Original Article

Robot-assisted radical nephroureterectomy with extended template lymphadenectomy for upper tract urothelial carcinoma: An outcome analysis

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ABSTRACT

Introduction: Robot-assisted radical nephroureterectomy (RANU) with extended template lymphadenectomy (E-LND) is the leading treatment option for nonmetastatic upper tract urothelial carcinoma. Due to the rarity of this disease, there is a lack of consensus regarding the best approach and the extent of lymphadenectomy. We report our technique and its initial outcomes from the retrospective evaluation of a prospectively maintained database of 11 consecutive cases of RANU + E-LND. To the best of our knowledge, our series represents the first published experience of this procedure from India.

Materials and Methods: RANU was performed in 11 patients (including two patients with simultaneous radical cystectomy) with the da Vinci Xi system. Pelvic and upper ureteric tumors were operated without re-docking or repositioning, using the port hopping feature. For the lower ureteric tumors, the patient was repositioned and the robot was re-docked to ensure completeness of pelvic lymphadenectomy. E-LND was performed in all the patients as per the templates described in previous studies.

Results: Median age was 67.5 years (range 52–71). Median console time and blood loss were 170 min (range 156–270) and 150 cc (range 25–500), respectively. Median hospital stay was 3 days (range 2–8). One patient developed paralytic ileus in the postoperative period (Clavien Dindo Grade 1). None had a positive surgical margin and the median lymph node yield was 22.5 (range 7–47). Median follow-up was 9 months during which one patient developed metastatic systemic recurrence. All other patients were disease free at the last follow-up.

Conclusions: A robotic approach to radical nephroureterectomy with E-LND is feasible and safe and does not appear to compromise the short-term oncological outcomes as defined by lymph node yields and margin positivity. At the same time, it offers the benefits of minimal invasion and results in swifter patient recovery from this extensive surgery.

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is a relatively uncommon malignancy and accounts for only 5%–10% of all the urothelial cancers.[1] Radical nephroureterectomy (RNU) with bladder cuff excision (BCE) with template-based lymphadenectomy is the current standard of care for UTUC. Due to the rarity of this disease, the overall available literature is limited to a few retrospective case series. The initial description of nephroureterectomy (NU) dates back to 1898 when Dentu and Albarran performed open NU for UTUC.[2] With the advent of minimally invasive surgery, the feasibility of a laparoscopic approach to NU was demonstrated by Clayman *et al*.[3] However, removing the bladder cuff laparoscopically was a challenge. The robot is potentially advantageous for RNU because of its three dimensional vision, improved dexterity, motion scaling, and intuitive movements. Robotic platform was used for NU in 2006 by Rose *et al*. by the retroperitoneoscopic

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approach.[4] Over the years, multiple variations in the patient positioning, port placement, robot positioning and surgical techniques have been described for robot-assisted radical nephroureterectomy (RANU) with an attempt to minimize operative duration without compromising the oncological principles. These vast majority of RANU series have focussed on the technique and the port position for NU with very limited description of extent of lymphadenectomy and its technique. In addition, to the best of our knowledge, there are no published series of RANU from the Indian subcontinent till date. Herein, we describe our step-by-step technique of RANU with extended template lymphadenectomy (E-LND) using the da Vinci Xi® (Intuitive Surgical, Sunnyvale, CaliforniaCA, USA) system. We have also evaluated the intraoperative and short-term postoperative outcomes to assess the safety and efficacy of this procedure.

MATERIALS AND METHODS

We conducted a retrospective analysis of our prospectively maintained database of 11 consecutive patients who underwent RANU for UTUC from July 2016 to November 2017, operated by single surgical team at a tertiary care oncology institute, with the da Vinci Xi system. Preoperative parameters such as age, gender, symptoms, biopsy report, cytology, imaging findings, status of disease in the bladder, and neoadjuvant chemotherapy (NACT) utilization were recorded. Intraoperative parameters such as port placement, side of surgery, console time, estimated blood loss (EBL), the requirement of repositioning and reinsertion of ports, and status of lymphadenectomy were also evaluated. Postoperatively, all details regarding the length of stay (LOS), complications by the Clavien Dindo grade, histopathology report, and need of adjuvant treatment were assessed.

Step-by-step procedure for RANU with the da Vinci Xi® system

Patient positioning

After induction of general anaesthesia, the patient is placed in a standard 75°–90° flank position with the operative side up and is catheterized while keeping the catheter in a sterile field for performing bladder leak test at a later juncture. All the pressure points are padded well. The ipsilateral arm is tucked by the side of torso to minimize obstruction to the robotic arms and/or the assistant.

Port placement

Pneumoperitoneum is created using the Veress needle and a standard working pressure of 15 mm Hg is maintained. All four robotic ports are placed in a straight line starting from the most cranial port which is placed around one finger-breadth below the costal margin in a para-rectal line, as per the patient habitus [Figure 1]. Rest of the ports are placed in a horizontal line maintaining a distance of 6–8 cm between the adjacent ports. Initial set of instruments passed through the ports from cranial to caudal are fenestrated bipolar, camera, monopolar scissors, and prograsp forceps. Two 12 mm assistant ports are placed, one in the midline just below the umbilicus and the other medial to and in between the upper two robotic ports in a triangulated manner. The upper 12 mm port is used for stapling the renal hilum and providing assistance during the renal part of the procedure, whereas the lower assistant port in the midline is a safety measure for vascular control in case of emergency during the paraaortic or the paracaval lymph node dissection and also provides assistance during the pelvic part of the surgery. Additional 5 mm port may be required for liver retraction for right-sided tumors. Initially, the robotic camera is targeted on the lower pole of the kidney whereas, for the lower ureteric and bladder dissection, the camera is moved one port caudad, and the visual target is shifted to the bladder approximating the site of the vesicoureteric junction (VUJ) [arrow-Figure 1]. Robotic instrument configuration during the pelvic steps is prograsp forceps, fenestrated bipolar, camera, and monopolar scissors, from cranial to caudal. This port hopping manoeuver enables a wider access in the pelvis to complete the BCE without the need of re-docking or repositioning.

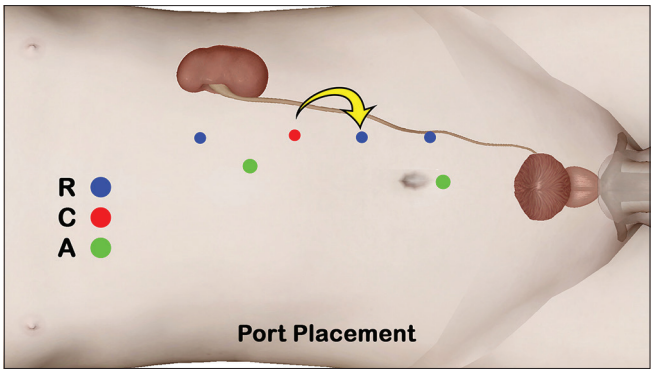

Figure 1: Port placement for da Vinci Xi system for left side Robot-assisted radical nephroureterectomy (R-Robotic working ports 8 mm, C-Camera port 8 mm, A-Assistant port 12 mm)

Nephrectomy and upper ureteric dissection

Nephrectomy starts in the standard manner with the initial incision along the line of Toldt, followed by mobilization of the colon medially. For right-sided tumors, the duodenum is kocherised to identify the vena cava. Lateral attachments of the kidney are left intact to avoid its medial displacement, which would make hilar dissection difficult. After this, the ureter and the gonadal vein are identified, and ureter is clipped below the level of the tumor to avoid tumor cell migration during renal mobilization [Figure 2a]. After creating a space anterior to the psoas, the ureter and the gonadal vein (on the left side) or the ureter alone (on the right side) along with its surrounding fatty tissue is lifted up by the fourth arm and the dissection proceeds cranially along the plane of the psoas muscle till the hilar structures are identified. Hilar dissection is carried out to bare the vessels. Superior pole mobilization is completed and adrenal is

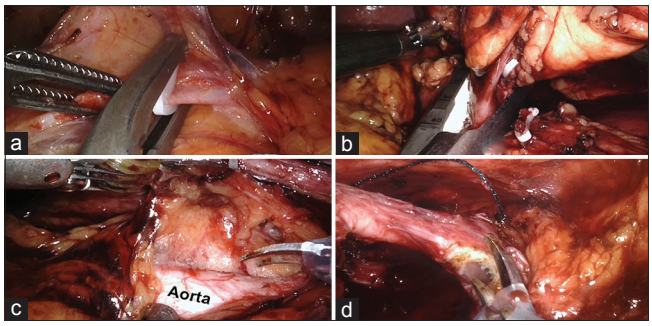

Figure 2: (a). Ureteric clipping before mobilization of kidney. (b) Stapling of renal hilum with endo GIA stapler. (c) Left paraaortic lymphadenectomy. (d) Bladder cuff excision

spared in all the cases unless indicated otherwise. Hilar control can then be obtained either with Hem-o-lok® clips or with Endo GIA® stapler [Figure 2b]. Appropriate use of the fourth arm helps in providing adequate exposure during the entire step, initially by retracting the colon medially to permit dissection of the ureter, and later on, allowing a safe hilar dissection by elevating the kidney laterally.

Retroperitoneal lymphadenectomy

Template-based lymphadenectomy is carried out at this stage along the great vessels [Figure 2c]. Care is taken to clip larger lymphatic channels to avoid lymph leak in the postoperative period. Lymph nodes are removed in different packets as per their location. It is a good practice to keep a rescue stitch (3-0 or 4-0 Prolene with a Hem-o-lok® clip at the end) available on the table at all times, as the dissection follows the major vessels.

Distal ureteric dissection and bladder cuff excision

As discussed previously, the distal ureteric dissection and BCE can be safely accomplished in most of the cases without the need for repositioning the patient or re-docking the robot. This is greatly facilitated by the newer da Vinci Xi® system which has the advantages of multi quadrant access due to its longer and thinner arms and a rotating boom configuration. After camera hopping and repeat targeting, the ureter is dissected down till the level of the bladder. The fourth arm can be used for giving traction on the ureter to complete the dissection extravesically. Once the dissection is completed till the VUJ, stay sutures (V loc 3-0) are taken on the bladder, proximal and distal to VUJ. Accurate placement of sutures is facilitated by clearing of the perivesical fat around the VUJ to identify the junction more clearly. These sutures help in providing traction during excision of the bladder cuff and prevent retraction of mucosa thereafter. An adequate bladder cuff is excised around the ureteric orifice to complete the NU [Figure 2d]. Watertight bladder closure is performed in two layers with mucosa to mucosa approximation with a V loc 2-0. The integrity of the closure can be checked at this time by instilling 200 ml of saline through the foley`s catheter. A pelvic drain is placed and the specimen is bagged.

The above technique is followed for patients with renal pelvic and upper ureteric tumors. However, for patients with lower ureteric tumors (below the crossing of the common iliac vessels), we prefer to change patient position from flank to supine, place new ports, and re-dock the robot. We believe that these steps provide better control and achieve appropriate oncological margins, decrease the need for traction on the lower ureter, and provide better access to perform a complete ipsilateral extended pelvic lymphadenectomy.

Specimen extraction

The specimen is extracted through a premarked Pfannenstiel incision, and wound is closed in layers.

Postoperative management

Patient is allowed a full liquid diet starting 4 h after reversal from anaesthesia. On postoperative day 1 (POD1), the pelvic drain is removed, the patient is ambulated and is advanced to a solid diet. Patient is usually discharged on POD 2 or 3 and the Foley catheter is removed after a week without a cystogram.

RESULTS

A total of eleven patients underwent RANU by a single surgical team from July 2016 to November 2017 at our institution [Table 1-demographic characteristics]. While nine patients underwent RANU alone, two patients underwent simultaneous RANU and robot-assisted radical cystectomy (RARC) for concurrent muscle-invasive bladder cancer and UTUC. The median age of the patients was 67.5 years (range 52–71) and 6 out of the 11 had a previous history of urothelial bladder cancer. Four of these had recurrent bladder cancer and were on maintenance intravesical BCG schedule and the other two had concurrent bladder and upper tract malignancies. Three patients had positive urine cytology and six underwent diagnostic ureteroscopic biopsy prior to extirpative surgery. Five patients had a right sided disease, the rest had left. Five patients had renal pelvic and upper ureteric mass, three had mid ureteric tumors, and the remaining three had lower ureteric masses. Seven patients underwent 18F fluorodeoxyglucose positron emission tomography-(FDG PET) computed tomography scan during work up, two of which showed avidity in the regional lymph nodes as well. One of these patients was subjected to FNAC of a 2.5 cm para-aortic lymph node mass, which was positive for malignancy. She received three cycles of Gemcitabine + Carboplatin NACT before the surgical procedure as she was ineligible for cisplatin chemotherapy. All the patients (except the two undergoing simultaneous RARC) underwent on table or pre-operative cystoscopy to rule out concurrent bladder malignancy. In five patients the procedure could be completed in flank position by utilising the camera hopping feature. Three patients were re-positioned from flank to supine for the pelvic part of the procedure and

Table 1: Demographic profile, intraoperative, and postoperative data

Variable	Result
Number of RANU cases, *n*	11
Side - right:left	5:6
Sex - male:female	9:2
Median age (range), years	67.5 (52-71)
Location	
Renal pelvic and upper ureteric	5
Mid ureteric	3
Lower ureteric	3
Median console time (range), min#	170 (156-270)
Median estimated blood loss (range), ml	150 (25-500)
Open conversion	1 (only for pelvic part of surgery)
Blood transfusion rate	0%
Median drain removal day (range), days	1 (1-2)
Median length of stay (range), days	3 (2-8)
Template-based lymphadenectomy	11 (100%)
Median lymph node yield (range)	22.5 (7-47)
Margin positivity	0%
Pathological grade*	
High grade	10
Low grade	0
Pathological T stage*	
pT1	5
pT2	1
pT3	4
Pathological Lymph node status	
N0	10
N1	1
30-day complications	1 (CD Grade 1- prolonged ileus)
30-day readmission rates	0%
Adjuvant chemotherapy	3
Median follow-up (range), months	9 (1-15)
Recurrence	1 (at 7 months of surgery- metastatic)

*One patient had papillary renal cell carcinoma in the final pathology report, #Excluding the two patients who underwent simultaneous radical cystectomy. CD=ClavienDindo grade, RANU=Robot-assisted radical nephroureterectomy

two underwent a concomitant cystectomy. After completing the nephrectomy and ipsilateral retroperitoneal lymph node dissection robotically, the patient with large positive paraaortic lymph node mass (post-NACT) was converted to open surgery through Gibson's incision for completing lower ureteric dissection, BCE, and E- pelvic lymph node dissection (PLND). This was required given gross adhesions between presacral lymph node mass and ureter and iliac vessels.

Median total console time (excluding the two patients who underwent simultaneous cystectomy) was 170 min (range 156–270). All patients underwent template-based lymphadenectomy. Median EBL was 150 cc (range 25–500). Pelvic drain was removed on day 1 after surgery in all the patients. Median LOS was 3 days (range 2–8). On histopathological evaluation, four had pT3 high-grade (HG) urothelial malignancy, five had pT1HG disease, and one had pT2HG disease. One patient was found to have papillary renal cell carcinoma in the final pathology report. Median lymph node yield was 22.5 (range 7–47). One patient had a single positive lymph node (1/27). Margins were free in all of them. None required readmission or blood transfusion. Except for one patient, none developed any postoperative complications in the first 30 days after surgery. This patient had a prolonged ileus which was managed conservatively (LOS-8 days) (CD Grade 1). A total of three patients were subjected to gemcitabine + carboplatin adjuvant chemotherapy in the follow-up (ineligible for cisplatin). Median follow-up was 9 months (range 1–15 months). One patient with node-positive disease developed systemic metastasis 7 months after surgery in spite of adjuvant chemotherapy and expired of metastatic disease after another 2 months. All other patients remained disease free at the last follow up.

DISCUSSION

In the current study, we have described our experience of 11 consecutive patients undergoing RANU and template-based extended lymph node dissection. On evaluation, we found this procedure to be a viable alternative to open surgery in terms of technical feasibility, safety, and short-term oncological outcomes while preserving the benefits of a minimally invasive approach leading to swifter patient recovery and early discharge. While this series may not represent a very high volume experience with this procedure, we do believe that it has several important points worthy of note.

First, to the best of our knowledge, it represents the first reported experience of RANU with E-LND from the Indian subcontinent. In the context of increasing availability and access to the robotic system in our country, this may serve to encourage surgeons to offer this procedure more often to our patients, thereby providing an opportunity to assess the pros and cons of this technique at a wider level.

Second, it adds to the recent (and as yet, sparse) literature on the use of the da Vinci Xi® platform for RANU.[5-7] While it is reasonable to assume that this platform would further facilitate RANU due to the improved reach of its arms (multiquadrant access) and the camera hopping feature, it has not yet been documented to a large extent. Lower ureteric dissection and BCE are often considered the Achilles heel of a minimally invasive RNU. It is not surprising, therefore, that in some initial series a robotic approach was utilized to perform this part of the procedure, while the renal dissection was still performed purely laparoscopically.[8,9] These initial attempts at utilizing the robot for the more complex pelvic component of the surgery has lead to consistent progress and technical modifications that have enabled the use of robotic system for the complete procedure.

Surgical teams globally have devised techniques to avoid repositioning and re-docking to minimize the operative time. Initial attempts date back to 2007 when Eun *et al*. published the concept of baseball diamond configuration of port placement and pivotal triangle for concurrent approach to both upper and lower tract with the da Vinci S® system in a porcine model.[10] They divided the baseball diamond into two triangles in which the camera could be switched as per requirement between the two 12 mm ports. For the pelvic part, they switched one robotic instrument arm to the lower 12 mm port through a dual port cannulation keeping robotic trocar attached to the arm. This increased the overall reach of the instruments. Park *et al*. reported their experience of 11 RANU procedures, five of which were operated using a hybrid port which enabled them to complete the pelvic part of the surgery without redocking and repositioning.[11] Hemal *et al*. described their technique of RANU in 15 consecutive patients using the da Vinci Si® system [Table 2].[12] Their port configuration utilized a 12 mm camera placed centrally and three robotic working ports placed in a triangulated manner. During the pelvic part of the dissection, robotic instruments were rotated in a circle around the camera port which avoided redocking or repositioning. Subsequently, the same group used barbed sutures for a watertight bladder cuff closure.[13] Lee *et al*. described placement of all four ports in line on a modified paramedian line which was drawn between the ipsilateral axilla and the insertion of rectus on the symphysis pubis.[14] Similarly, two other groups reported a larger experience (31 and 26 cases) of RANU with the da Vinci Si® system [Table 2].[15,16] After the launch of the Xi system in April 2014, Darwiche *et al*. described oblique in-line port placement to obviate redocking or repositioning in 10 patients undergoing RANU, utilizing the port hopping feature of the system, thereby reducing mean operative time to 184 min [Table 2].[5] Our current series represents another attempt in this continuum to translate the technological advancements in the robotic platform into standardized surgical steps for this complex procedure.

Third, in our series, all patients underwent a standardized template-based extended lymphadenectomy – a relative rarity in the context of the current RANU series reported in the literature. Multiple studies have emphasized the staging and therapeutic role of lymphadenectomy in cases of UTUC; however, there remain large gaps in our understanding of the indications, extent, and safety of this procedure as an adjunct to NU.[17-19] Recommendations from the National Comprehensive Cancer Network mentions that regional lymphadenectomy is indicated along with RNU in cases of HG, larger tumors of the renal pelvis with or without parenchymal invasion (Grade 2A).[20] Regional lymphadenectomy should also be performed in cases of ureteric tumors which are HG at the time of NU or distal ureterectomy.[20] Lymphatic metastases are seen in approximately 20%–40% of cases of UTUC depending on the stage of the primary tumor.[21] Multiple mapping studies have described templates of surgical lymphadenectomy in patients with UTUC and two groups in particular have pioneered in this filed.[22,23] They have reported that for right-sided pelvic and upper ureteric tumors, dissection of hilar, paracaval, retrocaval and interaortocaval lymph nodes covers all primary landing sites [Figure 3a]. For left-sided pelvic and upper ureteric tumors, the hilar and paraaortic regions constitute main areas of primary lymph node involvement [Figure 3a]. For mid and lower ureteric tumors, ipsilateral common iliac and PLND is recommended, respectively, along with the retroperitoneal template [Figure 3b and c]. We have utilized the template recommendations of these pioneer groups and have implemented them in our patient cohort. Rao *et al*. conducted a prospective clinical trial for feasibility and safety of retroperitoneal lymph node dissection during NU for UTUC which included 20 patients (6 RANU) and concluded that lymphadenectomy in cases of UTUC is a feasible procedure with acceptable morbidity.[24] Till date, the major series of RANU had a very limited focus on simultaneous lymphadenectomy. Lymphadenectomy was performed with a good safety profile in 16/20,[14] 14/31[15] and 22/40[25] cases in major series reported till date [Table 2]. Average lymph node yield was 14.1, 9.4, and 11 in these series, respectively. Our series compares favourably with the previously reported ones, both regarding lymph node yields (median 22.5), as well as the proportion of patients undergoing this procedure as an adjunct to RANU (100%).

In spite of the above highlights, there are significant limitations in our current report. Even though, to the best of our knowledge, our series is the first of its kind from India, it still represents a relatively small number of cases, performed at a tertiary care center, by a single surgical team. To some extent, this can be explained by the rarity of UTUC vis a vis other locations for urothelial malignancy. This emphasizes the need for multiinstitutional databases and collaborative efforts to provide a greater insight into the management of this disease. A lack of control arm in our study limits its comparison with an open or a laparoscopic approach for NU. Although this was not the primary aim of this study, such a comparison would have, without doubt, added value to our findings. In addition, due to the limited follow-up duration in our series, it is not possible to comment on the intermediate and long-term oncological parameters and survival outcomes of this procedure. However, the surrogate markers of lymph node yield and margin status do provide a certain level of confidence in the oncological efficacy of RANU + E-LND performed on our patients.

CONCLUSIONS

RANU with extended template-based lymphadenectomy provides a technically feasible and safe alternative to the other approaches for UTUC. The da Vinci Xi® system may provide greater technical ease in the conduct of

Table 2: Summary of different series of robot-assisted radical nephroureterectomy

Series	*n*	Robotic	OR time/ console time (range) min	EBL (range) ml	LND (selective or template)	LOS mean/median (range) days	Complications ClavienDindo (grade 1-2- minor) (grade 3-4-5- major)	LN yield mean/median (range)	Positive LN cases	Follow-up (mean/median) (range) months	PSM	Recurrence
Hemal *et al.*, 2011[12]	15	15	184 (147-250)	103 (10-300)	3/15 (selective)	2.73 (2-5)	Nil	4-9	Nil	NR	Nil	Nil - till short term follow up
Lee *et al.*, 2013[13]	20	20	161.3 (91-330)	98.9 (50-200)	16/20 (selective)	3 (1-16)	2/20 (minor)	14.1 (2-35)	3/16	13.5 (1-36)	1	1 - loco regional lymph node
Darwiche *et al.*, 2015[5]	10	10	184 (140-300)	121 (60-300)	5/10	2.4	2/10	NR	0/5	130 (15-210)	Nil	NR
Zargar *et al.*, 2014[14]	31	31	300	200 (100-375)	14/31	5 (3-6)	7/31 (1 major) (6 minor)	9.4 (3-21)	2/14	8 (0-32)	1	7 - bladder 4 - systemic
Badani *et al.*, 2014[15]	26	26	230 (128-310)	66 (25-100)	10/26	2 (1-15)	Nil reported (3 patients - medical problems e.g., GI bleed)*	NR	2/10	7.8 (2-17)	Nil	4 - bladder
Park *et al.*, 2009[11]	6 Standard port	6	247.3	106.7	NR	7	Nil	NR	NR	NR	Nil	NR
Park *et al.*, 2009[11]	5 hybrid port	5	193	270	NR	8.4	Nil	NR	NR	NR	Nil	NR
Rao *et al.*, 2011[16]	19	6	279 (146-500)	396 (100-1100)	19 (template-based dissection)	7.1 (4-18)	9/19 (1 major) (8 minor)	7 (2-17)	1/19	12 (2-24)	NR	8 - bladder 2 - contralateral upper tract urothelial tumors 2 - systemic
Pugh *et al.*, 2013[17]	43	43	247 (128-390)	131 (10-500)	22/43	3 (2-87)	6/43 (2 major) (4 minor)	11 (4-23)	4/22	9	1	6 -bladder 1 - contralateral upper tract urothelial tumors 2 - locoregional retroperitoneum
Our Series	11	11	170 (156-270)	150 (25-500)	11 (template-based dissection)	3 (2-8)	1/11 (minor)	22.5 (7-47)	1/11	9 (1-15)	Nil	1 - systemic

*Grade of complication not mentioned. NR=Not reported EBL=Estimated blood loss, LOS=Length of stay, LN=Lymph node, PSM=Positive surgical margin

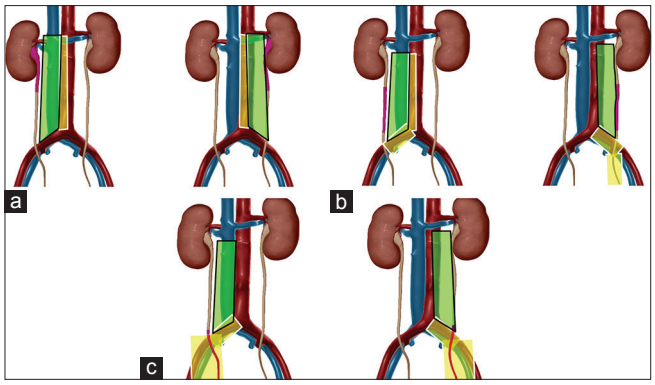

Figure 3: Schematic representation of template-based lymphadenectomy in cases of (a) renal pelvic and upper ureteric tumors,right side-hilar, paracaval, retrocaval and interaortocaval group, left side-hilar, paraaortic group. (b) Mid ureteric tumors, right side-paracaval, retrocaval, interaortocaval, right common iliac group, left side-paraaortic, left common iliac, left internal iliac group. (c) Lower ureteric tumors, right side-paracaval, right pelvic group, left side-paraaortic, and left pelvic group

this surgical procedure due to its inherent technological advantages. Multiinstitutional databases, collaborative efforts, long-term follow-up, and comparative analysis vis a vis other approaches for this procedure are the need of the hour for ensuring wider acceptability and applicability of our preliminary findings.

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