MINIMALLY INVASIVE AND ROBOTIC SURGERY

Status of robot-assisted radical cystectomy

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Purpose: Robot-assisted radical cystectomy (RARC) is an alternative approach for treatment of bladder cancer. We provide a critical review of the current status of RARC and pelvic lymph node dissection with a focus on feasibility, safety and oncological efficacy of the procedure.

Materials and methods: The PubMed literature database was reviewed for RARC series that have been reported in the English language until the present time. Surgical technique, operative parameters, pathologic outcome, complications and quality of life were examined. *Results:* RARC is progressing steadily. With nearly 500 published cases worldwide, RARC proves to be technically feasible and oncologically effective. It is associated with less blood loss, shorter hospital stay, and improved postoperative quality of life. Intracorporeal urinary diversion is still in the experimental phase, and effort is needed to make it technically easier and widely accepted.

Conclusions: With the worldwide rapid spread of robot-assisted surgeries, RARC is evolving as a reliable minimally invasive alternative to standard open surgery. Awaiting long term oncological results, adequately powered prospective randomized trials comparing open, laparoscopic and robotic approaches are urgently needed.

Key Words: bladder cancer, robot-assisted, radical cystectomy, urinary diversion

Introduction

Radical cystectomy and pelvic lymph node dissection is considered the standard treatment for muscle invasive bladder cancer. Robot-assisted radical cystectomy (RARC) has evolved in the past few years as an alternative to open radical cystectomy with the advantages of decreased postoperative pain and earlier return of bowel function. A critical review of the relevant literature is imperative to identify what has been achieved, and to identify the areas that need further improvement in the realm of RARC for invasive bladder cancer. Table 1 highlights RARC series reported in the English literature.¹⁻¹⁵

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Address correspondence to Dr. Khurshid A. Guru, Department of Urologic Oncology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, New York 14263 USA Open radical cystectomy and lymph node dissection. What are the standards?

One of the first detailed operative descriptions of radical cystoprostatectomy with pelvic lymphadenectomy was by Marshall and Whitmore in 1949.¹⁶ In the 1950s and early 1960s, the operation was associated with significant mortality and morbidity. With time, acquisition of surgical experience, improvement in medical technology and pharmacology, as well as the evolution of diversion techniques, radical cystectomy has evolved as the standard therapeutic modality for muscle invasive bladder cancer.¹⁷⁻²⁰

The 5 year disease free survival following radical cystectomy ranges from 50%-60%.¹⁷⁻²⁰ Evidence indicates that node positivity is a significant and independent prognostic factor and that adequate lymph node dissection has a direct impact on the survival.^{21,22} With radical cystectomy, the incidence of nodal disease is in the order of 25%. The pN stage among node

Author/ref	Ν	Urinary Diversion	Age	Mean OR Time	EBL	Hosp LOS	Complications
Menon et al ¹	17	Ileal conduit (3) Neobladder (14)	-	260 308	150	-	Re-exploration for postop bleed (1) Bilharziasis (13)
Beecken et al ²	1	Intracorporeal W neobladder	-	510	200	5	Nil
Yohannes et al ³	2	Ileal conduit	60	690	1118	6	Nil
Hemal et al ⁴	24	lleal conduit (4) W pouch (16) T pouch (2) Double chimney (2)	-	290	200	-	Minimal blood loss and morbidity
Sala et al ⁵	1	Intracorporeal W neobladder	65	720	100	5	Nil
Rhee et al ⁶	7	Ileal conduit	60	638	479	11	57% transfusion rate (4) Port site hematoma (1) Ileus (1)
Galich et al ⁷	13	Ileal conduit (6) Neobladder (5) Indiana pouch (2)	70	697	500	8	Enterovesical fistula + SBO (1) Abscess (1)
Abraham et al ⁸	14	Ileal conduit (14)	76.5	419	212	5.8	42.8% transfusion rate 28% complication rate: Ileus (2) Urine leak (1) MI (1) Incomplete transection of L obturator nerve
Lowentritt et al ⁹	5	Ileal conduit (4)	69.5	350	300	5	Initial open conversion for hypercapnea (1) not reported
Hemal et al ¹⁰	6	lleal conduit (5) Neobladder (1)	56	330	200	9.2	Partial wound dehiscence secondary to infection (1), Blood loss of 1L requiring 2 units of blood transfusion (1)
Murphy et al ¹¹	23	lleal conduit (19) Studer pouch (4)	64.8	368	278	11.6	23% complication rate. Transfusion (1), rectal injury/colostomy (1), anastomotic stricture, ureter leak (1), b/l femoral neuropathy, postop bleed
Park et al ¹²	1	Ileal conduit	59	340	600	-	-
Guru et al ¹³	67	Ileal conduit	67	436*	520	9*	Postop bleed / transfusion / return to OR (1)
Ng et al ¹⁴	83	Ileal conduit (47) Indiana pouch (10) Neobladder (26)	70.9	375	460	5.5	Cellulitis, dehiscence, renal failure, leak, FUO, PNA, UTI, abscess, pyelonephritis, ureteral obstruction, urinary fistula/ ileus, fungal infn, SBO, C.diff colitis, GI bleed, hematemesis, EC fistula, arrhythmia, MI, transfusion (1), rash, dehydration, DVT, PE
Pruthi et al ¹⁵	50	Ileal conduit (30) Neobladder (20)	63.9	302.4	268.2	4.5	FUO, anastomotic leak, others previously reported in Pruthi et al ¹²
EBL = estimated	blood	d loss; Hosp LOS = ler	ngth of	hospita	l stay;	FUO = d	fever of unknown origin; PNA = pneumonia;

TADLE 1. RAKC series reported in English interature	TABLE 1.	RARC series	reported in	English	literature
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EBL = estimated blood loss; Hosp LOS = length of hospital stay; FUO = fever of unknown origin; PNA = pneumonia; UTI = urinary tract infection; infn = infection; SBO = small bowel obstruction; EC fistula = enterocutaneous fistula; MI = myocardial infarction; DVT = deep vein thrombosis; PE = pulmonary embolism *unpublished data

positive cases indicates that 30%-40% are of the pN1 category. Therefore meticulous pelvic node dissection is mandatory to remove all involved nodes of pN1 and most of pN2 categories, thus improving the prognosis of pN1 cases treated by radical cystectomy to approximate that of organ confined disease.²¹ In 2004 Herr et al presented recommendations for standardization of open radical cystectomy (ORC) based on a collaborative group study across four institutions.²³ The authors recommended removal of at least 10-14 LNs and an acceptable positive margin rate was determined as < 10% overall and < 15% for pT3-4 tumors. Recently, Ghoneim and colleagues presented the Mansoura experience with 2720 consecutive cases with at least 5 years of follow up.¹⁸ They recommended a "standard" lymphadenectomy that include all the lymph nodes within the following boundaries: the mid common iliac vessels - proximally; the genitofemoral nerve - laterally; the circumflex iliac vein and lymph node of Cloquet distally; and the hypogastric vessels - posteriorly. Such a dissection would provide a yield of approximately 20 lymph nodes. These findings are in agreement with a retrospective clinical study by Mills et al and the autopsy data from Weingartner and associates that suggest 20 nodes determines the quality of a cystectomy.^{18,24,25}

Technique of robot-assisted radical cystectomy

Laparoscopic surgeons were the first to demonstrate the feasibility of radical cystectomy.³⁸ While the laparoscopic cystectomy was still in its infancy, robotic technology attracted the attention of urologists because of its superior three dimensional vision, seven degrees of freedom of movement, lack of tremor, intuitiveness of motion and superior ergonomics. The technique for RARC was developed based on the principles of open surgery with modification using the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). Since initial reports of RARC by Menon and colleagues, the technique has evolved and has been reproduced in many centers. Herein the technique adopted in Roswell Park Cancer institute, is described.

Preparation and port placement

Each patient is prepared as for open radical cystectomy. General anesthesia is achieved and both a nasogastric tube and Foley catheter are inserted. The patient's arms are adducted and padded, and the table is placed in the steep Trendelenburg position. Pneumoperitoneum is created using a Veress needle. A transperitoneal six port approach is used and the robot is docked between the patient's legs.

Operative steps for male cystoprostatectomy

Development of avascular spaces

Once the ports are placed the key landmarks in the pelvis are examined. The lateral paracolic spaces and any sigmoid attachments should be freed. The goal is to define three avascular spaces (periureteral, lateral pelvic space and anterior rectal spaces) to set up further dissection of the bladder.

Development of periureteral space

Peristalsis of the ureter with aid of magnification and three dimensional vision helps in defining the landmarks for separating out this space. The incision of the posterior peritoneum is carried out with separation of the visceral fascia and identification of the ureter in the loose areolar tissue. The periureteral space is opened with mobilization and dissection of the ureter distally up to the ureterovesical junction. Preservation of the periureteral adventitial tissue is critical to ensure ureteral viability. One of the caveats in this technique is to avoid early clipping and transaction of the ureter during initial dissection. The intact distal ureters act as a landmark in identifying the lateral pedicles and help the surgeon find the correct plane around the bladder to decrease the likelihood of a positive surgical margin in this location, Figure 1.

Development of lateral pelvic space

After development of the periureteral space, incision of the posterior peritoneum is carried parallel and lateral to the umblical ligaments onto the anterior abdominal wall above the superior pubis ramus, which helps



Figure 1. Anatomical landmarks for the technique of spaces (periureteral space).



Figure 2. Lateral pelvic space.

develop the lateral pelvic space. This avascular areolar space is opened following the medial curve of the rami of the pubic bone. The vas deferens is seen traversing across underneath the posterior peritoneum and is divided lateral to the obliterated umbilical ligament to access the lateral pelvic space. The bladder is still left attached to the anterior abdominal wall and provides natural anterior retraction. Both the periureteral and lateral pelvic spaces are separated by the ureter and the postero-lateral pedicle arising from the internal iliac vessels. The external iliac vessels, obturator nerve and vessels constitute the lateral boundary of both the spaces , Figure 2.



Figure 3. Anterior rectal space.

Development of anterior rectal space

Once the periureteric and lateral avascular spaces are defined bilaterally the anterior rectal space is developed. The two lateral incision of the posterior peritoneum are joined together at the peritoneal reflection of the pouch of Douglas. The dissection of this space is carried distally as far as the apex of the prostate. The plane between the anterior sheath of Denonvilliers fascia and the rectum is usually easily accessible. Blunt dissection following the anterior rectal wall is continued caudally. Careful blunt and sharp dissection using a cold round tip scissors is preferred to separate the rectum from the prostatic apex , Figure 3.

Control of vascular pedicles and mobilization of neurovascular bundles

The bladder is left suspended from the anterior abdominal wall while posterior dissection is completed. Anterior and lateral traction on the bladder using the fourth arm with a Cobra grasper will help expose the lateral vascular pedicles of the bladder. The distal UV junction is identified and the ureters are ligated with two Weck hemo-lok clips. The distal ureteral margins are sent for frozen section. An endovascular stapling device or hemo-lock clips and scissors can be used to secure the lateral pedicles in an expeditious fashion. In patients with locally advanced disease and need for non nerve sparing radical excision we advocate wider excision of pedicle and use the endovascular stapler. After controlling the inferior vesical vessels, the endopelvic fascia is opened bilaterally. The prostate is dissected off the rectum distally to the apex if possible.

Anterior exposure and apical dissection

Incision of the median and medial umbilical ligaments to release the bladder from the anterior abdominal wall is carried out once the posterior dissection is complete. The bladder will drop posteriorly. Dissection of the retropubic fat is performed and the superficial dorsal vein is cauterized. Suture ligation of the deep venous complex is performed; further release of the prostate is accomplished once the deep dorsal vein complex is incised. The urethra is incised and the specimen is placed in a retrieval bag and removed from the pelvic cavity. We use a large specimen bag (similar to one used for kidney specimen) that is placed through the 15 mm port. The pelvic cavity is irrigated and the area is examined for any bleeding. Control of any bleeding and irrigation of the pelvis with sterile water is thoroughly performed with approximately 1 liter of irrigation. A frozen section of the urethra can be done.

Lymph node dissection (LND) and lymph node yield in RARC

Surgical technique: (release and roll technique)

A 0° lens is used for LND although a 30°-down lens is helpful in the deep, narrow pelvis. Lymphadenectomy is performed with the following anatomical boundaries: common iliac up to the aortic bifurcation proximally, genitofemoral nerve laterally, circumflex iliac vein and node of Cloquet distally/caudally, and hypogastric vessels posteriorly. All nodal tissue is removed by skeletonizing the vessels. Dissection begins caudally and proceeds to the level of the aortic bifurcation with exposure of the triangle of Marcille. Nodal tissue is submitted in separate nodal packets from both sides as follows: (i) aortic bifurcation to common iliac package; (ii) genitofemoral nerve to external iliac artery package; (iii) node of Cloquet and external iliac vein package; (iv) obturator package proximally to the hypogastric artery.

The nodal packages are placed in EndoCatch bags, labeled right and left (United States Surgical Corps., Norwalk, CT, USA) for LN retrieval and prevention of port-site recurrence. After completion of the node dissection aggressive sterile water irrigation is carried out again and thorough hemostasis is achieved.

Practical tips during LND

We prefer performing LND after cystectomy for several reasons. Cystectomy provides adequate space to

perform LND and preserves the tissue planes of the bladder to prevent oncological compromise.

Exposure and development of the triangle of Marcille separate the major vessels from the pelvic wall and facilitate appropriate application of three dimensional vision, magnification, and maneuverability of the Endowrist (Intuitive Surgical, Sunnyvale, CA, USA), to perform LND and complete clearance of the obturator fossa.

Cold scissor dissection and bipolar point cauterization are used for small blood vessels and lymphatic channels to prevent bleeding and lymphocele formation. Avoiding the monopolar hook prevents thermal vascular injury.

Pneumoperitoneum pressure is decreased frequently to < 12 mmHg, as this enables distension of the external iliac vein.

Lymph node yield in RARC

As previously highlighted bilateral pelvic lymphadenectomy is considered to be an integral part of radical cystectomy. Both the adequacy of lymphadenectomy and the number of nodes retrieved have been the subject of criticism of minimally invasive cystectomy. The surgical extent of the dissection reported in RARC series was either to the common iliac bifurcation (termed standard) or to aortic bifurcation (extended). Most of the RARC series, have reported adequate lymph node procurement, the average number varying from 12 to 23 lymph nodes, a figure comparable to the open series, Table 2. Wang et al found

CABLE 2. Lymph node yield in robotic cystectomy series								
Author	No. of cases	Type of L.N. dissection*	Mean L.N. yield (range)	Patients with N+ disease (%)	_			
Menon et al ¹	17	S	12 (4-27)	1 (5.8)				
Hemal et al ⁴	24	Е	3-27	1 (4.2)				
Rhee et al ⁶	7	S	-	-				
Galich et al ⁷	13	S	-	2 (15.4)				
Abraham et al ⁸	14	Е	23.3 (15-31)	3 (21)				
Lowentritt et al ⁹	5	Е	12 (9-16)	1 (25)				
Hemal et al ¹⁰	6	S	12 (4-19)	1 (17)				
Murphy et al ¹¹	23	S	16 (8-24)	2 (8.7)				
Guru et al ¹³	67	Е	18 (6-43)	17 (25)				
Ng et al ¹⁴	83	S	17.9 (7.5-28)	13 (15.7)				
Pruthi et al ¹⁵	50	Е	19 (8-37)	8 (16)				

S = standard lymphadenectomy up to the bifurcation of the common iliac artery proximally; E = extended lymphadenectomy up to the aortic bifurcation

no differences in the number of lymph nodes retrieved between RARC and ORC group (20 versus 17).²⁶ Guru et al reported the feasibility and safety of performing adequate robotic extended lymph node dissection.13 They noted that the lymph node yield increased with progression of the learning curve. The number of lymph nodes retrieved during lymphadenectomy may be influenced by the way the nodes were retrieved (en bloc or separately), the way they are interpreted and processed by the pathology team, and by the number of nodes in a given patient, which can vary. Therefore, we advocate thorough anatomical dissection around the pelvic vessels and complete clearance of all the nodal tissue within the anatomical boundaries previously discussed, focusing about such extent of dissection is more important than worrying about the number of lymph nodes retrieved.

Complications of robot-assisted radical cystectomy

Since the first report of RARC by Menon et al in 2003, more than 500 cases have been published worldwide.1 Estimated blood loss (EBL) reported in robotic series is in the range 100 mL-1100 mL, Table 1, with most reporting an average of < 500 mL and transfusion rates below 2%. Complication rates following RARC ranges from 6% to 27%.^{1,2,4-6,8,11-13,26-29} Most complications are comparable the open approach, and management would likewise be identical. Wang and colleagues compared outcomes in 21 ORC cases versus 33 RARC cases, and complication rates were similar in both groups.²⁶ In a prospective study, Ng et al compared complication rates in 187 consecutive patients who underwent robotic versus open radical cystectomy. In this study, the robotic cystectomy cohort experienced fewer postoperative complications than those undergoing open cystectomy. Robotic cystectomy was an independent predictor of fewer overall and major complications.¹⁴ Similarly in a prospective randomized study Nix et al found no significant difference in overall complication rates between both groups.⁴⁰

Abraham et al compared their experience with laparoscopic assisted radical cystectomy (LARC) and RARC in 34 patients (20 LARC versus 14 RARC).⁸ Robot-assisted approach was associated with less blood loss, fewer postoperative complications, and earlier return of bowel function. Still, published series are limited with respect to patient number and long term follow up. Therefore, complication rates have not been well established for comparison. Table 3 lists the postoperative complications within 6 weeks following RARC according to Dindo- Clavien classification.

Surgical margins in RARC

Three dimensional vision allows for better surgical precision in excising local disease and sparing nerves in suitable cases with robot-assistance. However, due to lack of tactile feedback, concerns regarding the adequacy of local excision and soft tissue surgical margin (STSM) status arose.

Surgical margin status following radical cystectomy has not been has not been diligently studied. Herr et al analyzed a data set from the SWOG (Southwest Oncology Group) 8710 study of 268 patients treated with radical cystectomy, 25 (9.3%) of whom had positive STSM.³⁰ Positive STSM was associated with shorter overall survival in multivariate analysis. In addition, the probability of local recurrence was significantly higher in patients with positive STSM. In a study of 1589 patients treated with radical cystectomy for bladder cancer by Dotan et al, the incidence of positive soft tissue surgical margin STSM was 4.2%.³¹ Risk factors for positive STSM were female gender, locally advanced cancer, presence of vascular invasion and mixed histology. While none of the patients with organ confined disease had evidence of positive STSM, 9% of the patients with extravesical disease had positive STSM.³¹

Similarly, in RARC series positive STSM were reported only in cases with non-organ confined tumors and only in continuous series in which no case selection was performed, Table 4. These findings suggest that presence of tumor at the surgical margin is usually not a surgical error (cutting through the bladder), but rather is associated with infiltration of the soft tissue boundaries of the bladder. Wang et al in a prospective study of 54 patients (33 robotic, 21 open) reported 3 patients with positive STSM in the ORC group and 2 patients in the RARC group.²⁶ Guru et al studied the impact of tumor volume on surgical and pathological outcomes following RARC.³² Bulky tumors were associated with higher stage disease, and higher rate of margin positivity. Therefore, in patients with large volume tumors, wider dissection of perivesical tissue is recommended to decrease the margin positive rates.³²

Urinary diversion following RARC

There are several approaches adopted for urinary diversion following RARC including: a) extracorporeal through a 5 cm-7 cm midline infraumblical incision which is also utilized to retrieve the specimen, b) combined intracorporeal and extracorporeal technique: in which the orthotopic neobladder is fashioned extracorporeally, then it is internalized, the abdominal wound is closed and completion of the urethra vesical

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Grades	Organ	Description	Net	pon phe	ž Gali	Sú Por	mant ow	entrit Her	ale Au	Qua Cur	j ² 200	Profili
Grade I	system Other	Wound infection (opened at bedside) FUO						1		• • • • • • • • • • • • • • • • • • •	4	?
Grade II	Cardiac	Afib Arrhythmia MI				1				• • • • • • • • • • • • • • • • • • •	4 1 1	
	Pulmonary	PE Pneumonia								• · · · · · · · · · · · · · · · · · · ·	2 1	
	Gastro- intestinal	C.diff colitis Ileus SBO		1	1	2				• • • • • • • • • • • • • • • • • • •	3 13	
	Renal	UTI									14	
	Other	Sepsis DVT Depression Transfusion Postop bleed Abscess Fungal infection Pyelonephritis Bilharziasis Port site metastasis	1 13	4	1	6			1 1	1 1	2 5 0 1 2 5 1 1	
Grade IIIa	Renal	Ureteral obstruction Urinary leak Renal failure Anastomotic stricture				1			1 1		3 2 4 0	1 ?
	Other									•	0	
Grade IIIb	Gastro- intestinal	Rectal injury EC fistula			1				1	•	0 1	
	Renal	Urinary fistula									1	
	Other	Dehiscence Open conversion Return to OR Nerve injury	1			1	1		1	1	1 0 ?	2
Grade	ICU mgmt	nemia								•	1	2
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	Deatti		. :	. :						•		

TABLE 3. Modified Dindo-Clavien classification system of complications

*Note: Series without complications mentioned were not included in table.

argin positivity		Selection	No. of cases	Author
> T2 (%)	<			
-	-	С	17	Menon et al ¹
0	0	С	24	Hemal et al ⁴
0/1	0	S	7	Rhee et al ⁶
0/6	0	С	13	Galich et al ¹³
1 (7.1)	-	С	14	Abraham et al ¹⁴
0/3	0	С	5	Lowentritt et al ⁹
5/6	0	С	6	Hemal et al ¹⁰
0	0	S	23	Murphy et al ¹¹
-	-	С	67	Guru et al ¹³
6/32 (19)	0	С	83	Ng et al ¹⁴
0/17	0	S	50	Pruthi et al ¹⁵
			314	Total
	0	S	50 314 S = selected series	Pruthi et al ¹⁵ Total *C = continuous series

TABLE 4. Margin status in robotic cystectomy series

anastomosis is carried out with robotic assistance,¹ and c) total intracorporeal diversion. The first case reported of RARC with intracorporeal ileal orthotopic neobladder was by Beecken et al in 2003.² Operating time was 8.5 hours and blood loss was 200 mL. Balaji et al demonstrated the feasibility of RARC with intracorporeal ileal conduit in three cases with mean operative time of 11.5 hours.²⁶ Sala et al described a case of RARC with intracorporeal fashioning of an ileal neobladder with total operative time of 12 hours.⁵

Intracorporeal orthotopic urinary diversion is still time consuming and a technically challenging procedure. Evolution of new techniques and advances in development of absorbable stapling devices might help in future widespread usage of this approach.

Quality of life following RARC

Health related quality of life (HRQOL) outcomes in bladder cancer patients undergoing cystectomy are an important component of assessment of bladder cancer treatment modalities. Radical cystectomy with urinary diversion is a major debilitating operation that can affect the satisfaction with life in the aftermath. Treatment related morbidity, including urinary dysfunction, regardless of type of diversion, can be significant. Also, the vast majority of patients will have sexual difficulty after surgery.^{33,34}

Gilbert et al used a specific quality of life questionnaire, the bladder cancer instrument (BCI) to measure urinary, sexual, and bowel function as well as bother domains in patients with bladder cancer in 315 patients.³⁵ Scores were significantly lower among the cystectomy group compared to the native bladder group with intravesical treatment. Matsuda et al used the Functional Assessment of Cancer Therapy-Bladder (FACT-BL) questionnaire in patients 5 years after ORC, and found a long term negative effect on survivors.³⁶ This stemmed from concerns about cancer recurrence, follow up visits, complications, and restriction in social activities due to urine leakage, and changes in body image and sexual interest.

RARC has shown the potential to reduce hospital stay, pain and convalescence^{14,26,37} Yuh et al prospectively studied the effect of RARC on quality of life after surgery.³⁹ FACT-BL questionnaires were administered to 34 patients before and after 1, 3 and 6 months period following RARC. Scores decreased significantly in the initial period after RARC and then progressively improved. Quality of life returned promptly to, or even exceeded baseline levels by 6 months after RARC.

Conclusion

RARC has evolved to provide a minimally invasive alternative to the standard open approach. It proves to be feasible and effective, provides adequate lymph node yield, and can be accomplished with complication rates comparable to open surgery. Although we await long term oncologic outcomes, short follow up data are similar to open surgery. Well designed prospective randomized trials comparing RARC, LRC and ORC are urgently needed to define their role in management of bladder cancer.

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