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Comparative analysis of genitourinary function after type C1 robotic nerve-sparing radical hysterectomy versus type C2 robotic radical hysterectomy

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ABSTRACT

Background: To compare the return of bladder function and genitourinary complications after type C1 robotic nerve-sparing radical hysterectomy (C1-RRH) to type C2 robotic radical hysterectomy (C2-RRH) in gynecologic cancers.

Methods: A retrospective analysis between C1-RRH (n = 42) and C2-RRH (n = 43) was performed. Operative outcomes and perioperative genitourinary complications between the two groups were analyzed.

Results: The C1-RRH group had shorter hospitalization (0.7 vs. 1.7 days, $p < 0.001$) and shorter DUC (1 vs. 28 days, $p < 0.001$). About 76% of C1-RRH group required a catheter for less than 1 week while 84% of the C2-RRH group did for more than 1 week (54% for 1–6 weeks; 30% > 6 weeks). In spite of the short stay after surgery (95% of C1-RRH ≤ 1 day), only two patients (4.8%) in C1-RRH group were admitted again because of urinary tract infection. C1-RRH was only independent predictor for early bladder function return within 1 week after surgery.

Conclusion: The C1-RRH showed early bladder function return and feasible outcomes in spite of early discharge. It can be considered as the first surgical option in gynecologic cancer patients who need RH to preserve their bladder function.

1. Introduction

Cervical cancer is one of the most common gynecologic cancers although a decline in its incidence has been noted during the last 5 years [1]. Radical hysterectomy (RH) has been standard treatment for patients with early stage cervical cancer, stage II endometrial cancer, and upper vaginal carcinoma since Wertheim performed the first RH with pelvic lymph node dissection (PLD) for cervical cancer patients in 1898 [2]. However, patients who undergo RH have suffered neurogenic bladder because of the disruption of the inferior hypogastric plexus (IHP) by parametrium resection [3–5]. The incidence of bladder dysfunction following RH has been reported to occur in 24%–70% [6]. A number of surgeons and research groups have tried to perform and clarify surgical procedures to minimize neurogenic complications and maintain the radicality of RH. Fujii showed the procedures for nerve-sparing RH (NSRH) by describing the anatomical nerve plexus in the pelvis [7,8]. In addition, Querleu and Morrow defined the NSRH as type C1 in the new classification system for RH [9]. Recently, Ditto's retrospective study showed NSRH upheld efficacy of conventional RH, without increasing recurrence and operative complication but improving postoperative genitourinary function [10].

The optimal instrumentation and surgical techniques for robotic surgery are evolving in the direction of easier minimally invasive surgery [11–14]. Robotic surgery has improved surgeons' dexterity, surgical precision, visualization, and ergonomics [15,16]. Because of the complexity of the pelvic nerve anatomy, the concept of combining NSRH and robotic surgical systems seems to be an ideal surgical approach. There were a great number of retrospective minimally invasive RH studies, including laparoscopic and robotic, showed feasible surgical outcomes and reasonable survival results. In spite of the potential strength of robotic surgical system to preserve nerve system during operation, there is very little data focusing on the robotic NSRH. Based on these considerations, our study is worthy to assess whether robotic NSRH has feasible surgical and functional outcomes though neither abdominal nor laparoscopic approach were compared. It is important to keep in mind that though several studies regarding similar outcomes have been already reported [17–20]. Because majority of the studies reported were about laparoscopic RH. The aim of this study was to

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compare the return of bladder function and genitourinary complications after type C1 robotic NSRH (C1-RRH) to type C2 robotic RH (C2-RRH) in patients with early stage cervical cancer or endometrial cancer with spread to the cervix. To the best of our knowledge, this study is one of the largest series regarding the C1-RRH and the first study comparing C1-RRH with C2-RRH.

2. Materials and methods

2.1. Patients

This study was approved by the Institutional Review Board at University of Nevada, Reno. Between April 2008 and October 2016, we identified 86 consecutive patients who underwent RRH and PLD for early stage cervical cancer or endometrial cancer with spread to the cervix and reviewed their medical charts retrospectively. Of these, one patient was converted to laparotomy without any surgical procedure by robotic instruments due to morbid obesity. This patient was excluded from the analysis. The enrolled 85 patients in this study were divided into 2 groups based on the approach of surgery (C1-RRH group, n = 42, and C2-RRH group, n = 43). A single surgeon (P. C. Lim) performed all surgery. The patient's status was estimated in terms of operating time, estimated blood loss, days of hospitalization (DOH), perioperative complications, and days of urinary catheter required (DUC). In addition, their subjective genitourinary symptoms were evaluated at 2 years after surgery. The urinary catheter of all patients were removed routinely immediately after surgery. If postvoid residual urine volume (PVR) measured after spontaneous voiding was less than 150 ml, they were allowed to go home and visited the office after 2 weeks. If they could not void or their PVR > 150 ml, they had two options. One was that they discharged after recatheterization and visited our office after 4 days. At that time, the urinary catheter was removed and PVR was checked again. The other was that they stayed at hospital overnight and checked both spontaneous voiding and PVR in the next morning. If they had good result, they could visit the office after 2 weeks. The DUC were divided into 3 subgroups: < 1 week, 1–6 weeks, and > 6 weeks. The operating time was defined as the time from the first incision to the closure of the incision. In addition, we classified complications into minor and major complications. Minor complication included urinary tract infection (UTI) with fever > 38.5 °C. Major complications included the situation requiring a secondary surgical procedure to perform adequate hemostasis and repair of urinary tract injuries or bowel perforation.

All continuous data were expressed as mean ± standard deviation, and categorical data were reported as an absolute number or percentage. Frequency distributions were compared using the Chi-square test and Fisher's exact test, and mean or median values were compared using the Student's t- and Mann-Whitney U-tests. Progression-free survival (PFS) was calculated from the date of RH to date of disease progression or recurrence or date of last contact or disease-relevant death. Overall survival (OS) was calculated from the date of RH to date of last contact or death resulting from any cause. PFS and OS were estimated using the Kaplan–Meier method, and the differences in survival were compared using the log-rank test. All calculated p values were 2 sided, and $p < 0.05$ was considered statistically significant. Data were analyzed using SAS/STAT software, version 9.4 (SAS Institute Inc., NC, USA).

2.2. Surgical techniques

The da Vinci Si or Xi Surgical System (Intuitive Surgical, Inc., CA, USA) was used. We used three robotic arms and one camera port. The instruments and accessories included Prograsp forcep, Monopolar spatula, Maryland bipolar forcep, Vessel sealer, and Mega suture-cut needle driver. A 12-mm trocar for the camera was inserted into the umbilicus. One 8-mm trocar for the left robotic arm and two 8-mm trocar for the right robotic arms were placed 8 cm apart bilaterally to the umbilicus. In addition, a 12-mm accessory assistant port was placed in the lower abdomen lateral to the left outer robotic port at the level of the anterior superior iliac spine. The C1-RRH surgical procedure was achieved in the following manner. The round ligament was transected, and the pararectal and paravesical spaces were developed. PLD was performed as usual manner while preserving the genitofemoral and obturator nerve. The lymph nodes were removed en bloc and extracted through the accessory 12-mm port using an endobag. The parametrial complex was developed. The anterior division of hypogastric vessels were identified. The superior vesical artery, uterine artery, vaginal artery, and deep uterine vein were skeletonized, isolated and dissected. Robotic Hem-o-Lok clips (Intuitive Surgical, Inc., CA, USA) were used to secure the uterine artery and deep uterine vein at their origin. Beneath the deep uterine vein, the branches of the pelvic splanchnic nerves were identified. The parametrium was developed. The ureter was then dissected away from the medial peritoneal attachment. The mesoureter that encompassed the neurovascular bundles of the cervical (IHP-CF) and vesical (IHP-VF) nerve fibers of IHP was identified 1 cm dorsal to the ureter. The mesoureter with the IHP nerve fibers likewise was dissected away from the medial leaf of peritoneal attachment. The Okabayashi's and Latzko's space was developed. These spaces were achieved by placing the Vessel sealer directly dorsal to the ureter as it entered the ureteric tunnel. The IHP-CF and IHP-VF were skeletonized, separated, and identified. The IHP-CF was resected while laterally the IHP-VF was preserved. We identified the distal part of IHP-VF and separated it from the paravaginal tissues during resection of the ventral parametrium. The IHP-VF resided lateral and caudal to the vesicouterine ligament and the distal ureter. After separating blood vessels in both anterior and posterior leaf of the vesicouterine ligament, we excised the ventral parametrium and the paracolpium. The uterosacral ligament was then divided. The rectovaginal space was developed follow by development of vesicouterine space. Finally, the entire parametrium was resected by excising the dorsal parametrium. Colpotomy was then performed and the vagina was circumferentially excised. For the closure of the vaginal cuff, we performed continuous running sutures intracorporeally using a barbed suture.

3. Results

A summary of subject characteristics are described in Table 1 and there was no statistical difference between the two groups. Operative outcomes are shown in Table 2. Compared to the C2-RRH group, the C1-RRH group had shorter operating time (174.7 vs 204 min, $p = 0.008$), shorter hospitalization (0.7 vs 1.7 days, $p < 0.001$), and shorter DUC (1 vs 28 days, $p < 0.001$). When the DUC were divided into 3 subgroups, about 76% of the C1-RRH group required a catheter for less than 1 week while 84% of the C2-RRH group did for more than 1 week (54% for 1–6 weeks; 30% > 6 weeks). Although the C2-RRH cohort showed higher perioperative complication rate (37% vs 14%, $p = 0.036$), most of complications were UTI which did not require additional procedures. They were appropriately treated with antibiotics and had no sequelae. For the C1-RRH group, the rate of major complications was 2.4% (1/42) and this patient developed vesicovaginal fistula 3 months post completion of adjuvant radiotherapy. She underwent robotic vesicovaginal fistula repair six months after C1-RRH. For the C2-RRH group, the rate of major complications was 4.7% (2/43) and they sustained dissectional cystotomy during C2-RRH and underwent primary bladder repair without any further sequelae. The C1-RRH had shorter DOH than the C2-RRH (0.7 vs 1.7, $p < 0.001$). Because the DOH data of both the two groups did not follow a normal distribution statistically, the DOH was divided into 3 subgroups: 0, 1, and ≥2 days to show the distribution of all patients. There was no statistically significant difference of the incidence of unexpected visit after surgery between the two groups. Five patients in the C1-RRH group visited emergency room after surgery due to UTI symptoms (4 patients) or

Table 1
Clinicopathologic characteristics.

	C1-RRH (n = 42)	C2-RRH (n = 43)	p value
	Number of patients (%)		
Mean age (years, SD)	49.6 ± 13.3	46.5 ± 13.3	0.278
Mean body mass index (kg/m^2, SD)	26.9 ± 4.9	26.7 ± 6.9	0.877
Tumor stage			0.057
Cervical cancer IB1	29 (69)	37 (86)	
Cervical cancer IB2	5 (11.9)	4 (9.3)	
Cervical cancer IIA1	0	1 (2.3)	
Endometrial cancer II	8 (19)	1 (2.3)	
Tumor size (cm, IQR)[a]	2 (2.4)	1.5 (2.5)	0.427
Histology			0.059
Squamous cell carcinoma	23 (54.8)	25 (58.1)	
Adenocarcinoma	11 (26.2)	17 (39.5)	
Endometrioid adenocarcinoma	8 (19)	1 (2.3)	
Tumor grade			0.267
Well differentiated	10 (23.8)	14 (32.6)	
Moderately differentiated	23 (54.8)	16 (37.2)	
Poorly differentiated	9 (21.4)	13 (30.2)	
Lymphovascular space invasion	14 (33.3)	8 (18.6)	0.121
Parametrium invasion	0	5 (11.6)	0.055
Lymph node metastases	7 (16.7)	8 (18.6)	0.815
Vaginal cuff margin involvement	2 (4.8)	0	0.241

C1-RRH, type C1 robotic nerve-sparing radical hysterectomy; C2-RRH, type C2 robotic radical hysterectomy; SD, standard deviation; IQR, interquartile range.
[a] Cervical cancer patients only.

Table 2
Operative outcomes.

	C1-RRH (n = 42)	C2-RRH (n = 43)	p value
	Number of patients (%)		
Operating time (min)	174.7 ± 46.4	204.0 ± 52.1	0.008
Median estimated blood loss (ml, IQR)	87.5 (50)	100 (125)	0.058
Transfusion	1 (2.4)	0	0.494
Days of hospitalization			< 0.001
Mean (days)	0.7 ± 0.6	1.7 ± 1.0	
Median (days, IQR)	1 (1)	1 (1)	
0	14 (33.3)	1 (2.3)	
1	26 (61.9)	23 (53.5)	
≥2	2 (4.8)	19 (44.2)	
Number of lymph nodes retrieved	27.1 ± 10.0	28.7 ± 9.6	0.444
Days of urinary catheter required (days, IQR)	1 (9)	28 (35)	< 0.001
< 1 week	32 (76.2)	7 (16.3)	
1–6 weeks	10 (23.8)	23 (53.5)	
> 6 weeks	0	13 (30.2)	
Perioperative complications			0.036
Major	1 (2.4)	2 (4.7)	
Minor	5 (11.9)	14 (32.6)	
Visit to emergency room after discharge	5 (11.9)	11 (25.6)	0.107
Re-admission after discharge	2 (4.8)	5 (11.6)	0.250
Chronic symptoms 2 years after surgery			
Voiding difficulty	2 (4.8)	4 (9.3)	0.414
Overactive bladder	3 (7.1)	2 (4.7)	0.625
Stress urinary incontinence	0	1 (2.3)	1.000

C1-RRH, type C1 robotic nerve-sparing radical hysterectomy; C2-RRH, type C2 robotic radical hysterectomy; IQR, interquartile range.

blood clots in urinary catheter (1 patient). In spite of the short stay after surgery (95% of C1-RRH ≤ 1 day), only two patients (4.8%) of the C1-RRH group were admitted again because of UTI. Of 11 patients who visited emergency room unexpectedly in the C2-RRH group, four patients had UTI symptoms, three had urinary retention, and four

Table 3
Univariate and multivariate analyses for delayed bladder function return after 1 week.

	Univariate analysis	Multivariate analysis	
	p value	p value	HR (95% CI)
Age > 50 years	0.045	0.765	1.21 (0.35–4.15)
Body mass index	0.427		
C1-RRH	< 0.001	< 0.001	0.06 (0.02–0.19)
Tumor stage IB2/IIA1	0.054	0.375	2.53 (0.33–19.72)
Endometrial cancer	0.042	0.473	0.39 (0.03–5.05)

evaluated for abdominal pain or vomiting. Five patients of the C2-RRH required readmission to the hospital for pelvic abscess, urinary retention, UTI, abdominal pain monitoring, and abdominal ascites. There was no statistical difference of chronic genitourinary symptoms at 2 years after surgery between the two groups. C1-RRH was only independent predictor for early bladder function return within 1 week ($p < 0.001$) (Table 3). In the survival analysis, the median duration of the follow-up was 52 months (range 2.5–124). The recurrence rate of C1- and C2-RRH group was 7.1% (3/42) and 9.3% (4/43), respectively. The mean PFS of C1- and C2-RRH group was 76.7 and 113.6 months, respectively. There was no statistically significant difference between the two groups ($p = 0.811$). The mean OS of C1- and C2-RRH group was 78.7 and 116.8 months, respectively. There was no statistically significant difference between the two groups ($p = 0.902$) (Fig. 1).

4. Discussion

We focused on comparison of the return of bladder function and genitourinary complications between C1-RRH and C2-RRH in this study. Our results showed that the C1-RRH was associated with early bladder function return and early discharge of patients with minimal morbidity. In addition, the C1-RRH was only independent factor for early bladder function return after surgery. Although we had no specific indication for C1-RRH, we can ascertain that the cohorts of both two groups were matched properly by no difference of clinicopathologic factors (Table 1). In addition, we analyzed all patients who underwent RRH with PLD at the same period to minimize selection bias for comparison.

A number of studies have showed feasible operative outcomes of NSRH, including bladder function. Chen et al. evaluated the clinical outcomes of autonomic nerve and vascular injury within the cardinal ligament during NSRH compared to RH [21]. They reported PVR was greater in RH compared to NSRH. In addition, the mean time to achieve PVR < 50 ml was shorter in NSRH than in RH. In a meta-analysis, Wu and colleagues showed laparoscopic NSRH caused more satisfactory micturition, shorter catheterization time, and early bladder function recovery. In addition, NSRH group had better results in urodynamic assessments compared to conventional RH group [20]. In spite of the favorable outcomes as surgical treatment, NSRH is not performed routinely in patients with gynecologic cancers. The challenge of performing NSRH is identifying the anatomical landmark, development of the Okabayashi's space, Latzko's space, IHP-CF, and IHP-VF. In addition, there are some concerns regarding whether less resected specimens during NSRH can be related to poor prognosis. However, a number of studies showed that NSRH did not induce the lack of radicality [10,22–24]. A meta-analysis demonstrated that the time to bladder function recovery after NSRH was shorter than RH without the increase of recurrence rate [22]. Additionally, Roh et al. showed that NSRH was effective in preserving bladder function without sacrificing oncologic safety using a randomized controlled study that enrolled 92 patients with cervical cancer [23]. In our survival analysis, it seemed that the PFS and OS of C2-RRH group was longer than the C1-RRH group. Because most of the C2-RRH was performed in earlier period

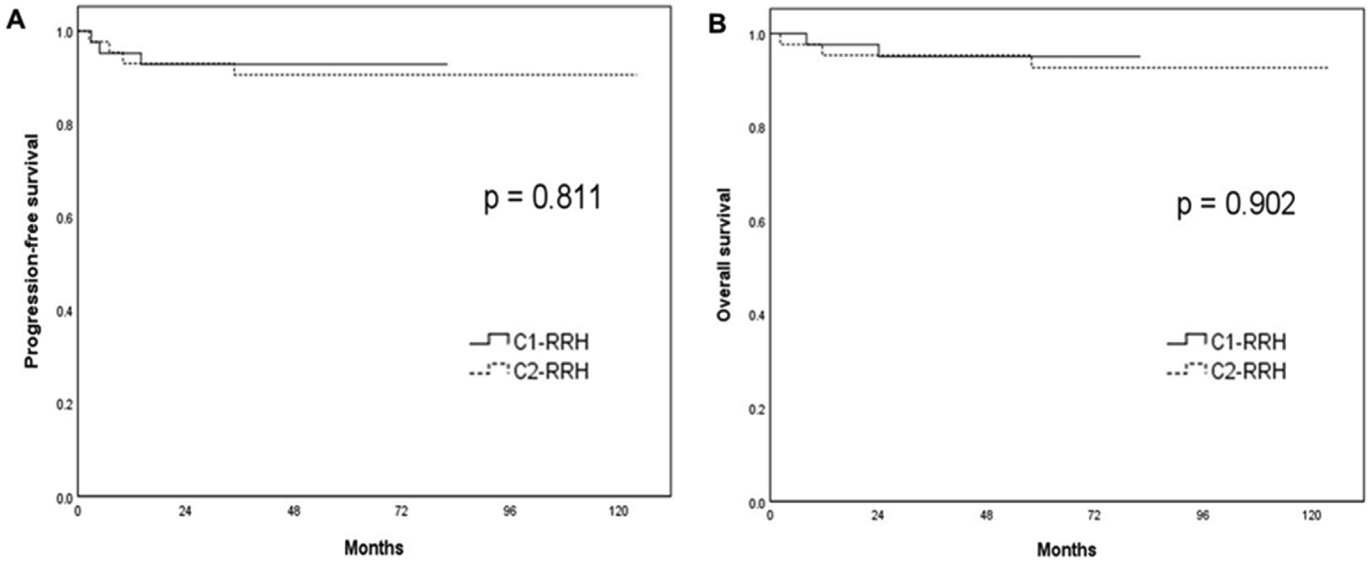

Fig. 1. Progression-free survival (A) and overall survival (B) stratified by type C1 and C2 robotic radical hysterectomy.

based on the surgery date, patients who underwent C2-RRH were followed up for longer time than C1-RRH group. However, there was no difference of recurrence rate between C1- and C2-RRH group (7.1% vs 9.3%).

Robotic surgery is becoming more widely accepted in the management of gynecologic disease. The technologic advantages of robotic surgery help surgeons to perform difficult operations that need to understand complex pelvic anatomy. Magrina et al. described the technique and feasibility C1-RRH and there are limited clinical studies [25–27]. Lee et al. evaluated short-term clinical outcomes of C1-RRH with extended PLD [26]. They showed that C1-RRH did not compromise the radicality and its surgical technique was feasible. In addition, they could resect more metastatic lymph nodes without disturbing voiding function. While this study was the case series of 28 patients who underwent C1-RRH, our study showed the favorable outcomes of C1-RRH with more number of patients compared to C2-RRH.

In our study, the shorter operating time of C1-RRH could be attributed to the learning curve of the surgeon as majority of C1-RRH cases were performed at the second half of the study period. The DOH was divided into 3 subgroups and there was clear difference between the two groups. Out of the 42 patients in C1-RRH, 14 patients (33.3%) were discharged on the same-day of surgery and 26 patients (61.9%) on post operation day (POD) 1. The remaining two patients were discharged on POD 2 and POD 3. In contrast to the C1-RRH group, 54% (23/43) of the C2-RRH group were discharged on POD 1 and 44% (19/43) on POD 2 or more. One patient was discharged on the same-day. The DOH data did not follow a normal distribution statistically. It was attributed to the small number of the analyzed cohorts in this study. Despite approximately 95% of the C1-RRH discharged on the same-day or POD 1, only two patients (4.8%) were admitted for UTI. They were treated with intravenous antibiotics and were subsequently discharged without complication. The DOH after RH is directly related to the time when urinary catheter can be removed. Most of gynecologic surgeons have thought that it would be safe to remove urinary catheter several days after RH. Because they were concerned that the resection of parametrial tissues might cause the injury of nerves which are related to bladder functions. However, there was no evidence that it was related to the higher incidence of genitourinary or perioperative complications based on previous reported studies [28–30]. In this study, our results showed the robotic nerve-sparing technique was related to early bladder function return in spite of early discharge.

Our study has several limitations. Firstly, we did not perform urodynamic studies to evaluate urinary functions objectively. Secondly, the number of enrolled patients was comparatively small to speculate the difference of the two groups. For pathologic results, there was statistically borderline significance between the two groups. If the number of enrolled patients is many, there may be statistically significant difference of pathological outcomes. However, we did not regard them as critical problem of this study because we focused on the functional outcomes of RH rather than oncologic results. Finally, we could not avoid selection bias completely because this was retrospective study. In addition, we could not exclude that surgeon's learning curve influenced on the operative outcomes. However, it takes long time to get proficiency for RRH regardless of the kinds of surgical approaches, including laparotomy, laparoscopy, and robotic surgery. Therefore, surgeons need to track their own surgical procedures and patients' outcomes carefully during reaching the completion of learning curve. Although our study was a retrospective study, we had our own standards for discharge and urinary catheter removal plan and they were applied to all patients. There is minimal data in describing comparison between C1-RRH and C2-RRH. Therefore, the strength of our study is comparing the genitourinary function and morbidity between the two robotic approaches.

In conclusion, the C1-RRH is associated with early bladder function return. Moreover, it is feasible and safe in spite of early discharge after surgery. The C1-RRH can be considered as the first surgical option in gynecologic cancer patients who need RH to preserve their bladder function.

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Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2019.05.003.

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