The Feasibility and Safety of Reproductive Organ Preserving Radical Cystectomy for Elderly Female Patients With Muscle-Invasive Bladder Cancer: A Retrospective Propensity Score-matched Study

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OBJECTIVE To evaluate the feasibility and safety of reproductive organ preserving radical cystectomy (ROPRC) compared to radical cystectomy (RC) for elderly female patients with muscle-invasive bladder cancer.

METHODS We retrospectively studied 135 elderly female patients (aged ≥75 years) who underwent RC followed by cutaneous ureterostomies at our center between January 1, 2007 and December 31, 2017. Eighty-four patients treated with RC, and 51 patients treated with ROPRC, were grouped into 45 pairs. Patient demographics, extensive peri-operative, and oncological data were then recorded and evaluated.

RESULTS In the matched group, the incidence of short-term and long-term complications in the ROPRC group were lower than the RC group (18.0% vs 28.0%, $P = .035$; 12.0% vs 22.0%, $P = .030$). Furthermore, operative time was shorter, estimated blood loss was lower, and bowel recovery was quicker in the ROPRC group (207.5 minutes vs 267.9 minutes, $P < .001$; 500 mL vs 600 mL, $P = .024$; 3.0 days vs 4.0 days, $P < .001$, respectively) compared to the RC group. The recurrence free survival ($P = .658$), overall survival ($P = .604$), and cancer-specific survival ($P = .361$) were all equivalent when compared between the 2 groups with a median follow-up period of 34.0 and 38.0 months, respectively. The surgical approach (RC vs ROPRC) was an independent risk factor for short-term complications ($P = .045$), duration of operative time ($P < .001$), estimated blood loss ($P = .004$), and bowel recovery ($P < .001$).

CONCLUSION This propensity score-matched cohort study showed that ROPRC was both feasible and safe for elderly female patients with muscle-invasive bladder cancer compared to RC, and also had comparable oncological outcomes after a lengthy follow-up period. UROLOGY 125: 138–145, 2019.
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Bladder cancer is the 11th most commonly diagnosed cancer in the global population with incidence and mortality rates of 2.2/100,000/y and 0.9/100,000/y, respectively, for women.[1] Bladder cancer often occurs in patients older than 70 years of age.[2]

Radical cystectomy (RC) with pelvic lymph node dissection is the primary treatment for muscle-invasive bladder cancer.[3,4] However, this approach is associated with considerable morbidity and mortality, particularly in elderly patients with comorbidity.[5]

Although women are less likely to develop bladder cancer than men, women present with more advanced forms of the disease and a worse prognosis.[6] The classical form of RC in women involves the en bloc removal of the bladder, urethra, uterus, and a portion of the anterior vaginal wall.[7] However, though surgeries have been developed which preserve organ function and provide safe margins, the routine removal of reproductive organs during the course of female RC has been challenged.[2] Reproductive organ preserving radical cystectomy (ROPRC) exerts good impact on perioperative period safety, psychology,

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sexuality, and even potential fertility.[2] Nevertheless, the application of ROPRC must be balanced against the potential risk to oncological outcome.

As yet, there have been no randomized controlled trials addressing these issues, and only a limited number of small-sized retrospective studies. Frustratingly, the conclusions drawn from these previous studies were controversial.[6] The aim of this retrospective score-matched study was to evaluate the feasibility and safety of ROPRC compared to RC for elderly female patients with muscle-invasive bladder cancer.

METHODS

Patients

We retrospectively studied 602 patients who underwent RC with pelvic lymph node dissection at our center between January 1, 2007 and December 31, 2017; 467 patients were excluded from the study because of male sex, missing data, or an age <75 years. Ultimately, 135 patients were included in the final analyses, and divided into 2 groups (ROPRC and RC) (Supplemental Fig. 1).

Inclusion and Exclusion Criteria

The inclusion criteria were female sex, aged ≥75 years,[2] muscle-invasive stage (≥T2), and underwent RC with pelvic lymph node dissection followed by bilateral cutaneous ureterostomy. The exclusion criteria were patients with metastatic disease, salvage cystectomy, underwent nephrectomy prior to RC, and RC combined with other types of urinary diversion besides cutaneous ureterostomy.

Propensity Score-matching

We used the propensity score-matching (PSM) method to adjust baseline differences between the ROPRC and RC groups in an effort to derive more accurate conclusions. Multivariate logistic regression analysis was used to determine propensity scores for each patient based on age, body mass index (BMI), and the Charlson Comorbidity Index, which were demographics or unbalanced variables before PSM between the 2 groups.[8] ROPRC and RC were matched 1:1 using a caliper width of 0.2 for the propensity score through the nearest neighbor matching. We achieved a balance between the ROPRC and RC groups after PSM; 51 patients treated with ROPRC and 84 patients treated with RC were balanced into 45 pairs (Supplemental Fig. 2).

Preoperative Preparation

All patients received perioperative prophylactic antibiotics and subcutaneous heparin. Standard mechanical and oral antibiotic bowel preparation was initiated 3 days prior to surgery in each patient.

Surgical Technique for ROPRC

Patients underwent surgery under general anesthesia in the Trendelenburg position. Preoperatively, gemcitabine (50 mg) plus normal saline (50 mL) were introduced into the bladder via an indwelling urethral catheter. Gauze was then placed in the vagina so that the border between the bladder wall and the vagina could be identified easily. Then, a standard lower midline abdominal incision was made. Bilateral pelvic lymphadenectomy was performed first; this involved the removal of lymph nodes around the common, external, and internal iliac vessels, as well as the obturator vessels.

The bladder wall was then separated from the peritoneum. The vesical pedicle was ligated and transected at the origin from the internal iliac vessels. The endopelvic fascia was incised and the urethra was separated from the anterior vaginal wall. The plane between the posterior bladder wall and the vaginal wall was separated by a combination of blunt and sharp dissection. The vesicle, and part of urethra which was approximately 5 mm distal to the vesicourethral junction, were removed en bloc. In cases of hydronephrosis or tight adhesion between the posterior bladder wall and the anterior vaginal wall, a portion of the anterior vaginal wall was removed, together with the specimen, en bloc. Sutures (PDS 2-0) were then inserted transversely to close the vagina. The margin of the urethra, ureters, and part of the vaginal wall was assessed using frozen section pathology at the time of surgery in order to ensure we had sufficient excisional range.

The ureters were brought out from the abdomen in an extraperitoneal manner through a V-shaped incision, and anchored to the fascia and the skin. Single J stents were then placed into the ureter.

All of the above procedures were performed using an extraperitoneal approach, and the uterus and ovaries were left intact.

Surgical Technique for RC

A classic RC was performed, with excision of the bladder, adjacent vagina, and uterus, which were removed en bloc after bilateral pelvic lymphadenectomy.

The peritoneum was incised in the Douglas cavity just below the vaginal fundus. After approaching the vesicourethral junction, the vagina wall was opened circumferentially. The vaginal wall was closed with PDS 2-0 running suture transversely.

Briefly, all of the procedure was performed using a standard intraperitoneal approach; the other processes were the same as surgical technique for ROPRC.

Outcome and Follow-up

Patient demographics (age and BMI), comorbidity (Charlson Comorbidity Index[9]), past history (prior bladder cancer surgery and smoking), disease characteristics (tumor stage and pathological type), extensive intraoperative factors (duration of surgery, estimated blood loss, and blood transfusion), and postoperative factors (time to bowel recovery, length of hospital stay, time to drain removal, and morbidity), and oncological data (recurrence and survival rates) were recorded.

Morbidity was classified according to the Clavien-Dindo classification[10] and 3 months after surgery was considered to represent the boundary between short-term and long-term complications. Bladder cancer was classified according to the 2009 TNM classification.[11] Histological grading was performed according to the 2004 World Health Organization grading system.[6] Follow-up data were obtained through telephone calls and office visits for blood pressure readings and oncology data.

Statistical Analysis

Continuous variables with a normal distribution are reported as the mean ± standard deviation. Non-normal continuous variables are expressed as the median (interquartile range). Categorical variables are reported as numbers (percentage). An independent sample Student's *t* test was used to compare the means of 2 continuous normally distributed variables and the Mann-Whitney *U* test was applied to compare the means of 2 continuous non-normally distributed variables. Pearson's

chi-square test or Fisher's exact test was used for categorical variables. Recurrence and survival rates were calculated using Kaplan-Meier curves with a log-rank test. The adjusted odds ratio and 95% confidence interval were determined by binary logistic regression and the β coefficient was calculated by multiple linear regression. Statistical analyses were performed using SPSS 22.0 for Windows (SPSS, Inc., Chicago, IL). Values of $P < .05$ (2-tailed) were considered to be statistically significant.

RESULTS

In total, 135 patients were included in the final analysis, and divided into 2 groups (ROPRC [51 patients] and RC [84 patients]). We achieved a balance of baseline variables between the 2 groups after PSM; 51 patients treated with ROPRC and 84 patients treated with RC were balanced into 45 pairs.

In the matched group, the mean age of the patients in the ROPRC and RC groups was 77.7 and 78.8 years ($P = .132$), respectively. The BMI was 21.0 and 21.5 kg/m^2 ($P = .734$), and the mean Charlson Comorbidity Index was the same when compared between 2 groups ($P = .054$). Analysis showed that in the ROPRC group, 13.0% of patients had a previous history of smoking, and 16% of the patients had prior bladder cancer surgery (transurethral resection of bladder tumor) in the ROPRC; these results were similar to those of the RC group.

Mean age and Charlson Comorbidity Index, at baseline, were unbalanced between the ROPRC and RC groups prior to PSM. A balance was obtained after adjusting these variables with PSM. Other variables, such as tumor stage, and pathological type were not significantly different when compared between the 2 groups before and after PSM (Table 1).

The incidence of short-term and long-term complications in the ROPRC group were lower than that in the RC group (18.0% vs 28.0%, $P = .035$; 12.0% vs 22.0%, $P = .030$). Of the long-term complications, there was a lower incidence of urinary tract infection in the ROPRC group compared to the RC group (5.0% vs 16.0%, $P = .004$). There was also a significantly shorter operative time, lower estimated blood loss, and quicker bowel recovery in the ROPRC group (207.5 minutes vs 267.9 minutes, $P.< .001$; 500 mL vs 600 mL, $P = .024$; and 3.0 days vs 4.0 days $P < .001$, respectively) compared to the RC group.

The blood transfusion volume (200 mL vs 200 mL, $P = .680$), length of hospital stay (13.0 days vs 13.0 days, $P = .728$), and time to drain removal (4.0 days vs 4.0 days, $P = .238$) were similar when compared between the 2 groups. No patients died in the ROPRC group and 2 patients (4.4%) died in the RC group, postoperatively. The recurrence free rate ($P = .658$), overall survival ($P = .604$), and cancer specific survival (CSS) ($P = .361$) were also comparable between the 2 groups over a median follow-up period of 34.0 and 38.0 months in the ROPRC group and RC group, respectively. The recurrence free survival, overall survival (OS), and CSS of patients in the ROPRC group at 5 years were 67.1%, 41.6%, and 72.9%, and 71.4%, 49.8%, and 61.4% in the RC group, respectively (Table 2, Fig. 1).

The surgical approach (ROPRC vs RC) was a significant and independent risk factor for short-term complications, as determined through multivariate binary logistic regression analyses by adjusting for confounding variables; the odds ratios of ROPRC compared to RC were 0.372 ($P = .045$). The surgical approach also influenced the operation duration ($\beta = -54.5$, $P < .001$), estimated blood loss ($\beta = -331.1$, $P = .004$), and bowel recovery ($\beta = -1.0$, $P < .001$), as determined by multiple linear regression analyses (Table 3).

DISCUSSION

While classic RC in females is very helpful in removing advanced bladder cancer or nondetected disease of genital organs, it can also damage both reproductive and sexual function.[12] Moreover, bladder cancer mostly occurs in elderly patients, and is usually associated with more comorbidity, thus resulting in a higher risk of morbidity and mortality. ROPRC may reduce the risk of surgery because of its reduced excision range. However, it has not been established whether ROPRC compromises oncological outcome, and standard surgical indications have not been defined.[13] The aim of the present study was to confirm the feasibility and safety of ROPRC compared to RC for elderly female patients with muscle-invasive bladder cancer. Thus, this current PSM cohort provides a fair retrospective comparison.

After PSM, we first balanced the baseline variables. The ROPRC group had a lower incidence of short-term and long-term complications than the RC group. There was also a shorter operative time, less estimated blood loss, and quicker bowel recovery in the ROPRC group. Recurrence free survival, OS, and CSS were comparable between the 2 groups after a lengthy period of follow-up. The surgical approach (RC vs ROPRC) was a significant and independent risk factor for short-term complications, the duration of operative time, estimated blood loss, and longer bowel recovery, as determined by multivariate logistic regression analyses.

Complications can be divided into 2 types: those that were related to RC and those that were related to urinary diversion. All of the patients included in this study were elderly with a higher Charlson Comorbidity Index, so we use bilateral UC as a form of urinary diversion. This technique type is the simplest, can be performed quickly, and is often associated with fewer complications compared to the other types of urinary diversions.[3,5] In the literature, the reported incidence of complications for elderly patients after RC ranged from 28% to 64%[14]; this wide variation was mainly caused by different reporting systems and lengths of follow-up periods. In line with these previous results, our study demonstrated that the incidence of short-term and long-term complications were 40% and 26.7%, respectively, in the ROPRC group, which were less than in the RC group (62.2% and 48.9%). It is noteworthy that there was a significant statistical difference between the 2 groups with regard to Clavien I short-term and long-term complications, however, the incidence of Clavien II-V complications were the same when compared between the 2 groups. Surgical time was shorter, and estimated blood loss lower, in the ROPRC group compared to the RC group, because of the reduced extent of excision. Furthermore, we actively excised part of the anterior vaginal wall, featuring the entire specimen, when there was adhesion or suspicious vaginal infiltration; this

Table 1. Demographics and clinical data of patients aged ≥75 years who underwent RC in this cohort according to the study group

Variable	Propensity Before 135 Patients			Propensity After 90 Patients		
	RC	ROPRC	*P* Value	RC	ROPRC	*P* Value
Number of patients (%)	84.0 (100)	51.0 (100)		45.0 (100)	45.0 (100)	
Follow-up period, mo	37.0 (16.5-80.5)	34.0 (8.0-58.0)		38.0 (15.0-52.0)	34.0 (8.5-59.5)	
Demographic characteristics						
Mean age (y)	79.5 ± 4.2	77.5 ± 2.5	<.001	78.8 ± 4.2	77.7 ± 2.6	.132
BMI (kg/m^2)	21.5 (20.1-25.3)	21.5 (20.7-24.2)	.758*	21.5 (20.0-25.6)	21.0 (20.7-24.2)	.734*
Past history						
Past history of smoke	31.0 (36.9)	14.0 (27.5)	.269	16.0 (35.6)	13.0 (28.9)	.499
Charlson Comorbidity Index	3.0 (3.0-4.0)	5.5 (4.0-5.0)	<.001*	4.0 (3.0-5.0)	4.0 (4.0-5.0)	.054*
Prior bladder cancer surgery	34.0 (40.5)	18.0 (35.3)	.549	16.0 (35.6)	13.0 (28.9)	.499
Tumor data						
T stage (pathology)			.951†			1.000†
T2	66.0 (78.6)	40.0 (78.4)		36.0 (80.0)	36.0 (80.0)	
T3	11.0 (13.1)	6.0 (11.8)		6.0 (13.3)	5.0 (11.1)	
T4 (vaginal wall infiltration)	7.0 (8.3)	5.0 (9.8)		3.0 (6.7)	4.0 (8.9)	
N stage (pathology)			.884†			.591†
N1	3.0 (3.6)	3.0 (5.9)		2.0 (4.4)	3.0 (6.7)	
N2	4.0 (4.8)	3.0 (5.9)		1.0 (2.2)	3.0 (6.7)	
N3	1.0 (1.2)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)	
Pathologic type			.849†			.645†
TCC low grade	12.0 (14.3)	9.0 (17.6)		6.0 (13.3)	9.0 (20.0)	
TCC high grade	52.0 (61.9)	30.0 (58.8)		26.0 (57.8)	26.0 (57.8)	
TCC with squamous or adenoid	12.0 (14.3)	8.0 (15.7)		9.0 (20.0)	3.0 (13.3)	
Squamous cancer	3.0 (3.6)	2.0 (3.9)		1.0 (2.2)	2.0 (4.4)	
Adenoid cancer	2.0 (2.4)	2.0 (3.9)		1.0 (2.2)	2.0 (4.4)	
TCC with sarcoma	3.0 (3.6)	0.0 (0.0)		2.0 (4.4)	0.0 (0.0)	
Hydronephrosis	12.0 (14.3)	9.0 (17.6)	.815†	5.0 (11.1)	7.0 (15.6)	.817†

BMI, body mass index; RC, radical cystectomy; ROPRC, reproductive organ preserving radical cystectomy; SD, standard deviation; TCC, transitional cell carcinoma.

Continuous variables with normal distribution were reported as the mean ± SD; non-normal continuous variables were expressed as median (interquartile range); categorical variables were reported as number (percentage). Independent samples Student's *t* test was used to compare mean of 2 continuous normally distributed variables and the Mann-Whitney *U* test was run to determine mean of 2 continuous non-normally distributed variables, The chi-square test or Fisher' exact test was used for categorical variables.

* Mann-Whitney *U* test.

† Fisher's exact test.

procedure can lead to less blood loss and a better surgical margin than direct separation. Patients in the ROPRC group also had quicker bowel recovery; this is one of the main reasons as to why all procedures were conducted extraperitoneally as this had minimal influence on organ in the abdomen cavity.

Some retrospective studies have reported that the oncological outcome was safe in ROPRC, and comparable to classic RC in selected patients.[13,15,16] This was because the incidence of concomitant gynecological malignancy and gynecological infiltration by bladder cancer were very low.[17-19] Djaladat et al reported that the vaginal wall is the most commonly involved reproductive organ, with an incidence of 5%.[20] Our data also demonstrated that the oncological outcome was equivalent between our 2 groups. In this study, there were only 8.9% and 6.7% of cases in the ROPRC group and the RC group, respectively, in which the vaginal wall had been infiltrated by tumor. There was no involvement of the uterus, ovaries, and fallopian tubes in either of the 2 groups, and no concomitant reproductive malignancies were detected in the RC group either.

For patients who had vaginal infiltration in the ROPRC group, we just resected part of the anterior wall of the vagina with the entire specimen collectively; we then carried out frozen section pathology on the margin of the urethra, ureters, and vaginal wall at the time of surgery in order to obtain sufficient surgical range. Consequently, there was no tumor recurrence in gynecological organs after a long period of follow-up in either the ROPRC group or RC group. We therefore suggest that frozen section pathology of the surgical margin had a beneficial oncological effect for female patients, even those who had vaginal wall infiltration (stage T4a). This expands the indication criteria for ROPRC, in which tumor stage usually falls within stage T3.[9,13,19,21,22] There have been no previous studies reporting adaptions of this procedure for ROPRC.[23]

The recurrence free survival rate at 5 years was 67.1% and 71.4% in the ROPRC group and RC group, respectively, a little lower than previous data which showed an incidence of 83.8%-100%, in a systemic review.[24] This was mainly due to the fact that most of our patients (80% of the ROPRC and 86.7% of the RC group) were higher risk with muscle invasion and high grade bladder cancer.

Table 2. Perioperative and prognostic data of patients aged ≥75 years who underwent RC in this cohort according to the study group

Variable	Propensity Before 135 Patients			Propensity After 90 Patients		
	RC	ROPRC	*P* Value	RC	ROPRC	*P* Value
Number of patients (%)	84.0 (100)	51.0 (100)		45.0 (100)	45.0 (100)	
Follow up period, months	37.0 (16.5-53.0)	34.0 (8.0-53.0)		38.0 (15.0-49.0)	34.0 (8.5-54.0)	
Intraoperative data						
Duration of operative time (min)	263.0 ± 71.8	211.7 ± 50.0	<.001	267.9 ± 66.0	207.5 ± 50.0	<.001
Estimated blood loss (mL)	600.0 (400.0-1000.0)	500.0 (400.0-600.0)	<.001*	600.0 (400.0-1000.0)	500.0 (400.0-600.0)	.024*
Blood transfusion (mL)	300.0 (0.0-800.0)	300.0 (0.0-400)	.039*	200.0 (200.0-700.0)	200.0 (200.0-400.0)	.680*
Postoperative data						
Short-term complications (Clavien 1-5)	49.0 (58.3)	23.0 (45.1)	.135	28.0 (62.2)	18.0 (40.0)	.035
Blood transfusion rate	16.0 (19.0)	13.0 (25.5)	.377	7.0 (16.3)	10.0 (22.2)	.480
Reoperation	1.0 (1.2)	2.0 (3.9)	.557†	1.0 (2.3)	2.0 (4.4)	1.000†
Need to ICU admission	4.0 (4.8)	2.0 (3.9)	1.000†	3.0 (7.0)	1.0 (2.2)	.355†
Perioperative mortality	3.0 (3.6)	0.0 (0.0)	.290†	2.0 (4.4)	0.0 (0.0)	.494
Duration of postoperative hospital stay	12.0 (10.0-18.0)	13.0 (10.0-20.0)	.532*	13.0 (10.0-18.0)	13.0 (10.0-17.5)	.728*
Bowel recovery (d)	4.0 (3.0-5.0)	3.0 (2.0-4.0)	<.001*	4.0 (3.0-5.0)	3.0 (2.0-4.0)	<.001*
Time to drain removal	4.0 (3.0-5.0)	4.0 (3.0-4.0)	.051*	4.0 (3.0-5.0)	4.0 (3.5-4.0)	.238*
Long-term complications (Clavien 1-5)	32.0 (38.1)	14.0 (27.5)	.206	22.0 (48.9)	12.0 (26.7)	.030
UTI	23.0 (27.4)	7.0 (13.7)	.064	16.0 (37.2)	5.0 (11.1)	.004
Pyelonephritis	1.0 (1.2)	4.0 (7.8)	.067†	0.0 (0.0)	4.0 (8.9)	.117†
Stoma stenosis (need nephrostomy)	0.0 (0.0)	3.0 (5.9)	.052	0.0 (0.0)	3.0 (6.7)	.242†
Prognostic data						
Recurrence and metastasis rate	14.0 (17.3)	14.0 (27.5)	NA	11.0 (25.6)	13.0 (28.9)	NA
RFS rate at 5 y	74.1%	60.9%	.110#	71.4	67.1	.614*
Overall mortality rate	24.0 (29.6)	21.0 (41.2)	NA	16.0 (37.2)	19.0 (42.2)	NA
OS rate at 5 y	56.9	48.8	.074#	49.8	41.6	.582*
Cancer specific mortality rate	15.0 (18.5)	15.0 (29.4)	NA	10.0 (23.3)	14.0 (31.1)	NA
CSS rate at 5 y	74.1	60.9	.071#	61.4	72.9	.582*

CSS, cancer specific survival; NA, not applicable; OS, overall survival; RC, radical cystectomy; RFS, recurrence free survival; SD, standard deviation; UTI, urinary tract infection.
Continuous variables with normal distribution were reported as the mean ± standard deviation (SD); non-normal continuous variables were expressed as median (interquartile range); categorical variables were reported as number (percentage). Independent samples Student's *t* test was used to compare mean of 2 continuous normally distributed variables and the Mann-Whitney *U* test was run to determine the mean of 2 continuous non-normally distributed variables, The chi-square test or Fisher's exact test was used for categorical variables. Recurrence and survival were calculated using Kaplan-Meier curves with log-rank tests.
* Mann-Whitney *U* test.
# Log-rank test.
† Fisher' exact test.

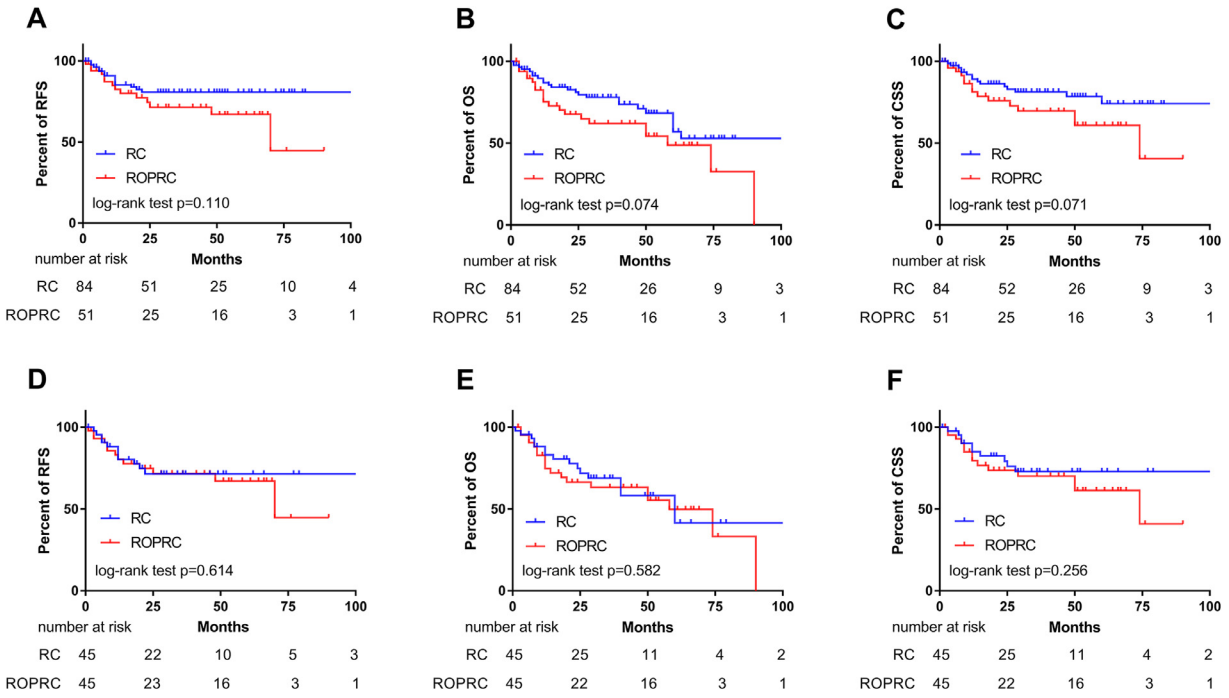

Figure 1. Survival curve of RC and ROPRC, before and after propensity score-matching. (**A**) Recurrence free survival before propensity score-matching. (**B**) Overall survival before propensity score-matching. (**C**) Cancer specific survival before propensity score-matching. (**D**) Recurrence free survival before propensity score-matching. (**E**) Overall survival before propensity score-matching. (**F**) Cancer specific survival before propensity score-matching. RC, radical cystectomy; ROPRC, reproductive organ preserving radical cystectomy. (Color version available online.)

In the present study, none of the local recurrence observed to occur in the pelvic cavity involved reproductive recurrence in the ROPRC group. Veskimae et al demonstrated that OS was 65%-100%, and CSS was 70%-100%, at postoperative 5 years, in a systemic review, which included 7 studies after a mean follow-up period of between 12 and 132 months.[24] In the present study, the OS and CSS at 5 years follow-up in the ROPRC group were 41.6% and 72.9%, respectively, and in the RC group were 49.8% and 61.4%, respectively. These figures were a little lower than those reported in previous studies. This may have been caused by patients in this study being older and having more advanced cancer. The 2 groups showed an equivalent survival outcome.

All of the procedures carried out in the ROPRC were conducted extraperitoneally. This had several obvious advantages. First, the abdomen cavity would not be contaminated when the bladder was perforated by excision. Second, reintervention would be easier and safer because of the intact nature of the peritoneum.[25]

Table 3. Multivariate regression of patients aged ≥75 years undergoing ROPRC versus RC

	Propensity Before 135 Patients			Propensity After 90 Patients		
Variable	OR/β	95% CI	*P*	OR/β	95% CI	*P*
Duration of operative time (min)*	−50.50	(−77.50, −23.50)	<.001	−54.5	(−80.9, −28.0)	<.001
Estimated blood loss (mL)*	−415.70	(−651.60, −179.50)	.001	−331.1	(−554.2, −108.0)	.004
Bowel recovery*	−1.00	(−1.40, −0.70)	<.001	−1.0	(−1.4, −0.6)	<.001
Short-term complications†	0.4131‡	(0.171-0.995)	.049	0.372§	(0.142-0.978)	.045
Long-term complications†	0.713‖	(0.317-1.602)	.413	0.415¶	(0.169-1.019)	.550

CI, confidence interval; OR, odd ratio.
The odds ratio and 95% confidence interval were determined by multivariate binary logistic regression and β coefficient was calculated by multiple linear regression.
* multiple linear regression.
† binary logistic regression.
‡ Propensity before adjusted Charlson Comorbidity Index, prior bladder cancer surgery, estimated blood loss, blood transfusion for short-term complications.
§ Propensity after adjusted tumor, prior bladder cancer surgery, estimated blood loss, blood transfusion for short-term complications.
‖ Propensity before adjusted N stage, prior bladder cancer surgery, estimated blood loss for long-term complications.
¶ Propensity after adjusted tumor Charlson Comorbidity Index for long-term complications.

Urethral recurrence in female patients after RC is rare, usually less than 1%.[26] In our study, there was no urethral recurrence; the reason for this may be that there was no skip lesion from the tumor location in the bladder, so we were able to confirm a sufficient surgical margin by using frozen section pathology.

Furthermore, ROPRC would be more beneficial for younger female patients who had an urgent desire for preserving sexuality and potential fertility; this technique also has a good psychological impact.[21] In fact, 50% of menopausal females are still sexually active.[27] ROPRC also has beneficial effects for improving voiding function, and in reducing the risk of pouch prolapse and neobladder-vaginal fistulization in patients after RC followed orthotopic neobladder.[17]

There were several limitations to this study. First, this was a retrospective study in a single situation with inherent selection bias, even though PSM was conducted to counter such bias. Second, the number of patients were limited and our follow-up period was relatively short. A large multi-center randomized controlled trial is now necessary to validate the feasibility and oncological safety of ROPRC after longer follow-up periods.

CONCLUSION

This propensity score-matched cohort study showed that ROPRC was both feasible and safe for elderly female patients with muscle-invasive bladder cancer compared to RC. ROPRC also showed comparable oncological outcomes after a lengthy follow-up period.

ETHICAL APPROVAL STATEMENT

Ethical approval (Ethics Committee No. 2018PS398K) was provided by the Institutional Research and Ethics Committee of the Shengjing Hospital Affiliated China Medical University in Shengyang, China. Informed consent was obtained from all eligible patients.

AUTHOR CONTRIBUTIONS

Ning Wen had full access to all the data in the study and takes responsibility for the integrity of the data, study concept and design,and the accuracy of the data analysis.

Acquisition of data, analysis, and interpretation of data were performed by Song Bai, Zichuan Yao, and Xianqing Zhu.

Drafting of the manuscript and critical revision of the manuscript for important intellectual content were by Song Bai.

Statistical analysis were the responsibility of Rongzhi Wang and Zidong Li.

Obtaining funding and other (figures) were performed by Song Bai, Zidong Li, and Yuzhong Jiang.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.urology.2018.09.035.

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