			Referent	
Positive	1.62	0.36–7.31	0.530	1.53	0.23–10.11	0.660
Surgical margin positive						
Negative		Referent			Referent	
Positive		0.88–9.30	0.080	2.89	0.78–10.66	0.110
Neoadjuvant chemotherapy						
No		Referent			Referent	
Yes	1.86	0.49–6.93	0.360	1.83	0.42–8.06	0.430
Adjuvant chemotherapy						
No		Referent			Referent	
Yes	1.43	0.44–4.66	0.550	0.80	0.17–3.72	0.780

HR, hazard ratio; CI, confidence interval.
*Statistically significant p-value <0.05.

the USRC group showed a greater decline in the postoperative questionnaire score, the difference was not statistically significant (p=0.130). Twelve months after radical cystectomy with continent urinary diversion, 28.8% of the patients underwent CIC (Fig. 4). Patients in the USRC group had significantly lower CIC rates than those in the SRC group (14.7% [5/34] vs. 48.0% [12/25], p=0.005). The complete continence rate 12 months postoperatively, defined as no pad, was 66.1% among all patients (Table 5). The continence rate was significantly higher in the USRC group than in the SRC group (85.3% [29/34] vs. 40.0% [10/25], p=0.001).

DISCUSSION

The main objective of bladder cancer treatment is to treat the disease while maintaining the urinary and sexual capabilities. Uterus-sparing surgery or sexual organ-sparing surgery would leave the reproductive organs and nerves intact to bring noticeable progression of functional outcomes [4]. However, concurrent hysterectomy or anterior pelvic exenteration during radical cystectomy remains the conventional treatment for high risk NMIBC and MIBC in females because of the proximity of the sexual organs and the bladder. Nonetheless, postoperative pathological data from previous studies have revealed that uterine invasion is rare. In a large study of 609 patients who underwent radical cystectomy, no patient had concomitant gynecological malignancies [1]. Gregg et al. [7] reported that 20 of 160 patients (12.5%) had uterine invasion. This is believed to be the highest uterine invasion rate reported so far (0.3%–12.5%) [7-13]. In our study, among the 36 patients who did not undergo preoperative hysterectomy, only two (5.5%) had uterine invasions. Since there is no anatomical barrier in the vesicocervical space, most urologists still recommend that hysterectomy be performed during cystectomy to reduce the probability of uterine invasion, especially in postmenopausal patients [4].

Broad utilization of USRC in unselected patients can compromise oncological outcomes, but there are no established guidelines for preserving the uterus or other sexual organs during radical cystectomy [1,12]. The risks of uterine invasion have been investigated in preliminary studies to determine which group of patients is suitable for USRC. Choi et al. [13] found that a hydronephrosis on CT, tumor size ≥4.8 cm on CT, and tumors located at the bladder neck

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Table 4. Univariate and multivariate Cox regression analyses of variables associated with recurrence-free survival

Prognostic factor	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (continuous variable)	0.99	0.95–1.03	0.560	1.004	0.97–1.05	0.840
Preservation						
Standard radical cystectomy		Referent			Referent	
Uterus-sparing radical cystectomy	1.62	0.70–3.69	0.230	0.46	0.19–1.11	0.840
Preoperative clinical stage						
<T2		Referent			Referent	
≥T2	2.78	1.12–6.91	0.030*	1.97	0.77–5.08	0.160
Pathologic stage						
<T2		Referent			Referent	
≥T2	3.81	1.62–8.93	0.002*	3.39	1.30–8.85	0.013*
Lymph node positive						
Negative		Referent			Referent	
Positive	2.99	1.26–7.10	0.010*	4.06	1.50–11.01	0.006*
Surgical margin positive						
Negative		Referent			Referent	
Positive	1.51	0.57–4.00	0.400	2.64	0.87–7.96	0.085
Neoadjuvant chemotherapy						
No		Referent			Referent	
Yes	3.57	1.59–7.99	0.002*	3.25	1.29–8.22	0.013*
Adjuvant chemotherapy						
No		Referent			Referent	
Yes	1.16	0.49–2.78	0.730	0.46	0.17–1.25	0.130

HR, hazard ratio; CI, confidence interval.
*Statistically significant p-value <0.05.

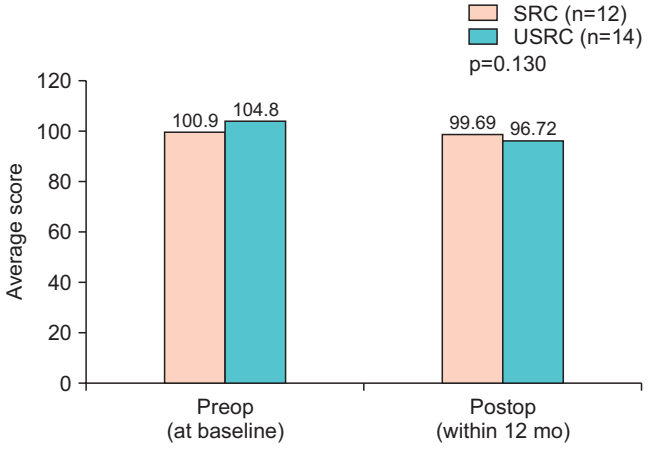

Fig. 3. Preoperative and postoperative mean Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index questionnaire total scores in patients (n=26) who underwent uterus-sparing radical cystectomy or standard radical cystectomy. USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy; preop, preoperatively; postop, postoperatively.

or trigone are risk factors for sexual organ invasion [12]. In another study by Ali-El-Dein et al. [11], the risk of secondary gynecologic organ invasion was increased by high-grade bladder tumors and positive lymph node status [12]. Therefore, patients with unifocal, organ-confined bladder cancer that is distant from the bladder neck, bladder base, and trigone can be considered suitable candidates for sexual organ-sparing cystectomy [1]. In this study, the indications for USRC were different from those reported in previous studies. If the patient had no metastasis in either preoperative imaging studies (CT or MRI) and no uterine invasion on pelvic MRI, she was considered suitable for USRC regardless of clinical T stage, tumor focality, tumor size, and tumor location. Among patients who were considered suitable candidates for USRC, the uterus was either preserved or removed based on the discretion of doctors and consensus from patients. Hysterectomy was performed on patients whose preoperative MRI indicated intraoperative uterine invasion or suspicion of uterine invasion. Hence, this study applied broader utilization of USRC in selected patients.

Achieving oncological control is the primary goal of radical cystectomy. Among the 86 patients, 40 (46.5%) underwent USRC and 46 (53.5%) underwent SRC alone. There were no significant differences between the two groups in terms of OS, CSS, and RFS. Cox regression analysis was used

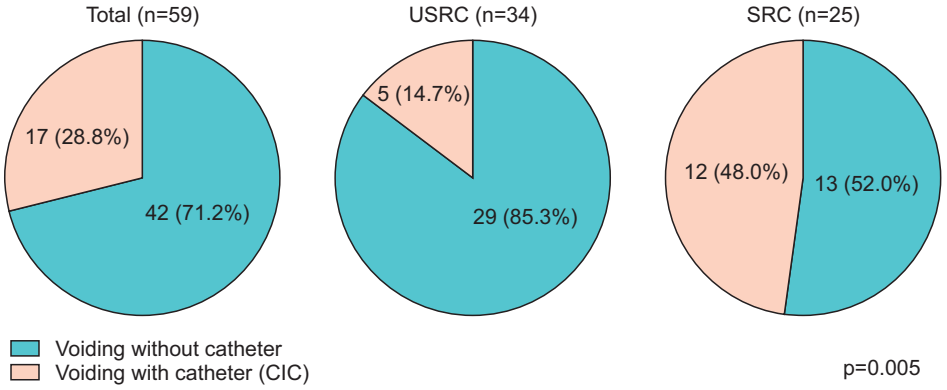

Fig. 4. Clean intermittent catheterization rate 12 months postoperatively in patients (n=59) who underwent uterus-sparing radical cystectomy or standard radical cystectomy. USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy; CIC, clean intermittent catheterization.

Table 5. Urinary continence rates 12 mo postoperatively in patients who underwent uterus-sparing radical cystectomy or standard cystectomy

Urinary continence, n (%)	Total (n=59)	USRC (n=34)	SRC (n=25)	p-value
Totally continent (pad=0)	39 (66.1)	29 (85.3)	10 (40.0)	0.001*
Socially continent (pad=1)	13 (22.0)	3 (8.8)	10 (40.0)	
Incontinent (pad>1)	7 (11.9)	2 (5.9)	5 (20.0)	

USRC, uterus-sparing radical cystectomy; SRC, standard radical cystectomy.
*Statistically significant p-value <0.05.

to reduce selection bias and adjust for the parameters that may affect the patient's prognosis: age, clinical stage, pathologic stage, lymph node positivity, surgical margin positivity, and neoadjuvant or adjuvant chemotherapy. The analysis showed that uterine preservation was not an independent predictor of OS (HR, 0.62; 95% CI, 0.18–2.11; p=0.450), CSS (HR, 0.99; 95% CI, 0.22–4.40; p=0.990), and RFS (HR, 0.46; 95% CI, 0.19–1.11; p=0.840). Thus, we inferred that this study's broad indication of uterine preservation, which depends mainly on preoperative pelvic MRI, did not negatively affect the oncological outcomes of the USRC group. Increasing evidence shows that diffusion-weighted MRI may provide more precise preoperative staging and may decrease clinical understaging in reproductive organ-sparing cystectomy candidates [1]. Moreover, pathologic stage ≥T2 significantly increased the HR in OS (HR, 6.14; 95% CI, 1.53–24.55; p=0.010), CSS (HR, 8.88; 95% CI, 1.80–43.86; p=0.007), and RFS (HR, 3.39; 95% CI, 1.30–8.85; p=0.013). Although this study included uterus-preserved patients with ≥cT2b disease, a higher pathologic stage increased the HR in all survival curves. Hence, careful consideration must be given to patients who are expected to have a higher T stage, although they have no uterine invasion on preoperative MRI. In one study, the 2-year OS in females who underwent radical cystectomy without gynecologic organ involvement was 73% [23]. In this study, the 2-year OS rates of the USRC and SRC groups were 82.0% and 85.9% (p=0.890), respectively.

In addition to achieving oncological control, optimizing functional outcomes is another challenge in radical cystectomy. Females who underwent radical cystectomy and neobladder substitution had a higher rate of incontinence and frequently required CIC due to incomplete bladder voidance than males [4,24]. One potential reason might be the lack of attention paid to nerve-saving during radical cystectomy in females. In females, the autonomic nerve of the inferior hypogastric plexus runs along lateral sides of the cervix and the rectum, leaving them vulnerable to injuries that could lead to incontinence and sexual dysfunction during pelvic surgeries, such as hysterectomy [1,4,25,26]. Gross et al. [4] reported that patients who underwent cystectomy with sexual organ preservation more often maintained both daytime and nighttime continence than those who underwent SRC. A continence rate of 87.5% was achieved for both day and nighttime continence. Although our study could not divide the continence rate into day and night due to a lack of information in the database, the 24-hour continence rate was 85.3% in the USRC group, which is in line with the study by Gross. This was significantly higher than the 24-hour continence rate in the SRC group (85.3% vs. 40.0%, p=0.001). Daytime and nighttime continence rates were reported to be 64%–100% and 50%–89%, respectively, in other studies regarding sexual organ-sparing [25]. Moreover, 'hypercontinence' (incomplete emptying of the bladder) is another complication that can arise from concomitant hysterectomy during radical cystectomy. The reported CIC rate ranges from 0% to 31% [25], and Gross et al. [4] reported that the rate of CIC was the same in both groups. In the current study, CIC rate was 28.8% in the entire cohort. Evaluating the CIC rate separately, the CIC rates of the USRC and SRC groups were 14.7% and 48.0% (p=0.005). The outcomes of this study showed that the continence rate was higher, and the CIC rate was lower after USRC than after SRC.

The present study has some limitations. The study was

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conducted retrospectively at a single center with a limited number of patients. A key limitation of this study was selection bias. Since there are still no clear guidelines for the application of USRC, the decision regarding whether to spare the uterus was based on the surgeon's discretion, which may have influenced the oncological outcomes. Nevertheless, this is inherent to the nature of this study, and we used Cox regression analysis to adjust for factors that may affect the oncologic prognosis of patients. Moreover, the follow-up period may be inadequate, and further long-term investigations are needed in the future. Lastly, sexual function and postoperative fertility were not evaluated in this study because of the limited data available. In the future, USRC may enable female patients to achieve better sexual and reproductive outcomes.

CONCLUSIONS

The standard utilized in this study is differentiated from that used in previous studies in that it decided whether to preserve the uterus of the female patients undergoing radical cystectomy depending primarily on the preoperative MRI results. For females, USRC resulted in higher continence rates and lower ISC rates than SRC without negatively affecting oncological outcomes. Hence, with thorough deliberation, USRC should be considered for females undergoing radical cystectomy and urinary diversion.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Jae Suk Park and Ja Hyeon Ku. Data acquisition: Chang Wook Jeong, Hyeon Hoe Kim, and Ja Hyeon Ku. Statistical analysis: Jae Suk Park. Data analysis and interpretation: Jae Suk Park, Hyeong Dong Yuk, Chang Wook Jeong, Cheol Kwak, and Ja Hyeon Ku. Drafting of the manuscript: Jae Suk Park. Critical revision of the manuscript: Jae Suk Park and Ja Hyeon Ku. Supervision: Hyeong Dong Yuk, Chang Wook Jeong, Cheol Kwak, Hyeon Hoe Kim, and Ja Hyeon Ku. Approval of the final manuscript: all authors.

REFERENCES

1. Niver BE, Daneshmand S, Satkunasivam R. Female reproductive organ-sparing radical cystectomy: contemporary indications, techniques and outcomes. Curr Opin Urol 2015;25:105-10.
2. Wong MCS, Fung FDH, Leung C, Cheung WWL, Goggins WB, Ng CF. The global epidemiology of bladder cancer: a joinpoint regression analysis of its incidence and mortality trends and projection. Sci Rep 2018;8:1129.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. Erratum in: CA Cancer J Clin 2020;70:313.
4. Gross T, Furrer M, Schorno P, Wuethrich PY, Schneider MP, Thalmann GN, et al. Reproductive organ-sparing cystectomy significantly improves continence in women after orthotopic bladder substitution without affecting oncological outcome. BJU Int 2018;122:227-35.
5. Tuderti G, Mastroianni R, Flammia S, Ferriero M, Leonardo C, Anceschi U, et al. Sex-sparing robot-assisted radical cystectomy with intracorporeal padua ileal neobladder in female: surgical technique, perioperative, oncologic and functional outcomes. J Clin Med 2020;9:577.
6. Hautmann RE, de Petriconi R, Kleinschmidt K, Gottfried HW, Gschwend JE. Orthotopic ileal neobladder in females: impact of the urethral resection line on functional results. Int Urogynecol J Pelvic Floor Dysfunct 2000;11:224-9; discussion 230.
7. Gregg JR, Emeruwa C, Wong J, Barocas DA, Chang SS, Clark PE, et al. Oncologic outcomes after anterior exenteration for muscle invasive bladder cancer in women. J Urol 2016;196:1030-5.
8. Chang SS, Cole E, Smith JA Jr, Cookson MS. Pathological findings of gynecologic organs obtained at female radical cystectomy. J Urol 2002;168:147-9.
9. Varkarakis IM, Pinggera G, Antoniou N, Constantinides K, Chrisofos M, Deliveliotis C. Pathological review of internal genitalia after anterior exenteration for bladder cancer in women. Evaluating risk factors for female organ involvement. Int Urol Nephrol 2007;39:1015-21.
10. Salem H, El-Mazny A. Primary and secondary malignant involvement of gynaecological organs at radical cystectomy for bladder cancer: review of literature and retrospective analysis of 360 cases. J Obstet Gynaecol 2012;32:590-3.
11. Ali-El-Dein B, Abdel-Latif M, Mosbah A, Eraky I, Shaaban AA, Taha NM, et al. Secondary malignant involvement of gynecologic organs in radical cystectomy specimens in women: is it mandatory to remove these organs routinely? J Urol

2004;172:885-7.

12. Huang H, Yan B, Shang M, Liu L, Hao H, Xi Z. Is hysterectomy beneficial in radical cystectomy for female patient with urothelial carcinoma of bladder? A retrospective analysis of consecutive 112 cases from a single institution. BMC Urol 2019;19:28.
13. Choi SY, Yoo S, Han JH, Jeong IG, Hong B, Hong JH, et al. Predictors of female genital organ involvement in radical cystectomy for urothelial carcinoma of the bladder: a single-center retrospective analysis of 112 female patients. Int J Surg 2017;47:101-6.
14. Kulkarni JN, Rizvi SJ, Acharya UP, Kumar KS, Tiwari P. Gynecologic-tract sparing extra peritoneal retrograde radical cystectomy with neobladder. Int Braz J Urol 2008;34:180-7; discussion 187-90.
15. Roshdy S, Senbel A, Khater A, Farouk O, Fathi A, Hamed E, et al. Genital sparing cystectomy for female bladder cancer and its functional outcome; a seven years' experience with 24 cases. Indian J Surg Oncol 2016;7:307-11.
16. Jeong CW, Suh J, Yuk HD, Tae BS, Kim M, Keam B, et al. Establishment of the Seoul National University Prospectively Enrolled Registry for Genitourinary Cancer (SUPER-GUC): a prospective, multidisciplinary, bio-bank linked cohort and research platform. Investig Clin Urol 2019;60:235-43.
17. Bertz S, Hartmann A, Knüchel-Clarke R, Gaisa NT. [Specific types of bladder cancer]. Pathologe 2016;37:40-51. German.
18. Kim M, Lee HE, Kim SH, Cho SY, Jeong SJ, Oh SJ, et al. Korean version of the functional assessment of cancer therapy (FACT)-vanderbilt cystectomy index (VCI): translation and linguistic. Urol J 2014;11:1961-7.
19. Cookson MS, Dutta SC, Chang SS, Clark T, Smith JA Jr, Wells N. Health related quality of life in patients treated with radical cystectomy and urinary diversion for urothelial carcinoma of the bladder: development and validation of a new disease specific questionnaire. J Urol 2003;170:1926-30.
20. Kim M, Oh SJ, Kwak C, Kim HH, Ku JH. Psychometric validation study of the Korean version of the Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index. PLoS One 2018;13:e0190570.
21. Khan A, Vuppalapati JK, Sarath LR, Mujeeburahiman M, D'souza N. Functional outcome of robotic-assisted intracorporeal versus extracorporeal neobladder following radical cystectomy: initial experience. Urol Ann 2021;13:9-13.
22. Thüroff JW, Mattiasson A, Andersen JT, Hedlund H, Hinman F Jr, Hohenfellner M, et al. The standardization of terminology and assessment of functional characteristics of intestinal urinary reservoirs. International Continence Society Committee on Standardization of Terminology. Subcommittee on Intestinal Urinary Reservoirs. Br J Urol 1996;78:516-23.
23. Avulova S, Chang SS. Role and indications of organ-sparing "radical" cystectomy: the importance of careful patient selection and counseling. Urol Clin North Am 2018;45:199-214.
24. Stenzl A, Jarolim L, Coloby P, Golia S, Bartsch G, Babjuk M, et al. Urethra-sparing cystectomy and orthotopic urinary diversion in women with malignant pelvic tumors. Cancer 2001;92:1864-71.
25. Veskimäe E, Neuzillet Y, Rouanne M, MacLennan S, Lam TBL, Yuan Y, et al. Systematic review of the oncological and functional outcomes of pelvic organ-preserving radical cystectomy (RC) compared with standard RC in women who undergo curative surgery and orthotopic neobladder substitution for bladder cancer. BJU Int 2017;120:12-24.
26. Gross T, Meierhans Ruf SD, Meissner C, Ochsner K, Studer UE. Orthotopic ileal bladder substitution in women: factors influencing urinary incontinence and hypercontinence. Eur Urol 2015;68:664-71.

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