Erectile Function and Long-term Oncologic Outcomes of Nerve-Sparing Robot-Assisted Radical Cystectomy: Comparison With Open Radical Cystectomy

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Purpose: We performed nerve-sparing robot-assisted radical cystectomy (nsRARC) and compared the operative outcomes of nsRARC and open radical cystectomy (ORC).

Materials and Methods: The data of 38 patients that underwent ORC or nsRARC for bladder cancer between July 2009 and April 2014 (23 ORC and 15 RARC) were retrospectively analyzed. Data were collected on patient demographics, pathologic stages, perioperative outcomes, and oncologic outcomes as well as on erectile function. Five-year overall survival and cancer-specific survival were analyzed using the Kaplan-Meier method. Erection function recovery was defined as the ability to achieve penetration $\geq 50\%$ of the time and to maintain an erection sufficient enough for penetration $\geq 50\%$ of the time at 12 months after surgery.

Results: No significant differences were found between the nsRARC and ORC groups in terms of age, sex, body mass index, American Society of Anesthesiologists physical status, or clinical stage. Mean estimated blood loss was significantly less in the nsRARC group (205.3 mL vs. 394 mL, $p=0.011$), but mean operative time was significantly greater (520.3 minutes vs. 415.0 minutes, $p=0.004$). Five-year overall survival and cancer-specific survival were 86.7% and 86.7%, respectively, for nsRARC, and 77.7% and 86.7% for ORC. With respect to erectile function, the overall postoperative potency rate at 12 months was 40.0% in the RARC group and 9.5% in the ORC group, and this difference was significant ($p=0.021$).

Conclusions: Our clinical experiences indicate nsRARC in selected patients is a feasible procedure in terms of oncologic outcome and that it preserves erectile function relatively effectively. (Korean J Urol Oncol 2018;16:32-37)

Key Words: Radical cystectomy • Robot

INTRODUCTION

Open radical cystectomy (ORC) is currently regarded the gold standard for the management of muscle-invasive bladder

cancer, extensive uncontrollable non-muscle-invasive cancer, and refractory carcinoma *in situ* (CIS).¹ Multiple studies have repeatedly demonstrated the feasibility and oncologic efficacy of ORC.²⁻⁵ However, despite the operative results obtained, this technique is associated with significant morbidity and negative effects on quality of life, which include incontinence and erectile dysfunction.⁶⁻⁸

Robot-assisted radical cystectomy (RARC) is being increasingly adopted as a minimally invasive alternative to ORC.⁹⁻¹¹ RARC has become the main treatment option for bladder cancer worldwide and has been widely applied to improve operative outcomes.¹²⁻¹⁴ More recently, several surgeons have re-

Received February 9, 2018, Revised March 19, 2018,
Accepted March 22, 2018

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finer surgical procedures and reported excellent outcomes for RARC. RARC involves advanced technologies and provides a 3-dimensional operative view, a laparoscopic instrument that mimics movements of the human wrist and hand, high-level resolution, enlarged images, and excellent lighting conditions. For these reasons, RARC preserves neurovascular bundles more effectively and enables anastomotic suture placement in narrow operative spaces without external loupes or a headlight.

We have performed nerve-sparing RARC (nsRARC) at our institution. Here, we describe our technique of nsRARC and report perioperative, oncologic, and functional outcomes.

MATERIALS AND METHODS

1. Patients

We retrospectively analyzed the data of 38 patients that underwent ORC or nsRARC for bladder cancer between July 2009 and April 2014 (23 ORC and 15 nsRARC). Institutional review board approval was obtained before data retrieval and analysis (KNUMC 2016-05-021-006). Choice of surgical procedure was based on patient's demand and surgeon's preference. Study participants were followed for at least 3 years. All 38 patients underwent radical cystectomy by a single experienced surgeon. Demographic data, operative parameters, pathologic data, postoperative complications, erectile function recovery rates, and oncologic outcomes were included in the analysis.

2. Surgical techniques

The nsRARC was performed using a 6-port transperitoneal approach and a 4-arm da Vinci Si robotic system. In brief, with

a patient placed on the operating table in the standard 30° Trendelenburg position. Using a 6-port transperitoneal approach, a 12-mm camera port is inserted 5 cm above the upper umbilical margin and two 8-mm robotic ports are placed 8 cm from the umbilicus, along the line between the umbilicus to the anterior spine of the iliac crest bilaterally. An additional 8-mm robotic port for the fourth arm is placed 8 cm directly lateral to the right-sided robotic port. A 12-mm assistant port (for retraction and stapling) is placed 8 cm directly lateral to the left-side robotic port. A further 5-mm assistant port (for suction and irrigation) is placed on the left side between the camera port and the left robotic port. Following docking of the robotic system, laparoscopic adhesiolysis is performed if required. Standard pelvic lymphadenectomy (both obturator- and external iliac nodes) was performed in all patients. Nerve sparing is conducted to the apex of the prostate according to the principles of intrafascial, tension (Figs. 1, 2), and energy-free radical prostatectomy with high anterior release of periprostatic nerves. Small penetrating arteries are secured with titanium clips. The posterior aspect of the prostate is dissected using a completely lateral approach, leaving Denonvillier's fascia in place. ORC was performed through a midline incision in the traditional manner.

All patients underwent extracorporeal urinary diversions. A 5- to 7-cm midline incision below the umbilicus is made for specimen removal and urinary diversion. In case of an ileal conduit, uretero-ileal anastomosis is performed over 6F double J stents using a 4-0 polydioxanone suture, and the distal end of the conduit is fashioned as a stoma at the right port site of the robot arm in Robot cases. Orthotopic neobladders were only

Fig. 1. Nerve sparing at left side on nerve-sparing robot-assisted radical cystectomy.

Fig. 2. Nerve sparing at right side on nerve-sparing robot-assisted radical cystectomy.

applied in nsRARC and performed using the Studer method and ureteral stents. Urethro-enteric continuous anastomosis is then performed intracorporeally after redocking the robotic system. A Jackson-Pratt drain is placed in the pelvic cavity and around the uretero-enteric anastomosis site. The drain and ureteral stents are removed 2–3 weeks after surgery.

3. Definition of erection function recovery

Erection function recovery was defined as the ability to achieve penetration $\geq 50\%$ of the time and to maintain an erection significant enough for penetration $\geq 50\%$ of the time, as per questions 2 and 3 of the International Index of Erectile Function (IIEF)-5 survey, at 12 months after surgery.

4. Follow-up evaluation

Patients were reviewed at 4 weeks after surgery, and checked by a renal ultrasound at 2 weeks after stent removal, by computed tomography at 3 and 6 months after surgery, and then at 6-month intervals. At these visits, they underwent a clinical examination, and hemoglobin, electrolytes, creatinine, chloride, bicarbonate, and urethral washing cytology tests were conducted.

5. Statistical analysis

Demographics and perioperative outcomes were analyzed using the chi-square test and the Mann-Whitney test. The chi-square test was used to analyze erectile function recovery rates at the above-mentioned times. Five-year overall survival and cancer-specific survival were determined using the Kaplan-Meier method. The analysis was performed using PASW Statistics ver. 18.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was accepted for p values of <0.05 .

RESULTS

No significant differences were found between the nsRARC and ORC groups in terms of gender, sex, body mass index, American Society of Anesthesiologists physical status classification and clinical stage. However, some operative parameters were found to be significantly different in the 2 study groups. In particular, mean estimated blood loss was significantly less in the nsRARC group (205.3 mL vs. 394.0 mL, $p=0.011$), but mean operative time was significantly greater (520.3 minutes vs. 415.0 minutes, $p=0.004$). Group mean hospital stays were not significantly different (23.1 days and 24.1 days).

Perioperative complications occurred in 3 patients (20.0%) in the nsRARC group (acute pyelonephritis in 2 and ileus in 1) and in 6 patients (26.1%) in the ORC group (ileus in 3, wound disruption in 2, and acute pyelonephritis in 1) (Table 1). According to the classification,¹⁵ all complications were grade I or II and all cases were managed conservatively.

In the nsRARC group, median follow-up was 80 months. Cancer recurrence occurred in 4 patients between 1 and 4 months after surgery, in a lung in all 4 cases. Two of these 4 patients died at 2 and 5 months after surgery, respectively. In the other 2 patients, recurrence occurred at 1 and 4 months, and they survived until 40 and 31 months. After nsRARC, 5-year overall survival and cancer-specific survival were 86.7% and 86.7%, respectively (Table 2).

In the ORC group, median follow-up was 42 months. Cancer recurrence occurred in 10 patients between 1 and 21 months; in a lung in 8 cases and a lymph node in 2 cases. Six of these

Table 1. Patients' characteristics and operative parameter

Characteristic	nsRARC (n=15)	Open (n=23)	p-value
Age (yr)	58.7 $\pm$ 9.6	61.9 $\pm$ 5.9	0.209
BMI (kg/m ²)	22.1 $\pm$ 1.7	23.0 $\pm$ 1.6	0.118
ASA PS classification			0.715
I	4	6	
II	11	16	
III	0	1	
Clinical T stage			0.073
Ta	0	6	
T1	4	6	
T2	11	8	
T3–4	0	3	
CIS (concomitant)			0.413
0	15	22	
1	0	1	
Operative time (min)	520.3 $\pm$ 103.1	415 $\pm$ 102.3	0.004
Estimated blood loss (mL)	205.3 $\pm$ 117.0	394 $\pm$ 253.2	0.011
Hospital day (day)	23.1 $\pm$ 7.1	24.1 $\pm$ 12.6	0.768
Complication (%)	3 (20.0)	6 (26.1)	0.666
Urodiversion			0.001
Ileal conduit	5	20	
Neobladder	10	1	
Urethrocuteanostomy	0	2	
Erectile function (%)	6 (40.0)	2 (8.7)	0.021

Values are presented as mean $\pm$ standard deviation, number, or number (%).

nsRARC: nerve-sparing robot-assisted radical cystectomy, BMI: body mass index, ASA PS: American Society of Anesthesiologists physical status, CIS: carcinoma *in situ*.

Table 2. Pathologic data and oncologic outcome

Variable	nsRARC (n=15)	Open (n=23)	p-value
T stage			0.065
T0	1	2	
T1	1	6	
T2	8	3	
T3	4	6	
T4	1	6	
N stage			0.999
N0	11	17	
N1	2	3	
N2	2	3	
Median follow-up (mo)	80	43	
Metastasis, n (%)	4 (26.7)	10 (43.5)	0.294
5-year cancer-specific survival rate (%)	86.7	86.7	
5-year overall survival rate (%)	86.7	77.7	

nsRARC: nerve-sparing robot-assisted radical cystectomy.

10 patients died between 1 and 32 months after surgery. The other 4 patients exhibited recurrence between 1 and 6 months; and survived between 41 and 50 months. After ORC, 5-year overall survival and cancer-specific survival rates were 77.7% and 86.7%, respectively (Table 2).

With respect to erectile function, overall postoperative potency rates at 12 months after surgery in the nsRARC and ORC groups were 40.0% and 9.5%, respectively, and this difference was significant ($p=0.021$) (Table 1).

DISCUSSION

Schlegel and Walsh¹⁶ performed nerve sparing open radical cystectomy with preservation of sexual function in the majority of their patients without compromising the curative nature of the procedure. Open radical cystectomy is standard treatment in patients with localized muscle invasive cancer or non-muscle invasive urothelial cancer refractory to intravesical therapy.¹ Nevertheless, erectile dysfunction and sexual dysfunction are important complications of cystectomy and urinary diversion.⁶⁻⁸ In a prospective study, Hekal et al.¹⁷ concluded erectile recovery was better and progressively returned to normal in a nerve sparing group, and Schoenberg et al.¹⁸ reported return of sexual function was more likely in younger patients.

Menon et al.¹⁹ in a feasibility study on nsRARC first reported that the procedure combines the oncological concepts of open

surgery with the technical nuances of robotic surgery. According to Karolinska Institute experience, the oncologic and functional outcomes and the complications of nsRARC are similar to those of ORC.²⁰ However, Canda et al.²¹ found only one of 11 preoperatively potent men remained potent after a relatively short follow-up of 9-month post-ORC. Haberman et al.²² concluded nsRARC enabled better recovery of potency without sacrificing oncologic outcomes even in patients with high risk disease as compared with historical open or laparoscopic series.

In the present study, preoperative potency was not evaluated and postoperative potency was assessed at 12 months after surgery using questions 2 and 3 of the IIEF-5 survey. The erection potency rate was excellent (40%) in the nsRARC group as compared with the 9.5% observed in the ORC group.

Recent studies have improved understanding of the pelvic neuroanatomy from the aortic bifurcation to the membranous urethra, and as a result, pelvic nerve preservation during uro-oncologic surgery has been improved.^{23,24} The autonomic nerve supplies afferents to the corpora cavernosa from the pelvic plexus, and these nerve fibers run directly beneath the distal ureter, medial to the umbilical artery, alongside the lateral aspects of seminal vesicles, and adjacent to the prostatic capsule. Furthermore, the distribution of nerve fibers within the posterolateral prostatic neurovascular bundle and the existence of mixed innervation in the posterior and lateral fiber courses at the level of the prostate and seminal vesicles explain how effects associated with resection of the periprostatic part that influence sexual function might be minimized.

In our experience, the use of an energy source in the region of autonomic nerve supply to the corpora cavernosa is limited. Furthermore, traction of the prostate may be performed only after total bilateral nerve sparing, though resection of the lateral prostate vesicular area without causing nerve damage is allowed, because of the relative absence of neuronal tissue at the ventral surface on the base of the prostate.

During nsRARC, we performed antegrade intrafascial dissection with high anterior release of the prostatic fascia to the lateral prostate. Nerve sparing is an important step during radical prostatectomy and substantially determines functional outcomes, and hence, every attempt should be made to preserve neurovascular bundles. We have adopted an antegrade approach for robot and open procedures, because this approach allows early control of prostatic pedicles, minimizes bleeding during nerve sparing, and does not require suturing of the deep dorsal

vein complex.²⁵

Recently studies have reported short-term complication rates of from 30% to 69.0% for RARC and long-term complication rates from 34% to 100%. In the present study, the overall complication rate was 30% and no major complication was encountered.²⁶

The nsRARC is expected to indication for younger patients and advanced age who wants to preserve sexual function. Generally, nerve sparing radical cystectomy is regarded to present risks of an increase in positive surgical margins and local disease recurrence. However, in the present study, there is no local recurrence. Furthermore, the high negative soft tissue surgical margin rate (100%) achieved suggests that our technique of nsRARC leads to satisfactory local control.

This study has some limitations that should be considered. First, no comparison was made between nsRARC and conventional RARC. Second, there is no data whatever on preoperative sexual function. Third, our results are inherently limited the single-center, retrospective design of the study and its small sample size. Nevertheless, the study shows that nsRARC produces satisfactory oncologic outcomes with secure local control, and suggests nsRARC better enables recovery of erectile dysfunction than ORC.

CONCLUSIONS

Our clinical experiences indicate nsRARC in selected patients is a feasible procedure in terms of its oncologic outcomes and ability to preserve erectile function relatively effectively. We believe that this technique has the potential to be adopted by urologic surgeons as a standard RARC procedure.

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

REFERENCES

- Witjes JA, Compérat E, Cowan NC, De Santis M, Gakis G, Lebre T, et al. EAU guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2013 guidelines. *Eur Urol* 2014;65:778-92.
- Mari A, Campi R, Tellini R, Gandaglia G, Albisinni S, Abufaraj M, et al. Patterns and predictors of recurrence after open radical cystectomy for bladder cancer: a comprehensive review of the literature. *World J Urol* 2018;36:157-70.
- Kim TH, Sung HH, Jeon HG, Seo SI, Jeon SS, Lee HM, et al. Oncological outcomes in patients treated with radical cystectomy for bladder cancer: comparison between open, laparoscopic, and robot-assisted approaches. *J Endourol* 2016;30:783-91.
- Bagi P, Nordsten CB, Kehlet H. Cystectomy for bladder cancer in Denmark during the 2006-2013 period. *Dan Med J* 2016 Apr;63(4). pii: A5217.
- Kiss B, Burkhard FC, Thalmann GN. Open radical cystectomy: still the gold standard for muscle invasive bladder cancer. *World J Urol* 2016;34:33-9.
- Moschini M, Simone G, Stenzl A, Gill IS, Catto J. Critical review of outcomes from radical cystectomy: can complications from radical cystectomy be reduced by surgical volume and robotic surgery? *Eur Urol Focus* 2016;2:19-29.
- Schoenenberger AW, Burkhard FC, Thalmann GN, Wuethrich PY. Influence and impact of cognitive trajectories on outcome in patients undergoing radical cystectomy: an observational study. *Urology* 2016;92:63-9.
- Bazargani ST, Djaladat H, Ahmadi H, Miranda G, Cai J, Schuckman AK, et al. Gastrointestinal complications following radical cystectomy using enhanced recovery protocol. *Eur Urol Focus* 2017 Apr 25 [Epub]. pii: S2405-4569(17)30088-3. <https://doi.org/10.1016/j.euf.2017.04.003>.
- Tang JQ, Zhao Z, Liang Y, Liao G. Robotic-assisted versus open radical cystectomy in bladder cancer: a meta-analysis of four randomized controlled trials. *Int J Med Robot* 2018 Feb;14(1). <https://doi.org/10.1002/rcs.1867>.
- Son SK, Lee NR, Kang SH, Lee SH. Safety and effectiveness of robot-assisted versus open radical cystectomy for bladder cancer: a systematic review and meta-analysis. *J Laparoendosc Adv Surg Tech A* 2017;27:1109-20.
- Miller C, Campain NJ, Dbeis R, Daugherty M, Batchelor N, Waite E, et al. Introduction of robot-assisted radical cystectomy within an established enhanced recovery programme. *BJU Int* 2017;120:265-72.
- Thress TM, Cookson MS, Patel S. Robotic cystectomy with intracorporeal urinary diversion: review of current techniques and outcomes. *Urol Clin North Am* 2018;45:67-77.
- Hussein AA, Ahmed YE, Kozlowski JD, May PR, Nyquist J, Sexton S, et al. Robot-assisted approach to 'W'-configuration urinary diversion: a step-by-step technique. *BJU Int* 2017;120:152-7.
- Simone G, Papalia R, Misuraca L, Tuderti G, Minisola F, Ferriero M, et al. Robotic intracorporeal padua ileal bladder: surgical technique, perioperative, oncologic and functional outcomes. *Eur Urol* 2016 Oct 22 [Epub]. pii: S0302-2838(16)30721-7. <https://doi.org/10.1016/j.euro.2016.10.018>.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-13.

16. Schlegel PN, Walsh PC. Neuroanatomical approach to radical cystoprostatectomy with preservation of sexual function. *J Urol* 1987;138:1402-6.
17. Hekal IA, El-Bahnasawy MS, Mosbah A, El-Assmy A, Shaaban A. Recoverability of erectile function in post-radical cystectomy patients: subjective and objective evaluations. *Eur Urol* 2009;55:275-83.
18. Schoenberg MP, Walsh PC, Breazeale DR, Marshall FF, Mostwin JL, Brendler CB. Local recurrence and survival following nerve sparing radical cystoprostatectomy for bladder cancer: 10-year followup. *J Urol* 1996;155:490-4.
19. Menon M, Hemal AK, Tewari A, Shrivastava A, Shoma AM, El-Tabey NA, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion. *BJU Int* 2003;92:232-6.
20. Wilson TG, Guru K, Rosen RC, Wiklund P, Annerstedt M, Bochner BH, et al. Best practices in robot-assisted radical cystectomy and urinary reconstruction: recommendations of the pasadena consensus panel. *Eur Urol* 2015;67:363-75.
21. Canda AE, Atmaca AF, Altinova S, Akbulut Z, Balbay MD. Robot-assisted nerve-sparing radical cystectomy with bilateral extended pelvic lymph node dissection (PLND) and intra-corporeal urinary diversion for bladder cancer: initial experience in 27 cases. *BJU Int* 2012;110:434-44.
22. Haberman K, Wittig K, Yuh B, Ruel N, Lau C, Wilson TG, et al. The effect of nerve-sparing robot-assisted radical cystoprostatectomy on erectile function in a preoperatively potent population. *J Endourol* 2014;28:1352-6.
23. Alsaid B, Karam I, Bessedé T, Abdlsamad I, Uhl JF, Delmas V, et al. Tridimensional computer-assisted anatomic dissection of posterolateral prostatic neurovascular bundles. *Eur Urol* 2010;58:281-7.
24. Alsaid B, Bessedé T, Karam I, Abd-alsamad I, Uhl JF, Benoît G, et al. Coexistence of adrenergic and cholinergic nerves in the inferior hypogastric plexus: anatomical and immunohistochemical study with 3D reconstruction in human male fetus. *J Anat* 2009;214:645-54.
25. Kwon SY, Lee JN, Ha YS, Choi SH, Kim TH, Kwon TG. Open radical prostatectomy reproducing robot-assisted radical prostatectomy: involving antegrade nerve sparing and continuous anastomosis. *Int Braz J Urol* 2017;43:1043-51.
26. Yuh B, Wilson T, Bochner B, Chan K, Palou J, Stenzl A, et al. Systematic review and cumulative analysis of oncologic and functional outcomes after robot-assisted radical cystectomy. *Eur Urol* 2015;67:402-22.