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Article

Combined Robot-Assisted Radical Cystectomy and Robot-Assisted Nephroureterectomy for Synchronous High-Risk Upper Urinary Tract and Bladder Cancer. A Single Center Retrospective Study and Review of the Literature

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Abstract

Background/ Objectives Simultaneous robotic-assisted radical cystectomy (RARC) and nephroureterectomy (RARNU), offers a minimally invasive alternative to open approach, for patients with synchronous bladder and upper urinary tract cancers, as well as in selected benign conditions. This study presents our single-center experience and includes a review of the relevant literature. **Methods** All patients undergoing combined RARC and RARNU between 2016 and 2023 were retrospectively identified. Clinical and demographic data—including preoperative pathology, operative and re-docking time, estimated blood loss, complications (Clavien-Dindo system), surgical margins, recurrence, morbidity, and follow-up—were collected. A rapid literature review was also conducted. **Results** From 2016 to 2023, 10 patients (mean age 67.4 years, range 56–77) underwent combined RARC and RARNU for upper/lower tract urothelial malignancy. Mean re-docking time was 68.2 min (range 51–100), operative time 524.5 min (range 380–690), and blood loss 427 cc (range 75–1170). A Pfannenstiel incision was used for en bloc specimen extraction, with no complications or incisional hernias. One case was converted to open surgery, and two required extracorporeal diversion. Postoperatively, five Grade 2, one Grade 3, and one Grade 5 complications were reported. All surgical margins were negative. Mean hospital stay was 11.5 days (range 5–29). At a mean follow-up of 21.7 months, one patient became dialysis-dependent and one experienced recurrence requiring further surgery. Literature review included 74 patients with comparable outcomes. **Conclusions** Combined RARC and RARNU is a feasible, minimally invasive option for selected patients. Although technically demanding, it offers acceptable safety and should be performed in high-volume, specialized centers.

Keywords: robot; robotic cystectomy; robotic nephroureterectomy; bladder cancer; upper urinary tract carcinoma

1. Introduction and Objectives

The occurrence of synchronous high-risk, recurrent or muscle invasive bladder cancer and upper urinary tract malignancy is rare and affects less than 3% of patients. Surgical management with simultaneous radical cystectomy and nephroureterectomy is the recommended approach in these cases. Furthermore, some benign conditions such as synchronous dialysis-dependent end-stage renal

disease or non-functioning kidney and contracted bladder or severe bladder dysfunction can also be indications for removal of the bladder and kidney at the same procedure [1,2].

Combined radical cystectomy and nephroureterectomy provides significant advantages for patients. Primarily, these combined procedures eliminate the need for multiple operations that require general anaesthesia, resulting in reduced morbidity. Additionally, the combined surgical approach can potentially lower overall costs and shorten the recovery period [3].

A few surgical teams have published their experience in performing open or laparoscopic en bloc cystectomy and nephroureterectomy [4,5]. However, the introduction of advanced robotic-assisted surgical systems in recent years has improved ergonomics and reduced the morbidity associated with the procedure. In addition, robotic-assisted radical cystectomy (RARC with totally intracorporeal urinary diversion is becoming increasingly popular among urological surgeons. Therefore, combined robotic-assisted radical cystectomy (RARC) and robotic-assisted nephroureterectomy (RARNU) procedures are increasingly being adopted globally. [5,6]

This study presents our departmental experience on simultaneous RARNU and RARC for urothelial cell cancer and discusses the relevant literature.

2. Materials and Methods

A retrospective chart review was conducted after obtaining approval from the Institutional Review Board. All consecutive cases of combined robot-assisted radical cystectomy (RARC) and robot-assisted nephroureterectomy (RARNU) performed in our department between 2016 and 2023 were identified. Relevant demographic and clinical data were collected retrospectively, including preoperative histopathology, operative and re-docking times, estimated blood loss, intraoperative and postoperative complications (classified according to the European Association of Urology [EAU] Intraoperative Adverse Incident Classification System and the Clavien-Dindo grading system, respectively), margin status, morbidity, and duration of follow-up.

In parallel, a narrative literature review was undertaken to contextualize our institutional outcomes. A comprehensive search of PubMed, the Cochrane Library, and Google Scholar was performed, in adherence to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The search aimed to identify studies reporting combined minimally invasive RARC and RARNU procedures. Duplicates, case reports, and studies that did not involve simultaneous or combined robotic/laparoscopic approaches were excluded. Studies meeting the inclusion criteria were assessed for eligibility and included in the final analysis.

The PRISMA flow diagram detailing the study selection process is presented in **Figure 1**.

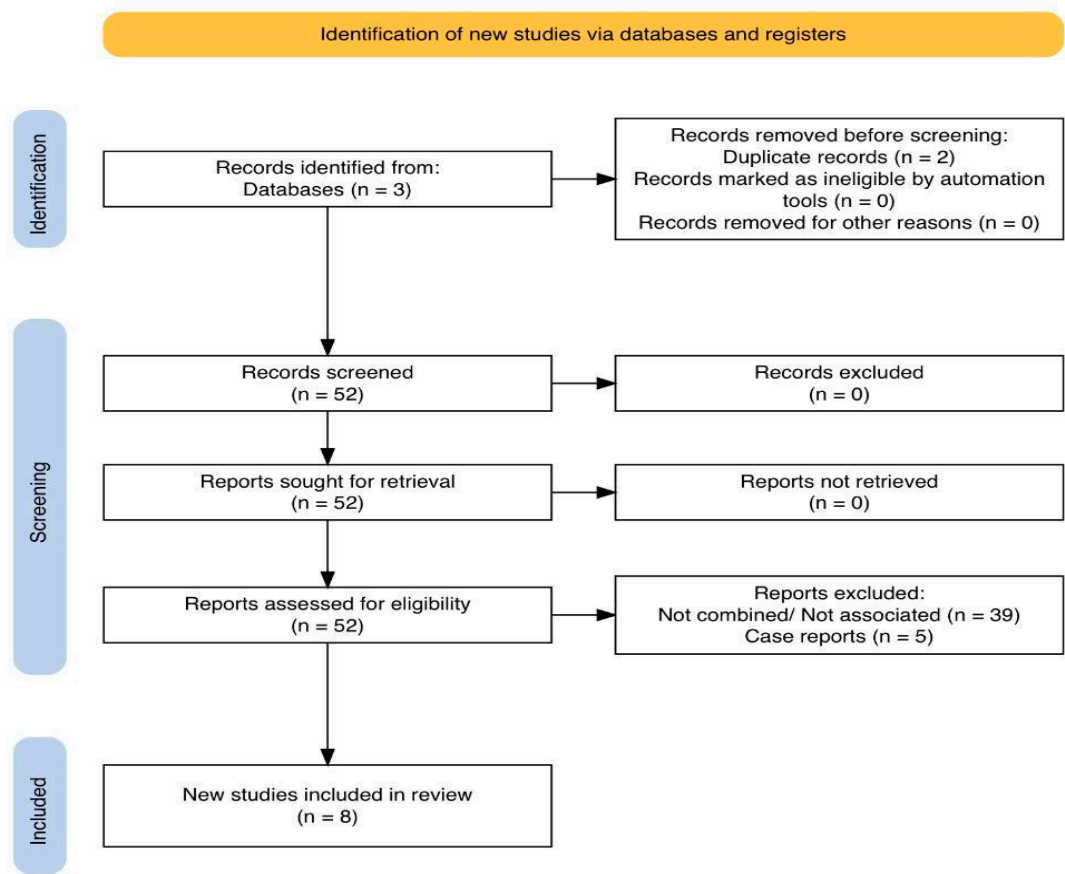


Figure 1. PRISMA Flow diagram.

3. Results

3.1. Cohort Study Results

Between 2016 and 2023, 10 patients (mean age 67.6 years, range 56-77) were offered RARC and RARNU for upper/lower tract urothelial malignancy in our department. A dedicated upper urinary tract robotic surgeon performed the RARNU and a dedicated pelvic robotic surgeon performed the RARC, with extended lymph node dissection and the urinary diversion, which for all patients was an ileal conduit formation. With a mean re-docking time of 68.2 min (range 51-100 min), mean operative time was 524.5 min (range 380-690 min) and mean blood loss was 427cc (75-1170cc).

Indocyanine green (ICG) 25mg in 10ml distilled water with 2ml solution intravenously, was administered prior to the ureteroileal anastomosis, to identify the vascularity of the ureteric distal end and hence prevented postoperative ureteroileal strictures.

Moreover, the bowel was handled minimally with Cadere forceps and the use of vicryl 2-0 stay sutures, which were cut short and clipped with Hem-o-Lok clips, in order to not directly touch the bowel.

A Pfannenstiel incision was used to extract the entire specimen en bloc at the end of the procedure, including the urinary bladder, ureter, and kidney, with a separate specimen bag used for lymph nodes. No complications or incisional hernias were observed. The two middle initial ports of the RARNU were repurposed as assistant and robotic ports during the RARC phase, while the most caudal RARNU incision was extended to facilitate the Pfannenstiel specimen extraction. Three additional robotic trocars were inserted for the RARC component. Figure 2 shows the trocar arrangement for RARNU and RARC.

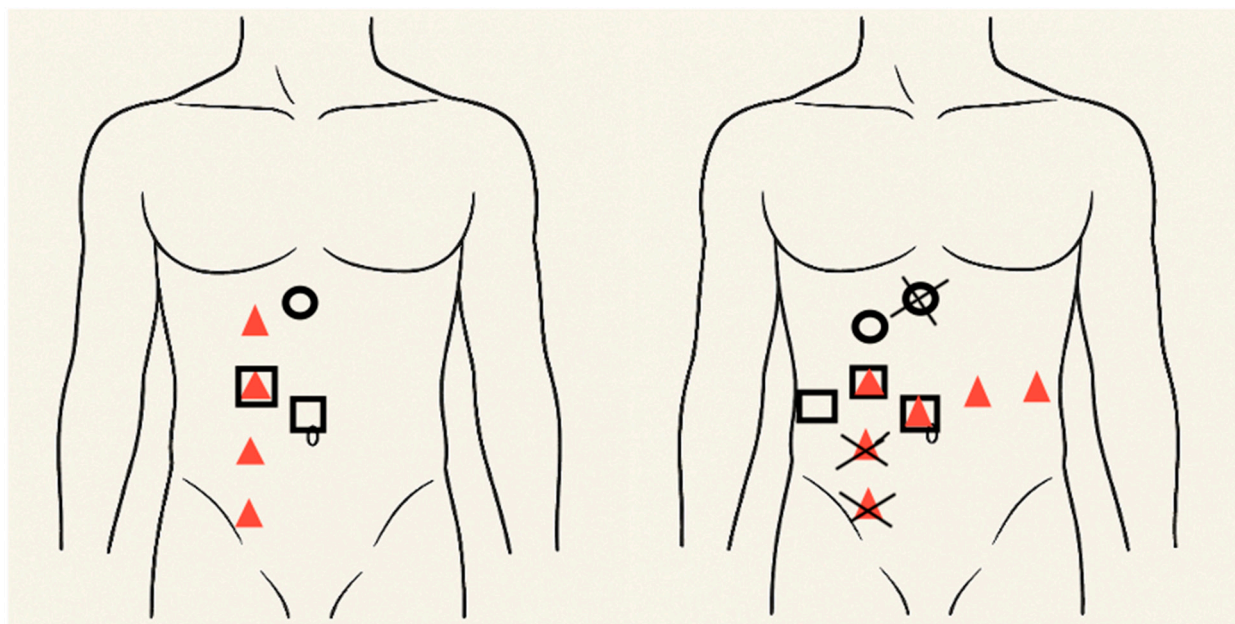


Figure 2. Port placement for RANU (a) and RARC (b). The squares indicate 12-mm ports. The circles indicate 5-mm assistant ports. The triangles indicate the robotic ports (8-mm). Cross marks indicate port holes that were not used in RARC.

One case was partly converted to open (part of RNU) and 2 cases required extracorporeal ileal conduit diversion. Five Grade 2 complications (50%), one Grade 3 (10%) and one Grade 5 complication (10%) were recorded postoperatively. All margins were clear and mean hospital stay was 11.5 days (range 5–29 days). At mean follow-up of 21.67 months (range 3–50 months) one patient (10%) has become dialysis-dependent because of a recurrence that required further surgical intervention (radical urethrectomy and contralateral nephroureterectomy).

3.2. Rapid Literature Review

From our rapid literature review, 74 patients underwent combined minimal invasive radical cystectomy and nephroureterectomy from 8 case series that were identified and included in our study. In 5 studies both parts of the procedure were done robotically (53 patients). In 1 study both the cystectomy and nephroureterectomy were done laparoscopically, while 2 case series used the laparoscopic approach for the upper tract and the robotic approach for the bladder.

There was no need for conversion to open or intraoperative complications reported in any of the studies. In most of the case series the reason for combining RARC and RARNU was simultaneous bladder and upper urinary tract urothelial carcinoma. However, in 3 of the included studies the initial diagnosis in some patients was nonfunctioning kidney or end stage renal disease (15% median of all 8 studies) although there were no cases of preoperative benign bladder diagnosis. Furthermore, there were 2 cases of urothelial bladder cancer with squamous differentiation and 1 squamous cell carcinoma of the bladder.

One study compared open and robotic simultaneous approaches. This study showed 1 case of positive surgical margins in the robotic arm, whereas the recurrences were 3 for open and 2 for robotic cases. 1 patient from the open series died within 6 months from surgery. Moreover, 3 patients from the open arm of the study had higher than 3 Clavien- Dindo complications, in comparison to none from the robotic arm. In total, only 6 patients (8.1%, 6/74) that underwent simultaneous RARC and RARNU (or laparoscopic either part) had high grade (>3) complications, including 2 deaths, in the postoperative follow up (<90 days). Only 9 patients that underwent robotic procedures were transfused (12.16%, 9/74), while almost all patients of the open simultaneous approach needed

transfusion (94%, 16/17). The exact number of units was not reported in all studies but 1 patient was reportedly transfused with 2 units of blood.

During postoperative follow up, there was 1 case of metachronous urothelial cell cancer of the contralateral kidney 24 months after the initial procedure and 2 patients with tumor progression at 4 & 62 months, as well as 3 cases of positive surgical margins The results of the studies are shown in Table 1.

Table 1. Results of studies with combined robot-assisted cystectomy (RARC) and robot-assisted nephroureterectomy (RARNU). LRC= Laparoscopic radical cystectomy, LRNU=Laparoscopic radical nephroureterectomy. RNU= radical nephroureterectomy.

Study	Jour nal/ Year	Numb er of patient s/ Age	Approa ch	Intraoperati ve complicatio ns/ conversion to open	Operative time	EBL (estimate d blood loss)	Hospit al stay	Postoperati ve complicati ons (Clavien- Dindo ≥3)	Follow up/ Recurrences
Ou et al. [1]	J Endo ur 2011	8/ 66.9 (mean)	RARC & RARNU	0	group II (252.5±35.0 min) vs group I (360±25.8 min) (mean)	group II (332.5±53. 8 mL) vs group I (660±137.4 mL) (mean)	7.75 days (mean)	no	28.1 months (mean)/ 0
Barros et al. [2]	Int Braz J Urol 2008	8/ 76.5 (media n)	LRC & LRNU	0	540 min (median)	755 ml (median)	7.5 days (media n)	(1)4a (fistula) (1)5 (death)	9 months/ 1 metastases/ 1 death
Pisipati et al. [3]	Can Urol Asso c J. 2014	6/ 71 (media n)	RARC & RARNU	0	300 min (mean)	416.7ml (mean)	10.2 days (mean)	no	not reported
Yajima et al. [5]	Curr Urol. 2021	3/ 75 (media n)	RARC & LRNU	0	435 min (Median)	377ml (median)	26 days (media n)	(1) 3b (incisional hernia)	8 months (median)/ 0
Buse et al. [6]	BMC Urol 2021	19/ 73 (mean)	RARC & RARNU	0	324 min (Median)	220ml (median)	not report ed	(1) 3b (post op hernia) (1) 5 (death/ pulmonary embolism)	23 months (median)/ 1 contralateral kidney recurrence & 3 deaths
Buse et al. [7]	J Robo t	11/ 74 (mean)	RARC & RARNU	0	287 min (median)	235ml (median)	15 days (media n)	(1) 3b (port hernia)	7 months (median)/ 1 contralateral

	Surg 2016								kidney recurrence
Kamei et al. [8]	Asia n J Endo sc Surg 2022	10 & 17/ 69.2 ± 6.2 (RARC) , 70.0 ± 8.4 (open)	10 RARC & lapRNU vs 17 OPEN RC & RNU	0	560.8 ± 80.7min (rarc), 487.1 ± 98.7 (open)	291.0 ± 268.8ml (rarc), 2790.0 ± 1341.4ml (open)	17.8 ± 4.2 (RARC) , 30.7 ± 14.7 (open)	(3/17) Grade>=3 (open) (1/17) 5 (death)	6 months/ Recurrence: 2 robotic, 3 open. Mortality: 1 open
Lin et al. [9]	J Chin Med Asso c 2014	9	RARC & RARNU	0	295 min (mean)	470ml (mean)	not report ed	no	not reported

4. Discussion

The present study evaluates the feasibility, safety, and outcomes of combined robot-assisted radical cystectomy (RARC) and robot-assisted radical nephroureterectomy (RARNU) in patients with synchronous high-risk upper urinary tract and bladder urothelial carcinoma. Our findings, contextualized within the existing literature, contribute to the growing body of evidence supporting this complex, minimally invasive approach.

The presence of concurrent muscle-invasive urothelial cell carcinoma (UCC) or recurrent high-risk superficial UCC of the bladder and synchronous UCC of the upper urinary tract is uncommon [1,2,10–12]. A simultaneous radical nephroureterectomy and radical cystectomy as a one-step procedure can be performed to reduce anesthetic risk and morbidity for the patients. There is a very small number of available studies reporting on combined unilateral or bilateral nephroureterectomy and radical cystectomy mainly comprising of small case series and case reports.

Our series demonstrates that simultaneous RARC and RARNU is technically feasible in a specialized center with an experienced multidisciplinary robotic team. The mean operative time (524.5 min) and mean estimated blood loss (427 cc) observed in our cohort are consistent with previously published case series, where operative times ranged from 252 to 560.8 minutes [1,8] and blood loss from 220 to 775 cc [2,6] . The need for re-docking and coordinated teamwork between upper tract and pelvic surgeons is reflected in the operative metrics, but these did not translate into increased intraoperative complications or conversion rates, with only one conversion to open surgery in our series. The use of a Pfannenstiel incision for en bloc specimen extraction proved effective, with no incisional hernias or wound complications, mirroring the safety profile reported in other studies. Furthermore, the use of indocyanine green (ICG) to recognize the vascularity of the remaining ureter before ileal conduit diversion in our series eradicated postoperative ureteric stricture incidences.

All patients in our series had negative surgical margins, with only one recurrence requiring further surgical intervention during follow-up. These results are in line with published data, where positive margin rates remain low and recurrence rates are not increased compared to open or staged procedures. A recent meta-analysis reported 2-year and 5-year overall survival rates of 68% and 44%, respectively, for simultaneous radical cystectomy and nephroureterectomy, with a 2-year progression-free survival rate of 91% [13]. These outcomes underscore the aggressive nature of synchronous urothelial carcinoma but do not suggest inferior cancer control with the combined robotic approach.

A recent systematic review and comparative analysis aimed to investigate the indications, clinical outcomes, and procedure safety of simultaneous RC and RNU [10]. From a total of 28 studies including 947 patients, 32,9% underwent laparoscopic surgery while 25.2% robot- assisted surgery [10]. The outcomes of the different surgical approaches could not be compared in the systematic review, because of study heterogeneity and limitations, however robotic-assisted surgery was found to be associated with lower blood transfusion rate but also, with longer operative times when compared to open surgery, while all remaining outcomes were found to be similar [8,10].

Simultaneous RC and RNU was shown to have a higher rate of intraoperative and postoperative complications with increased risk of re-operation, when compared to RC alone, and thus it is a treatment option that should be cautiously used in well-informed patients, who are relatively fit or in whom the expected benefits outweigh the procedure-related risks [10].

Simultaneous RARC and RARNU provide a single-stage solution for patients with multifocal or synchronous high-risk urothelial malignancies, reducing the need for multiple anesthetics and hospitalizations. This is particularly advantageous for patients with significant comorbidities, end-stage renal disease, or non-functioning kidneys, where minimizing perioperative risk is crucial [10]. Apart from that, the robotic approach has comparable oncological and functional results with the traditional open approach, while demonstrating lower postoperative morbidity and mortality [14]. However, careful patient selection and treatment in specialized centers remain essential to optimize outcomes and safety.

The retrospective design and small sample size limit the generalizability of our findings, as is the case with most published series. Larger, multicenter prospective studies with longer follow-up are necessary to better define the oncological efficacy, complication rates, and optimal patient selection criteria for combined minimally invasive approaches [10,13].

5. Conclusions

In summary, our experience and the available literature suggest that combined RARC and RARNU is a safe and effective option for selected patients with synchronous high-risk upper and lower urinary tract urothelial carcinoma. The robotic approach offers perioperative advantages without compromising oncological outcomes in specialized, high volume centers, though further studies are warranted to confirm these findings in larger cohorts.

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