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*Research article*

# Robot-assisted radical cystectomy and en bloc nephroureterectomy for synchronous upper and lower tract urothelial carcinoma: A multi-center case series

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**Abstract:** *Introduction:* Synchronous upper and lower urothelial carcinoma is uncommon, accounting for approximately 1.8% of patients with urothelial malignancy. Currently, there are no international guidelines for management when the conditions occur concomitantly. En bloc robot-assisted radical cystectomy (RARC) and nephroureterectomy (RANU) represent one management option for selected patients; however, available data remains limited due to the rarity of cases. We report the perioperative and short-term oncological outcomes from a multi-center cohort undergoing combined RARC and RANU. *Methods:* A multi-center, retrospective review was conducted. Patients undergoing combined RARC and RANU or laparoscopic nephroureterectomy between October 2016 and May 2022 for synchronous upper and lower tract urothelial carcinoma were identified and entered into a retrospective database following written consent. Perioperative and oncological parameters were recorded and analyzed using Microsoft Excel. *Results:* Five patients underwent combined RARC and RANU with three undergoing RARC and laparoscopic nephroureterectomy. Age ranged between 44 and 80 years (median 68 years). Seven had RARC with unilateral nephroureterectomy, and one had RARC, bilateral

RANU, and pelvic exenteration. Median console time was 280 minutes, and the median overall operative time was 420 minutes. Three patients had intracorporeal ileal conduit urinary diversion. No cases required conversion to open surgery, and mean blood loss was 201 mL. Mean inpatient stay was 9.9 days. Three patients experienced minor postoperative complications (Clavien-Dindo grade ≤ II). Surgical margins were clear in all cases, and there was no 30- or 90-day mortality. During the mean 15.5-month follow-up, three patients developed metastatic disease progression with an average time to metastasis of 10.3 months. All patients with metastatic recurrence died from cancer-related disease progression during follow up. One patient had nodal recurrence but is in remission after adjuvant chemotherapy. *Conclusion:* Concurrent RARC and RANU is a technically feasible management option in selected patients; however, the risk of metastatic recurrence and cancer-related mortality remains significant. Further prospective studies are required to optimize patient selection, assess long-term oncological outcomes, and clarify the role of perioperative systemic therapy in the management of pan-urothelial carcinoma.

**Keywords:** cystectomy; nephroureterectomy; robot-assisted surgery; bladder cancer; ureteral cancer

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**Abbreviations:** RANU: Robot-assisted nephroureterectomy; RARC: Robot-assisted radical cystectomy

## 1. Introduction

Urothelial cancer can arise from both the upper and lower urinary tract and, in some cases, may necessitate a combined approach for extirpative surgical management. Synchronous upper and lower urinary tract cancers account for less than 2% of patients with urothelial malignancies [1], and hence, there is limited data on outcomes of combined robot-assisted radical cystectomy (RARC) and nephroureterectomy (RANU).

Surgical resection remains the gold standard for upper and lower urinary tract malignancies individually [2,3]. Current EAU guidelines recommend radical cystectomy for high-risk/muscle-invasive bladder cancer (MIBC) and radical nephroureterectomy for high-risk upper tract urothelial cancer (UTUC) when the conditions occur in isolation [3,4]. However, a paucity of data in the literature means that no current international guideline makes a clear recommendation for treatment when the conditions are concomitant.

Surgical management strategies for concurrent upper and lower tract urothelial carcinoma include staged procedures or a combined approach using open, laparoscopic, or robotic techniques. A combined approach may minimize cumulative anesthesia exposure, blood loss, overall operative time, and hospital stay in this high-risk patient cohort, while potentially improving resource utilization. While there are some data reported on surgical outcomes of combined RARC and RANU [1,2,5–9], these are largely confined to small, retrospective cohort studies and case reports, with few studies providing detailed analyses of perioperative course and longer-term oncological outcomes.

In 2011, Ou et al. reported simultaneous robot-assisted laparoscopic nephroureterectomy and radical cystectomy in eight uremic patients, demonstrating technical feasibility, although long-term oncological outcomes were not reported [6]. Subsequently, Buse et al. described 19 patients undergoing simultaneous en bloc robot-assisted radical cystectomy and nephroureterectomy, reporting no conversion to open surgery and low mid-term mortality after a median follow-up of 23 months [1].

More recently, Zein et al. performed a systematic review of 947 patients, comparing outcomes of combined RARC and RANU to radical cystectomy alone. Combined procedures were associated with higher complication rates, specifically renal injury, readmission, and unplanned reoperation, highlighting the complexity of a combined approach and the need for careful patient selection [10].

Collectively, these studies suggest that simultaneous radical cystectomy and nephroureterectomy is technically feasible and can be performed safely in appropriately selected patients with acceptable short-term oncological outcomes. However, further analyses of surgical benchmarks and oncological outcomes in combined, robot-assisted procedures are required.

We report a three-center, eight-patient case series on combined RARC and RANU, with the aims of describing surgical details and oncological outcomes, characterizing the postoperative course (including cancer recurrence and all-cause mortality), and assessing the surgery's technical feasibility.

## 2. Methods

### *2.1. Patient population and study design*

All patients undergoing combined RARC and RANU between October 2016 and May 2022 across three institutions were identified, and data were collected in a retrospective database. The three units included two in the United Kingdom and one in Hong Kong.

Patients undergoing open surgery and those having had a cystectomy and nephroureterectomy performed at different times for metachronous disease were excluded.

Preoperative staging included a CT scan of the chest, abdomen, and pelvis (CT CAP) and CT urogram (CTU), with one unit also performing bladder MRI. All patients had histological confirmation of bladder tumor. Histological confirmation of upper tract cancer was not required for inclusion. In the presence of concordant cross-sectional imaging and direct visualization strongly suggestive of upper tract malignancy, biopsy was omitted following multidisciplinary team discussion, given the potential risks of tumor seeding and bleeding with limited additional diagnostics. All patients included in the study had clinically node-negative (cN0) disease with no metastatic disease preoperatively, although only one patient had histological confirmation of upper tract disease prior to surgery. Cytology results were not routinely available at the time of writing.

Written consent was obtained from all patients. Ethics approval was not required due to the retrospective nature of the study.

### *2.2. Data collection and statistical analysis*

Data were collated and entered into a spreadsheet, with descriptive statistical analysis conducted using Microsoft Excel. Given the small sample size of eight, inferential analysis was not performed.

### *2.3. Surgical team and technique*

#### 2.3.1. Nephrectomy and cystectomy

All procedures were conducted using the da Vinci Xi four-arm surgical system and were carried out by experienced consultant robotic urological surgeons, with two consultants involved in each case.

Patients were initially placed in the lateral position, depending on the laterality of the upper tract resection. An open Hasson technique was used for the initial transperitoneal access, and three further 8 mm robotic ports were inserted (Figure 1). The AirSeal® insufflator system was used to maintain the pneumoperitoneum in all cases, and the robot docking process was completed. The stepwise approach entailed identification of the gonadal vein, with division if required, followed by identification of the ureter. The ureter was dissected down to the level of the common iliac bifurcation with early clipping where proximal upper tract disease (i.e., tumor in renal pelvis/calyceal or proximal ureter) was present. Following this, the renal hilum was visualized and vessels individually divided with Weck® Hem-o-lok® clips or a stapler device, depending on anatomy, allowing for subsequent mobilization of the kidney with the robotic Vessel Sealer device. The patients were then repositioned into a lithotomy head-down position, and additional ports were inserted for pelvic access. The superior and inferior vesical pedicles were divided bilaterally using the Vessel Sealer device, and the specimen was fully isolated by dividing the dorsal venous complex and urethra. In male patients, prostatectomy was also performed. In female patients, hysterectomy and bilateral salpingo-oophorectomy were performed. This technique allowed the bladder, kidney, and ureteral specimens to be removed en bloc with the associated pelvic organs, without breach of urothelial integrity, minimizing urinary leakage and potential tumor seeding.

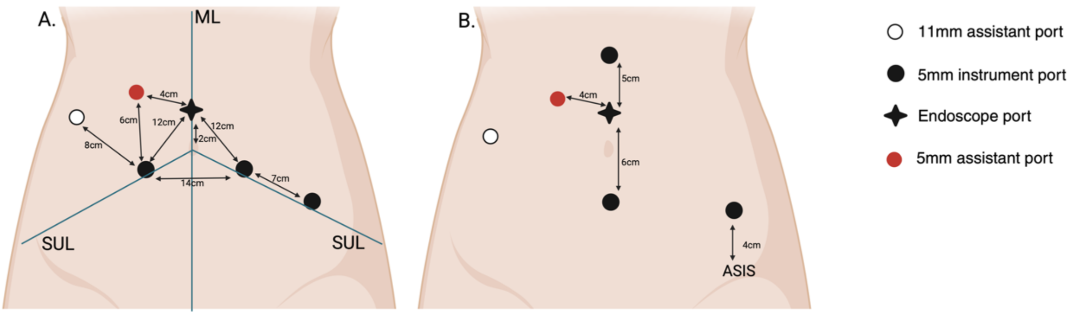


**Figure 1.** Port placement. A: Robot-assisted radical cystectomy; patient in head-down lithotomy position. Camera port 2 cm superior to the umbilicus, ports 2 and 4, placed 10 cm lateral to the left and right of the camera port, respectively. Assistant port is 4 cm inferior to the port line and 8 cm away from the port 4 on the right. Port 1 is placed 4 cm inferior to the port line, as far laterally on the left as possible. B: Robot-assisted nephroureterectomy; patient in left-lateral position. Port 2 is moved 4 cm superior to the anterior superior iliac spine (ASIS), port 1 is re-sited to 5 cm superior to the camera port, and port 4 is re-sited 6 cm inferior to the umbilicus.

2.3.2. Pelvic lymph node dissection

A bilateral pelvic lymph node dissection was performed robotically in all patients, including the obturator, internal, and external iliac lymph node packets up to the level of the common iliac bifurcation.

2.3.3. Urinary diversion

All patients underwent ileal conduit formation for urinary diversion. Decision on an intracorporeal or extracorporeal approach was left to the surgeon's discretion. Conduit isolation from the subterminal ileum and restoration of small bowel continuity were performed with a staple device in all cases. Due to the nature of this surgery, only a single ureter required anastomosis to the conduit. Where the left ureter was used, it was transposed across to the right side of the abdomen under the sigmoid mesocolon as standard for a right-sided stoma formation.

2.3.4. Systemic therapy

The use of neoadjuvant and adjuvant systemic therapy was determined by the treating multidisciplinary teams at each institution based on individual patient factors, including renal function, tumor characteristics, performance status, and anticipated risks. Detailed rationale for the inclusion or omission of systemic therapy was not consistently available due to the retrospective nature of the study.

## 3. Results

Across the three centers, eight cases were included in the study.

### *3.1. Patient demographics*

The mean and median age of the patients was 64 and 68 years, respectively (range 44–80 years), with a male-to-female ratio of 5:3. The American Society of Anesthesiologists (ASA) physical status classification was ASA 2 (mild systemic disease) in three patients and ASA 3 (severe systemic disease) in five patients, indicating a significant comorbidity burden for 62.5% of patients. The median Charlson Comorbidity Index score was 4.0, and none of the patients underwent prior cardiopulmonary exercise (CPET) testing due to resource constraints of participating centers.

The mean BMI (data available for seven of the eight cases) was 27.6 (range 22.3–38). One patient had previously undergone laparoscopic abdominal surgery.

All patients had pre-operative blood tests. Mean creatinine and eGFR were 97 µmol/L (range 68–161) and 68 mL/min (range 37–90; maximum eGFR measurement was capped at 90 using the MDRD calculation), respectively. The mean hemoglobin was 121 g/L (range 106–158).

### *3.2. Surgical indication*

The indications for cystectomy were muscle-invasive bladder cancer (four patients), BCG-refractory non-muscle-invasive bladder cancer (three patients), and multifocal disease (one case). Preoperative bladder tumor stage is shown in Table 1. The indication for nephroureterectomy was due to upper tract urothelial malignancy in seven out of eight cases (87.5%) and due to end-stage renal failure in the remaining case.

A single patient underwent neoadjuvant chemotherapy (methotrexate-vinblastine-doxorubicin-cisplatin regimen) preoperatively, with none of the patients receiving any form of radiation prior to surgery.

**Table 1.** Preoperative patient and tumor characteristics.

| Case | Sex | Age | BMI | ASA | Pathological stage of bladder cancer (preoperatively) | Upper tract biopsy | Preoperative upper tract imaging modality | Upper tract status (preoperatively) | Neoadjuvant chemotherapy |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 71 | 26.4 | 3 | G2pTa | Yes | CT CAP, MRI bladder | Left upper tract TCC | - |
| 2 | M | 69 | 38 | 3 | G3pT1 | No | CT urogram, CT chest, MRI prostate, bone scan | Left upper tract TCC | - |
| 3 | M | 80 | 27 | 3 | G2pTa | No | CT CAP | Left upper tract TCC | - |
| 4 | M | 54 | 23 | 2 | G2pTa + CIS | No | MRI bladder, CT CAP | Left renal pelvis TCC | - |
| 5 | F | 60 | 22.8 | 2 | G3pT2 | No | CT urogram | End-stage renal failure | - |
| 6 | M | 44 | 33.8 | 2 | G3pT1 | No | CT urogram | Left upper tract TCC | - |
| 7 | F | 67 | 22.3 | 3 | G3pT2 | No | CT urogram | Right upper tract TCC | Methotrexate, vinblastine, doxorubicin, and cisplatin |
| 8 | F | 72 | - | 3 | G3pT1 | No | CT urogram | Left upper tract TCC | - |

### *3.3. Intraoperative parameters*

Five surgeries were completed as fully robotic, and three were completed as robot-assisted radical cystectomy with laparoscopic nephrectomy. The median operative time was 420 minutes (range 360–543 minutes), with no total operative time recorded for one case. No cases were converted to open surgery.

Urinary diversion was conducted in the form of ileal conduit formation in all cases. Intracorporeal conduit formation was performed in three cases and extracorporeal in one. The technique was not specified in the remaining four cases.

A level II pelvic lymph node dissection was carried out in all four cases conducted at Lister Hospital. Level I dissection was undertaken for the cases conducted at Royal Berkshire Hospital and Prince of Wales Hospital.

None of the patients required intraoperative transfusion with a mean blood loss of 201 mL (range 40–600 mL), with data unavailable for one case. There were no intraoperative complications, and no rectal injuries were reported in any case.

### 3.4. Perioperative outcomes

All patients followed an enhanced recovery pathway in the immediate postoperative period. The 30-day and 90-day mortality rates were both zero. Surgical margin status was negative in all cases.

Three of the patients suffered postoperative complications (Table 2). One had a wound infection, one had a collection around the ileal conduit, and one had an acute coronary syndrome (ACS) event. The infection and collection were treated with antibiotics, and the ACS was managed with antiplatelet therapy. The complications were classified as Clavien-Dindo grade I (infection) and II (collection and ACS).

The mean duration of inpatient hospital stay was 9.9 days.

Preoperative mean creatinine level was 97 µmol/L (range 68–161), and postoperative mean creatinine was 136 µmol/L (range 87–251).

**Table 2.** Surgical and perioperative outcomes.

| Case | Cystectomy approach | Nephroureterectomy approach | Length of hospital stay (days) | Complication | Clavien-Dindo classification |
|---|---|---|---|---|---|
| 1 | Robotic | Robotic | 9 | Wound infection | I |
| 2 | Robotic | Robotic | 14 | - | - |
| 3 | Robotic | Robotic | 14 | Urosepsis, collection around the ileal conduit | II |
| 4 | Robotic | Robotic | Unknown | - | - |
| 5 | Robotic | Robotic | 7 | - | - |
| 6 | Robotic | Laparoscopic | 8 | - | - |
| 7 | Robotic | Laparoscopic | 7 | - | - |
| 8 | Robotic | Laparoscopic | 10 | Acute coronary syndrome | II |

### 3.5. Mid-term oncological outcomes

Operative histology for seven patients confirmed transitional cell carcinoma (TCC), with one squamous metaplasia, i.e., pT0 (Table 3). Exact postoperative histology was unavailable for three cases. Two patients had incidental prostate cancer, both with a Gleason score of 4 + 4 = 8. In terms of lymph node sampling, a mean of 13 lymph nodes was sampled (range 6–29). Two cases had positive nodes (two and one positive nodes, respectively).

At the time of writing, five out of eight patients are alive. Of the three patients who died, all three had Grade-3 disease confirmed histologically, with one having positive lymph nodes. All three deaths were due to cancer-related disease, i.e., disease progression and metastasis.

**Table 3.** Histopathological findings and oncological outcomes.

| Case | Bladder pathology | Upper tract pathology | Number of lymph nodes sampled | Number of positive lymph nodes | Metastatic disease at follow-up (July 2022) | Time to recurrence (months) | Survival status at follow-up (July 2022) |
|---|---|---|---|---|---|---|---|
| 1 | G2(HG)pTa TCC | G2(HG)pTa TCC | 9 | 0 | No | - | Alive |
| 2 | G3(HG)pT1 TCC | G3(HG)pT1 TCC | 9 | 0 | No | - | Alive |
| 3 | G2(LG)pTa TCC | G2(LG)pTa TCC | 17 | 0 | No | - | Alive |
| 4 | T0 | G3(HG)pTa TCC | 9 | 0 | No | - | Alive |
| 5 | HGpT1 | T0 | 6 | 0 | Yes | 8.7 | Deceased |
| 6 | Unknown | Unknown | 19 | 1 | No | - | Alive |
| 7 | Unknown | Unknown | 8 | 2 | Yes | 6.3 | Deceased |
| 8 | Unknown | Unknown | 29 | 0 | Yes | 15.8 | Deceased |

## 4. Discussion

Concomitant upper and lower tract urothelial carcinoma is uncommon [1]. Based on a review of the literature, Oldbring et al. reported a 1.7% incidence of patients with bladder cancer having subsequent ureteral or renal pelvis TCC in a study of 657 patients [11]. Similarly, Millán-Rodriguez et al. reported a 2.6% incidence of upper urinary tract malignancy in those with a primary bladder tumor in a study of 1529 patients [12].

The surgical oncological management of choice in patients with high-risk bladder cancer and synchronous upper urinary tract tumors who are deemed appropriate for resection is simultaneous cystectomy and nephroureterectomy, an approach that reduces the need for multiple major surgeries. Despite these advantages, concurrent RARC and RANU is recognized as a technically challenging surgery [9,10,13]. Additionally, these patients are often high-risk surgical candidates, as evidenced by the predominance of ASA 3 patients (62.5%) in this series.

Pisipati et al. conducted a case series of five patients who underwent simultaneous robotic RANU and RARC. Consistent with our cohort, no patients experienced any complications of Clavien-Dindo Grade III or above. In addition, overall hospital stays were also similar in length, with 9.9 days in our data and 10 days in their cohort [14].

Console and overall operative time were recorded, with a further breakdown of operative time in addition to this not specified. Future studies could examine this in further detail with regard to time for positioning, port insertion, establishing pneumoperitoneum, and docking/undocking, to establish steps during which efficiency could be improved. Combined RARC and RANU is a long procedure; however, the financial burden and duration of inpatient stay are likely to be lower when combined than with two separate operations. This is particularly important in low and middle-income countries.

In this cohort of patients, urinary diversion was performed in the form of ileal conduit formation, with three patients undergoing intracorporeal conduit formation. One patient underwent extracorporeal ileal conduit formation, and the remaining four were unspecified. There was no difference in console time or hospital stay between the two approaches.

Buse et al. examined mid-term oncological outcomes in 19 patients who underwent simultaneous en bloc RARC and RANU [1]. Similar to this previous study, oncological outcomes at a mid-term time frame were in keeping with survival rates for urothelial bladder cancer, indicating that the combined RANU and RARC approach can be conducted in a safe and effective way.

During follow-up, three patients died due to cancer-related disease progression. These findings are consistent with the aggressive nature of synchronous upper and lower tract urothelial carcinoma, which is an independent poor prognostic factor irrespective of management strategy [15,16]. Despite all patients being clinically staged N0M0 prior to surgery, pathological upstaging was observed in two cases, including one pN3 disease. These findings highlight the limitations of preoperative staging in this complex patient cohort. Reliance on cross-sectional imaging for nodal assessment may fail to detect occult nodal or systemic disease, while aggressive tumor biology may contribute to early metastatic progression.

At the time of analysis, only one patient received neoadjuvant chemotherapy. The rationale for omission of perioperative systemic therapy in the remaining patients was not consistently captured. Treatment decisions were likely influenced by a combination of patient factors, including comorbidities, renal function, multidisciplinary decision, and local treatment preferences. Given the observed rate of metastatic disease progression in this cohort, the role of systemic therapy in synchronous upper and lower tract urothelial carcinoma warrants further investigation; however, this remains beyond the scope of this study.

Evidence on staged management of synchronous malignancy is limited, and while our data suggest that combined surgery is feasible with acceptable perioperative outcomes, superiority over alternative management cannot be established in the absence of inferential analysis. Further comparative studies are required to assess the therapeutic efficacy of combined surgery over multimodal or sequential approaches.

The low incidence of synchronous upper and lower tract urothelial carcinoma and relatively modern robotic approaches to these surgeries mean that series describing this approach are small. While this limits statistical interpretation, we have been able to demonstrate that these complex multi-quadrant robotic operations can be undertaken in resource-limited settings. Although our data was obtained from high-income regions (Hong Kong and the United Kingdom), all participating centers were public hospitals with limited prior experience of combined robotic procedures and limited access to robotic platforms. A broader applicability of our findings will require validation across different health systems and lower-income settings. Given the burden that these patients are likely to have on the healthcare system and the aggressive nature of urothelial carcinoma, careful patient selection of those most likely to benefit from such radical surgery is crucial.

## 5. Limitations

This study has several limitations. The small sample size of eight restricts statistical analysis and the generalizability of our findings. The absence of a control cohort prevents direct comparison of perioperative outcomes between combined RARC and RANU and staged procedures. The small data set was insufficient for robust inferential statistical testing or correlation analysis, limiting interpretation to descriptive reports only. Long-term oncological outcomes were not analyzed due to the short mean follow-up period of 15.5 months. No standardized perioperative protocol was implemented across the three participating centers, which may have affected the postoperative course. Our study does not account for variation in surgeon experience and intraoperative technique.

Future studies should focus on large, prospective cohorts to validate the feasibility and efficacy of combined RARC and RANU across a variety of healthcare settings. Standardized perioperative procedures and benchmarks are required to improve reproducibility and enable robust inferential analyses. Extended surveillance is needed to analyze long-term oncological and functional outcomes, alongside the technical viability of synchronous RANU and RARC.

## 6. Conclusion

Although several thousand robotic procedures are carried out each year across the three centers, a very small proportion of patients require synchronous en bloc cystectomy and nephroureterectomy.

Our data from the eight patients undergoing synchronous RANU and RARC indicate that the combined approach for extirpative treatment can be safely undertaken by experienced robotic surgeons in a range of healthcare settings, with an acceptable operative time, limited blood loss, and a limited proportion of postoperative complications. However, the small cohort size and limited follow-up preclude definitive conclusions regarding oncological efficacy. Larger, prospective studies are required to validate our preliminary findings and assess long-term outcomes.

## Author contributions

Vishali Sharma, Elaina Gubbay and Kimberley Chan contributed to design and implementation of the research, analysis of the results and to the writing of the article. Ross Warner and Yogit Wagh contributed to implementation of the research and data collection. Prabhat Narayan contributed to data collection. Karel Decaestecker, Jeremy Teoh, Philip Charlesworth and Ben Pullar contributed to design, implementation of research and supervision of work and Nikhil Vasdev contributed to design, implementation of research and supervision of work.

## Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

## Ethics approval and consent to participate

This study was a retrospective, multicenter case series and used anonymized data collected during routine clinical care. In accordance with institutional and national regulations, ethics approval was not required. No identifiable patient information was used, and written consent was obtained from all patients.

## Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Conflict of interest

The author declares no conflict of interest.

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