

# Robot-assisted radical cystectomy with intracorporeal neobladder diversion: The Karolinska experience

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## ABSTRACT

**Introduction:** The aim of this report is to describe our surgical technique of totally intracorporeal robotic assisted radical cystectomy (RARC) with neobladder formation.

**Materials and Methods:** Between December 2003 and March 2013, a total of 147 patients (118 male, 29 female) underwent totally intracorporeal RARC for urinary bladder cancer. We also performed a systematic search of Medline, Embase and PubMed databases using the terms RARC, robotic cystectomy, robot-assisted, totally intracorporeal RARC, intracorporeal neobladder, intracorporeal urinary diversion, oncological outcomes, functional outcomes, and complication rates.

**Results:** The mean age of our patients was 64 years (range 37-87). On surgical pathology 47% had pT1 or less disease, 27% had pT2, 16% had pT3 and 10% had pT4. The mean number of lymph nodes removed was 21 (range 0-60). 24% of patients had lymph node positive disease. Positive surgical margins occurred in 6 cases (4%). Mean follow-up was 31 months (range 4-115 months). Two patients (1.4%) died within 90 days of their operation. Using Kaplan-Meier analysis, overall survival and cancer specific survival at 60 months was 68% and 69.6%, respectively. 80 patients (54%) received a continent diversion with totally intracorporeal neobladder formation. In the neobladder subgroup median total operating time was 420 minutes (range 265-760). Daytime continence and satisfactory sexual function or potency at 12 months ranged between 70-90% in both men and women.

**Conclusions:** Our experience with totally intracorporeal RARC demonstrates acceptable oncological and functional outcomes that suggest this is a viable alternative to open radical cystectomy.

**Key words:** Neobladder, oncological outcomes, radical cystectomy, robotic cystectomy, robot assisted radical cystectomy, totally intracorporeal, surgical technique

## INTRODUCTION

Open radical cystectomy with extended pelvic lymphadenectomy and urinary diversion remains the gold standard management for patients with invasive and high-risk bladder cancer unresponsive

to intravesical treatments.<sup>[1,2]</sup> Despite improvements in oncological and functional outcomes, open radical cystectomy is a surgical procedure associated with significant early and late complication rates, even in high volume centres of excellence.<sup>[3-5]</sup> Minimal invasive surgery was introduced to reduce morbidity and decrease hospital stay and laparoscopic radical cystectomy was first described in 1992, but technical difficulties associated with this approach limited widespread adoption.<sup>[6]</sup> With the introduction of robot-assisted laparoscopic surgery, robot-assisted radical cystectomy (RARC) has emerged as a more viable alternative to the open procedure.<sup>[7]</sup> RARC approaches are continually being refined and re-assessed and RARC has been gaining in popularity over the past decade.<sup>[8]</sup> In the majority of centers in USA performing RARC, the urinary diversion continues to be done with an extracorporeal approach.<sup>[9]</sup> The potential advantages of a complete intracorporeal procedure are less intraoperative blood loss, decreased bowel manipulation and exposure, reduced insensible losses, decreased morbidity

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from smaller incisions, reduced postoperative analgesic requirements, shorter hospital stay and earlier return to normal activities.<sup>[8]</sup> In this paper we describe our approach for RARC, extended pelvic lymph node dissection (ePLND) and intracorporeal neobladder formation. We report our oncological and functional outcomes from Karolinska, on 147 RARC completed with a totally intracorporeal approach, performed between December 2003 and March 2013. We also review the published literature on totally intracorporeal RARC with orthotopic neobladder, reporting oncological and functional outcomes and complication rates.

## MATERIALS AND METHODS

From December 2003 to March 2013, 668 radical cystectomies (521 open, 147 RARC) were performed at the Karolinska University Hospital. In December 2003 the first RARC, with intracorporeal neobladder was performed by surgeon PW. Surgeon PW and surgeon AH (since 2009), both experienced in open radical cystectomy and robot-assisted radical prostatectomy, have performed 147 RARC (118 male and 29 female) with totally intracorporeal urinary reconstruction for patients with clinically high-risk or muscle-invasive bladder cancer. 45 patients received neoadjuvant treatment (26 with ileal conduit, 19 with neobladder) and no patients received pre-operative radiotherapy. Contraindications for RARC were patients with a history of extensive abdominal surgery, severe cardiopulmonary disease, and bulky tumours; relative contra-indications were age >75 years and body mass index (BMI) >30. In the absence of contraindications and following appropriate discussion, patients chose between an open procedure and RARC with totally intracorporeal orthotopic ileal neobladder or ileal conduit. In this paper we focus on the 80 patients who underwent urinary diversion with an intracorporeal modified Studer neobladder. We used the standard da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA) for the first 20 patients and the da Vinci Si system for the remaining 60 patients. The technique has evolved with experience and the approach described in this paper has been used since 2008. All patients received preoperative intravenous broad-spectrum antibiotics (cefotaxime and metronidazole) and low-molecular-weight heparin (4000 units).

Postoperatively, patients were followed at 6 weeks; at 3, 6, 12, 18, and 24 months; and thereafter once a year. Postoperative functional outcomes regarding continence and potency rates were assessed. The International Index of Erectile Function (IIEF)- 5 score was used and a patient was defined potent if IIEF-5 score was at least 17 or if he could perform intercourse on more than half of the times attempted, with or without a phosphodiesterase inhibitor. A nurse interviewed the patients regarding urinary continence at 6 and 12 months, during the day and at night. Continence was defined as the usage of zero to one safety pad. Incontinence was defined as two or more wet pads.

Peri-operative parameters and outcome data were prospectively recorded in a secure, password protected database. Data are presented as frequencies and proportions, or as means or medians with data ranges. Survival curves were created using the Kaplan-Meier estimator.

## PATIENT SELECTION

Care should be taken in patient selection. The selection process includes preoperative investigation to ensure fitness for surgery as well as specific counselling about robotic technology. Patients with decreased pulmonary compliance who cannot tolerate prolonged Trendelenburg positioning are not candidates for the robotic-assisted technique. Furthermore, if the patient has a history of previous extensive abdominal surgery, RARC may be contraindicated. Relative contra-indications include patients aged >75 years, body mass index (BMI) >30 and those with bulky disease and such cases should be avoided early in the operative learning curve.

## PREOPERATIVE PREPARATION

In patients receiving an intracorporeal orthotopic neobladder, mechanical bowel preparation (osmotic laxative) may be used the day before surgery. All patients have a stoma site marked the day before surgery. Broad spectrum intravenous antibiotics are administered at the start of the procedure.

### Operative set-up

#### Patient position

After induction of general anesthesia, a naso-gastric tube and an 18 FG Foley urinary catheter are inserted. The patient is placed in lithotomy position with arms adducted and padded. The lower limb calves are wrapped with Flowtron pneumatic compression stockings and then placed and secured within stirrups where they can be abducted and slightly lowered on spreader bars [Figure 1a]. The table is

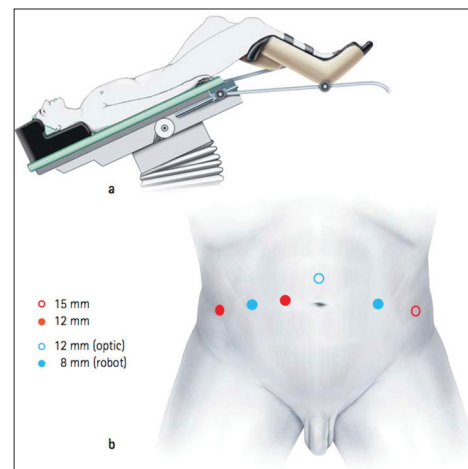


Figure 1: (a and b) patient positioning and port placement

placed in the 25° Trendelenburg position during the radical cystectomy and ePLND.

### Equipment

The technique is challenging, requiring conventional laparoscopic infrastructure as well as an assistant skilled in conventional laparoscopy. As well as standard laparoscopic surgical equipment, essential additional instruments are required: LigaSure® Covidien, surgical endoscopy clip applicators, laparoscopic Endo-Catch bags and laparoscopic stapler for intestinal stapling.

### Surgical technique

#### Trocar configuration

Port placement is critical for successful robotic surgery. A six-port technique is used with the camera port placed 5 cm above the umbilicus in the midline. The camera port is placed by a small mini laparotomy as described by Hasson<sup>[10]</sup> and the other ports are placed in view of the camera. A pneumoperitoneum pressure of 18 mmHg during the port placement can be helpful in creating additional tension on the abdominal wall. Two robotic ports are placed symmetrically and level with the umbilicus on the left and right side, lateral to the rectus sheath. A third robotic instrument port is placed just above and medial to the left anterior superior iliac spine through a 15-mm port thereby enabling laparoscopic stapling by the assistant when the third robotic port is temporarily disconnected. Two assistant ports are placed on either side of the right robotic instrument port [Figure 1b]. The pneumoperitoneum can then be reduced to 10-12 mmHg.

#### Male RC

- Step 1: Ureteric dissection. The peritoneum over the identified ureters is incised, ureters are dissected and divided close to the ureterovesical junction between two Hem-o-Lok® clips (Weck Pilling, NC, USA). A stay suture is placed on both proximal clips allowing easier identification of the ureters during construction of the urinary diversion. The distal ureteric margins may be sent for frozen section
- Step 2: Posterior dissection. An incision is placed in the peritoneum above the seminal vesicles exposing the seminal vesicles and vasa deferentia. The incision is extended laterally to join the peritoneal incision for ureteric dissection. The posterior dissection behind the seminal vesicles is developed to expose the Denonvilliers' fascia. The fascia is then opened and a surgical plane is developed between the Denonvilliers' (attached to the prostate) and the rectum. In non-nerve-sparing cases the seminal vesicles are left intact on the bladder and in case of nerve-sparing the seminal vesicles are divided close to the prostate, thereby avoiding undue damage to the erectile nerves that are in close proximity lateral to the seminal vesicles
- Step 3: Lateral dissection. A peritoneal incision is made

on both sides lateral to the umbilical ligaments and continued down to the external iliac artery entering the space of Retzius. The bladder is then mobilized from the pelvic wall until the endopelvic fascia can be clearly identified. It is important to leave the umbilical ligaments intact at this point so that the bladder does not fall down into the operating field. The vas deferens is divided and the lateral dissection is continued dividing the lateral pedicles with a LigaSure instrument (Tyco Healthcare). After division of the lateral pedicles, the prostatic base is identified and in non-nerve-sparing cases LigaSure dissection can be continued transecting the prostatic pedicles and dividing the neurovascular bundles. If nerve-sparing dissection is planned, a high release of the neurovascular bundle is performed with a strict athermal technique using Hem-o-Lok clips for haemostasis

- Step 4: Anterior dissection. The urachus and the median umbilical ligaments are coagulated with bipolar diathermy and then cut. The bladder is taken down, following the areolar tissue to stay in the correct plane. The pneumoperitoneum is then raised to 18 mmHg and the dorsal venous plexus complex is divided with cold scissors and a continuous haemostatic suture (2-0 Biosyn®) is placed after division to control the bleeding; haemostasis is checked after lowering the pneumoperitoneum. Preserving maximal urethral length, dissection is performed and a suture or Hem-o-Lok clip is placed on the prostatic apex to avoid spilling tumor cells into the operating field. When the specimen is totally freed it is immediately placed in an endocatch retrieval bag.

#### Female RC

For female radical cystectomy the required variations to the posterior and lateral dissections are described. The ovaries and uterus are usually removed depending on tumor stage and the age of the patient, after division of the ureters. The uterus is stretched anteriorly by the fourth arm and the infundibulo-pelvic (suspensory) ligaments and ovarian pedicles are divided. The uterine artery is identified and controlled by Hem-o-Lok clips. The uterus is retracted proximally and the junction between the vagina and uterus is identified; identification may be facilitated by manipulating a sponge in the vagina. After incising the vagina, the sponge is identified and the anterior wall of the vagina is taken with the specimen. Care is taken to preserve the autonomic nerves along the lateral walls of the vagina as they are responsible for sexual function. In cases when a vaginal-sparing dissection is planned and no suspicion of tumor invasion toward the uterus exists, the uterus can be dissected separately. The specimen is then removed via the vagina and the edges of the vagina are closed by continuous suture using the "clam shell" technique<sup>[11]</sup> with a 3-0 V-Loc® suture.

### Extended PLND

We find it preferable to perform the ePLND after the cystectomy, because of the increased working space in the pelvis when the bladder is removed. Dissection is started at the external iliac vessels at the node of Cloquet and is continued en-bloc up to the aortic bifurcation. The lateral border of the dissection is the genitofemoral nerve. After identification of the obturator nerve and vessels the obturator fossa, triangle of Marcille and the area along the internal iliac vessels including the presacral area are cleared of lymphatic tissue. Paravesical nodes are removed en bloc. Clips are used to prevent lymphocele formation. If a nerve-sparing procedure is performed, a meticulous dissection without diathermy is done to avoid damage to the autonomic nerves in the area lateral to the seminal vesicles and along the peri-rectal fascia. Following ePLND, the left ureter is tunneled under the sigmoid mesentery to the right side by gently lifting the colon with Cadiere forceps.

### Orthotopic neobladder, intracorporeal technique

After completing the radical cystectomy and the ePLND the urinary diversion is performed. For the urinary diversion the robot is undocked and the Trendelenburg position is decreased to 10-15° before re-docking, so as to facilitate the bowel dropping into the pelvis.

- Step 1: Anastomosis between the ileum and the urethra. The 0° lens is used for this initial step. The ileum is sufficiently mobilized to reach down to the urethra without tension. The anastomosis between the neobladder and urethra can then be made without tension, and this manoeuvre also ensures the neobladder will be placed correctly in the small pelvis during the whole procedure. A 20F opening is made on the antimesenteric side of ileum, using cold robotic scissors. The anastomosis is made according to the van Velthoven technique with two 16 cm 2-0 Quill® suture, allowing for 10-12 suture passes
- Step 2: Neobladder formation. The orthotopic neobladder is fashioned from a 50 cm segment of terminal ileum. The intestine is isolated using laparoscopic Endo-GIA with a 60 mm intestinal stapler. The stapler is inserted by the assistant surgeon, using the hybrid 15 mm port. The ileum is stapled 40 cm proximal to the urethro-ileal anastomosis. The continuity of the small bowel is restored by using an Endo-GIA with a 60 mm intestinal stapler, positioning the distal and proximal end of the ileum side-to-side with the anti-mesenteric sides facing each other. An additional transverse firing of the Endo-GIA staple is then used to close the open ends of the ileal limbs. The distal 40 cm of the isolated ileal segment is detubularized along its anti-mesenteric border with cold scissors, preserving a 10 cm intact proximal iso-peristaltic afferent limb for the entero-ureteric anastomoses. After detubularization, the posterior part of the Studer reservoir is closed using multiple running sutures (15 cm 3-0 V-Loc®) in a seromuscular fashion,

avoiding suturing the mucosa. After the posterior part is sutured, the distal half of the anterior part of the reservoir is sutured, using the same suture. The proximal half of the anterior part of the reservoir is left open and is closed in the last part of the procedure

- Step 3: Ureteric-neobladder anastomosis. The anastomosis between the ureters and the afferent limb is performed using the Wallace technique. Using the 4<sup>th</sup> arm the ureters are aligned holding the ties attached to the Hem-o-lok clips. The ureters are then incised and spatulated for 2 cm. The posterior walls of the ureters are sutured side-to-side, using a 15 cm running 4-0 Biosyn suture. Before the anastomosis between the ureters and the intestinal loop is made, two single-J 40 cm ureteric stents are introduced with the Seldinger technique through two separate 4 mm incisions at the lower part of abdominal wall. Using the Cadiere forceps the stents are pulled through the afferent limb and pushed up into the ureters on each side. The ureters are then sutured to the afferent limb of the Studer pouch, using two-times 16 cm 3-0 Quill suture. After the entero-ureteric anastomoses are completed the stents are sutured and fixed to the skin
- Step 4: Closure of the neobladder. The remaining part of the neobladder is then closed with a running 3-0 V-Loc suture. The balloon of the indwelling catheter is filled with 10 mL sterile water. The neobladder is then filled with 50 mL of saline to check for leakage. Extra suturing to secure a watertight reservoir and anastomosis is fundamental to decreasing post-operative complications. A 21F passive drain is introduced and placed in the small pelvis. The urethral catheter is removed after 21 days. We do not place a suprapubic catheter.

### Avoiding complications

Shoulder pads should be avoided due to the high risk of plexus damage. Care should be taken during the tunnelling of the left ureter behind the colon sigmoid and during the extended lymph node dissection to avoid damaging any vascular structures. It is important to check for leakage after the neobladder has been created.

### RESULTS

RARC with intracorporeal urinary diversion was performed in 147 patients. Mean age was 64 years (range 37 to 87). On surgical pathology 47% had pT1 or less disease, 27% had pT2, 16% had pT3 and 10% had pT4. The mean number of lymph nodes removed was 21 (range 0-60). 24% of patients had lymph node positive disease. Positive surgical margins occurred in six cases (4%), five patients receiving ileal conduit diversion with T3/4 disease and one patient receiving a continent diversion who had a positive ureteric margin that was misreported on frozen section at the time of operation. Mean follow-up since operation was



31 months (range 4-115 months). Two patients (1.4%) died within 90 days, one with intracorporeal ileal conduit from pulmonary embolism and the other with intracorporeal orthotopic neobladder from bronchopneumonia and associated cardio-respiratory arrest. Using Kaplan-Meier analysis, overall survival and cancer specific survival at 36 months were 78.5% and 80.4% and at 60 months were 68% and 69.6%, respectively (Figures 2 and 3).

80 (54%) received a continent diversion with intracorporeal neobladder formation. In the neobladder subgroup median total operating time was 420 minutes (range 265-760). Daytime continence and satisfactory sexual function or potency at 12 months ranged between 70-90% in both men and women.

## DISCUSSION

A totally intracorporeal RARC with neobladder formation technique aims to give patients equivalent oncological outcomes to open radical cystectomy with the benefits of a complete minimally invasive approach with less blood loss, lower peri-operative morbidity and complication rates, good functional outcomes, shorter recovery time and earlier return to normal activities.<sup>[8]</sup>

The number of specialist centers offering both standard RARC and totally intracorporeal RARC in the management of bladder cancer is increasing and the approach continues to evolve.<sup>[7]</sup> The accumulating long-term outcome experience of RARC is supported by encouraging short-term and intermediate outcomes.<sup>[12-15]</sup> Until recently, the majority of published oncological data has been on surrogate markers of oncological outcome, with a recent meta-analysis concluding that RARC is associated with higher lymph node yields compared to open radical cystectomy. The two surgical approaches appeared to be equivalent in terms of positive surgical margin rates.<sup>[16]</sup> In our series lymph node yields were satisfactory compared with other series, with a mean number of 26 lymph nodes in the extended PLND.<sup>[17]</sup> Our overall PSM rate of 4% is comparable

to open radical cystectomy and RARC series with PSM rates related to pre-operative staging [Table 1].<sup>[18]</sup>

Open radical cystectomy with extended pelvic lymphadenectomy remains the gold standard surgical treatment for muscle invasive and high-risk bladder cancer unresponsive to intravesical treatments. Open radical cystectomy provides good local cancer control with 50-70% 5-yr cancer-specific survival.<sup>[19]</sup> Radical cystectomy is an oncological procedure and any approach should primarily be judged by the long-term survival outcomes, which due to the comparatively recent introduction have until recently not been available for RARC. With RARC having been performed at Karolinska since 2003 we can contribute to the growing long-term outcome data for RARC. Using Kaplan-Meier analysis we showed a cancer-specific survival of 69.6% at 5 years (Figure 3).

The percentage of patients receiving continent urinary diversions is very variable and depends on the centre's experience and patient preference.<sup>[20]</sup> When looking at the functional outcomes in our series,<sup>[17]</sup> our results showed that the vast majority of patients were continent during the daytime and that preoperatively potent patients remained sexually active after surgery. It is evident that increasing age has a negative impact on functional outcomes including daytime continence and in achieving successful sexual function. This is an important factor to take into consideration when evaluating functional outcomes in a bladder cancer cohort outcome data, as cystectomy patients have a mean age of circa 70 years.<sup>[21]</sup>

Radical cystectomy by any approach has associated significant peri-operative complication and mortality rates.<sup>[22]</sup> Recent publications reported peri-operative complication rates from open radical cystectomy ranging from 49 to 64%, high-grade complication rates ranged from 13 to 40% and 90-d mortality ranging from 0 to 4.5%.<sup>[23-25]</sup> RARC is also associated with a high rate of

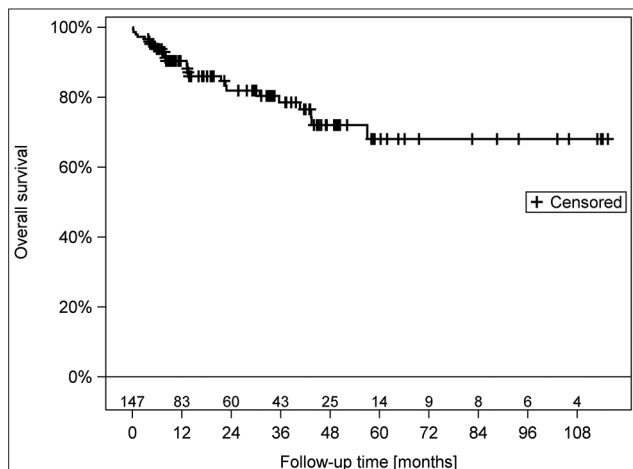


Figure 2: Overall survival

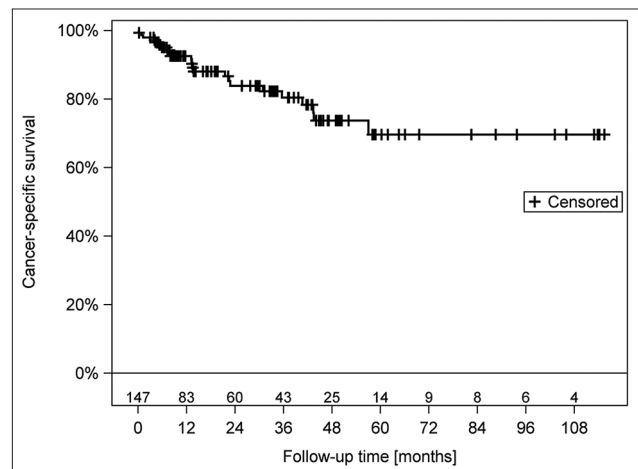


Figure 3: Cancer specific survival

**Table 1: Summary of robot-assisted intracorporeal neobladder series currently published**

Author and year	Patients (n)	Operating time (minutes)	EBL (ml)	Lymph node yield median (range)	PSM rate (%)	Hospital stay (days)	Complication rates	Functional outcomes at 12 months
Collins <i>et al.</i>	80	420	475	19 (0-52)	1	9	Clavien I-II complications for <30d and long-term (>30d) were 17% and 11%, respectively. Clavien III-V complications <30 days were 27% and long-term 19%	Daytime continence 87%. Night-time continence 80%. 72% of men received nerve sparing surgery with 69% potent post surgery
Goh <i>et al.</i> 2012 <sup>[34]</sup>	8	450	225	55 (44-74)	0	8	Clavien I-II complications for <30 d and 31-90d were 63% and 0%, respectively. Clavien III-V complications <30 days were 25% and 31-90d 13%	75% daytime continence. Night-time continence NR
Kang <i>et al.</i> 2012 <sup>[35]</sup>	1	585	500	29.7 (overall)	0	14	Post-operative paralytic ileus, no Clavien III-V complications	NR
Canda <i>et al.</i> 2011 <sup>[36]</sup>	25	594 (overall)	429.5 (over-all)	24.8 (8-46) (overall)	3.7 (overall)	10.5 (overall)	Overall results, Clavien I-II complications for <30d and 31-90d were 33% and 15%, respectively. Clavien III-V complications <30 days were 15% and 31-90d 11%	64.7% daytime continence. 17.6% night-time continence
Pruthi <i>et al.</i> 2010 <sup>[37]</sup>	3	330	221 (over-all)	NR	NR	5	NR	NR
Sala <i>et al.</i> 2006 <sup>[38]</sup>	1	720	100	NR	NR	5	0%	100% daytime continence. 0% night-time continence
Beechen <i>et al.</i> 2003 <sup>[39]</sup>	1	510	200	NR	NR	10	0%	NR

NR=Not reported, EBL=Estimated blood loss. If series includes results for intracorporeal ileal conduit diversion - reported as "overall" results

complications.<sup>[26,27]</sup> However, a robotic approach has been shown to reduce the complication rates compared to open radical cystectomy<sup>[28]</sup> and has also been better tolerated in elderly patient groups,<sup>[29,30]</sup> suggesting that RARC may be indicated in these susceptible patient groups.

The International Robotic Cystectomy Consortium (IRCC) recently published their accumulated RARC complication rates. On multivariable analysis, increasing age group, neoadjuvant chemotherapy, and receipt of blood transfusion were independent predictors of any and high-grade complications. 30 and 90-day mortality was 1.3 and 4.2%, respectively.<sup>[31]</sup>

Minimally invasive surgery has documented advantages over open surgery and a recent meta-analysis concluded that RARC is associated with lower overall peri-operative complications, higher lymph node yields, longer operation time, reduced blood loss and reduced transfusion rates, as well as a shorter length of stay compared to open radical cystectomy.<sup>[16]</sup>

Randomized controlled trials (RCT) comparing open radical cystectomy with laparoscopic and robotic approaches, are now being reported.<sup>[32,33]</sup> Whereas limitations of our study's outcome data include inherent bias due to the learning curve phase, future high-volume RCTs with long-term follow-up are awaited to confirm the findings of the current literature analysis. As totally intracorporeal RARC becomes increasingly

popular, robotic surgical techniques evolve and surgeons' skills plateau on their learning curve, future meta-analysis of the literature and prospective RCT's will further clarify the actual benefits of a totally intracorporeal RARC technique.

## CONCLUSIONS

We have presented our technique for RARC with intracorporeal neobladder formation. By adopting a step-wise approach to this complex surgery we have successfully developed a totally intracorporeal robotic cystectomy service that is replicable. RARC is primarily an oncological procedure and we have demonstrated good oncological outcomes and encouraging long-term cancer specific survival rates. We have also shown good functional outcomes with intracorporeal continent diversion. In our series, RARC with intracorporeal neobladder formation appears to be a viable alternative to an open approach, offering patients the advantages of a minimally invasive approach.

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