## ROBOTIC RADICAL CYSTECTOMY FOR BLADDER CANCER: CURRENT PERSPECTIVES

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### ABSTRACT

The most effective local treatment of muscle invasive bladder cancer and non-invasive, high-grade bladder tumours that recur or progress despite intravesical therapies, is open radical cystectomy (RC), extended pelvic lymph node (LN) dissection with urinary diversion. Performing these complex procedures using pure laparoscopy is extremely difficult. On the other hand, the surgical robot has the advantage of enabling the console surgeon to perform complex procedures more easily, providing three-dimensional (3D) and magnified views, higher grades of wristed hand movements, and decreased hand tremor, while the fourth robotic arm offers additional assistance and tissue retraction which facilitates the learning curve. The number of centres performing robot-assisted radical cystectomy (RARC) is increasing. Although most of the centres perform extracorporeal urinary diversion following RARC, very few centres - including ours - have reported their outcomes on RARC with total intracorporeal urinary diversion. Some of the articles, comparing open RC versus RARC, have suggested similar outcomes in terms of operative time, mean LN yield, positive surgical margin (PSM) rates, and complication rates, whereas others have suggested decreased estimated blood loss, transfusion rate, complications, length of hospital stay, wound problems, time to flatus, and time to regular diet in the postoperative period in RARC patients. The surgical technique of total intracorporeal RARC with urinary diversions is still evolving, and these complex robotic procedures seem to be technically feasible with good intermediate-term oncologic results, acceptable morbidities, excellent short-term surgical and pathological outcomes, and satisfactory functional results.

<u>Keywords</u>: Robotic radical cystectomy, bladder cancer, minimally invasive surgery, intracorporeal urinary diversion.

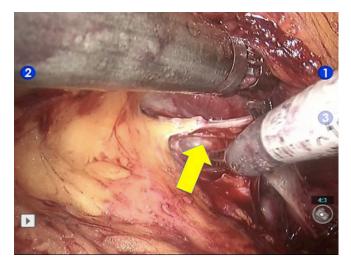
### INTRODUCTION

Open radical cystectomy (RC), bilateral extended pelvic lymph node (LN) dissection, and urinary diversion is the gold standard surgical approach in the management of muscle invasive bladder cancer in addition to high-grade, recurrent, noninvasive tumours.<sup>1</sup> However, minimally invasive surgical approaches have attracted great interest, particularly following the introduction of the da Vinci-S four-arm surgical robot (Intuitive Surgical, Sunnyvale, CA). Thus, robot-assisted radical cystectomy (RARC) is increasingly being performed worldwide. Herein, we summarised the current literature on RARC.

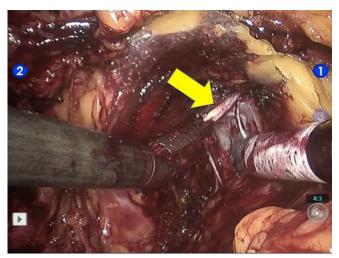
### RARC PROCEDURE

Briefly, the whole procedure consists of three main steps including neurovascular bundle (NVB)sparing RARC, robotic bilateral extended pelvic LN dissection, and extracorporeal or intracorporeal urinary diversion. (1A)

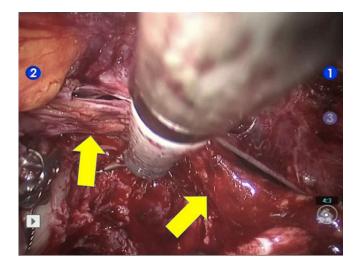
(1C)



(1B)



(1D)



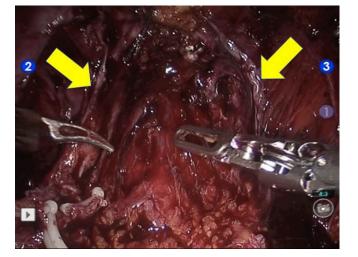


Figure 1A: High anterior release neurovascular bundle preservation (right side, arrow). Figure 1B: High anterior release neurovascular bundle preservation (left side, arrow). Figure 1C: Preserved neurovascular bundle (left side, arrows). Figure 1D: Preserved bilateral neurovascular bundles in the pelvis (arrows). Obtained from Prof Balbay and Dr Canda's own robotic surgical procedure.

#### Step 1: NVB-Sparing RARC

The surgical robot has the advantage of threedimensional (3D) and magnified image capability, higher grades of wristed hand movements, and decreased hand tremor.<sup>2</sup> In addition, the fourth robotic arm facilitates this complex surgery by means of additional assistance and tissue retraction in the abdomen and pelvis.<sup>2</sup> In our experience, technological details these give significant advantages to the operating console surgeon that facilitates dissection of tissues and particularly the NVBs (Figure 1A-D), which is expected to have impact on the postoperative functional an

outcomes and quality of life, namely urinary continence and penile erection.<sup>2,3</sup> Menon et al.<sup>4</sup> stated that NVB-sparing RARC combines the oncological principles of open surgery with the technical advantages of the surgical robot, allowing a precise, gentle, quick, and safe surgery. Of note, the presence of anatomic anomalies such as ureteric duplication could easily be surgically managed by using the surgical robot.<sup>5</sup>

A positive surgical margin (PSM) rate of <10% was suggested as surgical oncological sufficiency in open RC.<sup>6,7</sup> Due to the published RARC literature including the International Robotic Cystectomy Consortium (IRCC) series, a PSM rate of 0-8.9% was reported, which is in line with this requirement.<sup>8-12</sup> Most of the published literature comparing open versus robotic RC is retrospective and non-randomised, therefore a selection bias is inevitable in most of these studies. There are only two articles that prospectively compare open versus robotic approaches.<sup>13,14</sup> Estimated blood loss, guicker return of bowel function, and the lower use of inpatient narcotics were detected as the main advantages of the robotic approach.<sup>13,14</sup> A decreased complication rate seems to be another advantage of robotic surgery when compared to open approach. A number of comparative studies have reported decreased complication rates in the robotic groups due to modified Clavien classification,<sup>15,16</sup> whereas some others have reported similar complication rates.<sup>14,17</sup>

# Step 2: Robotic Bilateral Extended Pelvic LN Dissection

A LN yield of >15 LNs was suggested for surgical oncological sufficiency in open RC.<sup>18,19</sup> RARC seems to maintain sufficient LN yield due to the published literature.<sup>3,10,12,20</sup> In our experience, the advantages gained from the use of the robotic surgical instruments with magnified 3D vision, used during robotic extended pelvic LN dissection, lead to delicate dissection of the lymphatic tissues (Figures 2 and 3). In order to acquire a sufficient amount of LNs following completion of RARC, we suggest initially performing at least 50 cases of robot-assisted radical prostatectomy (RARP) with pelvic LN dissection to gain sufficient experience and confidence with extended pelvic LN dissection.

We use a total of six trocars for this type of robotic surgery. A 12 mm camera port is placed 2 cm above the umbilicus in the midline. Regarding the robotic arms, two 8 mm robotic trocars are placed at the level of umbilicus, 8 cm apart from the camera port. The fourth arm robotic trocar is placed 3 cm above the iliac crest, as lateral as possible, on the right side of the patient. Two assistant trocars are placed on the left abdomen of the patient. A 15 mm trocar for inserting bowel staplers and endobags is placed 3 cm above the iliac crest laterally, and the remaining 12 mm assistant trocar is placed between the camera and the second arm of the robot. Although the whole surgery can be performed with a 0° lens, we prefer to switch to a 30° lens when we start the intracorporeal Studer pouch reconstruction.



Figure 2: Extended lymph node dissection and appearance of skeletonised major pelvic vasculature (arrows).

Obtained from Prof Balbay and Dr Canda's own robotic surgical procedure.



Figure 3: Skeletonised abdominal aorta and vena cava inferior are seen. Please note titanium endoclips on the vasculature used for haemostasis. Obtained from Prof Balbay and Dr Canda's own robotic surgical procedure.

The patient is placed in a deep (30°) Trendelenburg position until the completion of robotic bilateral extended LN dissections and transposition of the left ureter. Thereafter, the patient is taken to a mild (5°) Trendelenburg position for intracorporeal Studer pouch reconstruction. LNs including external, internal, and common iliac, obturator, presacral, interbifurcation, preaortic, paracaval LNs within the boundaries between the genitofemoral nerves, psoas muscles, and ureters laterally, cut the edge of the endopelvic fascia over the NVBs and internal iliac vessels medially, inferior mesenteric artery (IMA) and accompanying vena cava superiorly are removed. Thereafter, the left ureter is transposed to the right gutter under the sigmoid colon. We use an endowrist 8 mm monopolar Maryland curved scissors (Intuitive Surgical, Sunnyvale, CA) on the right hand and an endowrist Maryland bipolar forceps (Intuitive Surgical, Sunnyvale, CA) on the left hand. For the fourth arm, we use a Cadiere forceps (Intuitive Surgical, Sunnyvale, CA).<sup>21</sup>

Due to the published literature oncologic outcomes of the RARC series including the IRCC outcomes, the mean LN yield has been reported to range between 15-21 LNs and PSM rate ranges between 1.4-7%.<sup>3,22-26</sup>

# Step 3: Extracorporeal or Intracorporeal Urinary Diversion

Urinary diversion is performed extracorporeally in most of the published literature relating to RARC. Including ours, only a few centres have reported their experience on intracorporeal urinary diversion including ileal conduit and Studer pouch reconstruction. Very recently, Tyritzis et al.<sup>22</sup> reported The Karolinska Institute's experience of 70 patients with RARC and totally intracorporeal modified Studer ileal neobladder formation, which is the largest published single institution series of this particular robotic technique. The median follow-up was 30.3 months in their series. The surgical margins were negative in all but one patient (98.6%). Perioperative complications (Clavien 3-5) occurred in 22 of 70 patients (31.4%) between postoperative 0-30 days. Comparatively, Clavien 3-5 complications occurred in 13 of 70 patients (18.6%) in postoperative 31-90 days. The overall complication rate was calculated as 58.5% within postoperative 90 days. Recurrence-free, cancer-specific, and overall survival rates at 24 months were 80.7%, 88.9%, and 88.9%, respectively. They also reported functional outcomes in their series. Of the patients, daytime continence rates were 70-90% and satisfactory sexual function or potency was reported both in men and women at 12 months. They concluded that totally intracorporeal neobladder diversion has satisfactory and comparable outcomes when compared to open series.

In our experience with 27 cases, the mean operation time was 9.9±1.4 hours (range, 7.1-12.4)

and estimated blood loss was 429±257 mL (100-1,200). Regarding surgical oncologic parameters including SMs mean LN yield, SMs were negative in all-but-one patient who had pT4b disease and whose mean LN yield was 24.8 (9.2, 8-46). Postoperative pathological stages were as follows: pTO (n=5), pTis (n=1), pT1 (n=1), pT2a (n=5), pT2b (n=3), pT3a (n=6), pT3b (n=2), pT4a (n=3), and pT4b (n=1). Positive LNs were detected in six patients. Incidental prostate cancer was detected in nine patients. The mean length of hospital stay was 10.5±6.8 days (range, 7-36) and the mean follow-up time was 6.3±2.9 months (range, 1.8-11.3). In the perioperative (0-30 days) period, nine minor (Grade 1 and 2) and four major (Grade 3-5) complications were detected as described in modified Clavien classification. On the other hand, there were four minor and three major complications in the postoperative (31-90 days) period. Regarding our functional outcomes, of the available 18 patients: 11 were fully continent, 4 had mild day-time incontinence, and 2 had severe day-time incontinence.<sup>3</sup>

Our technique of robotic intracorporeal Studer pouch formation was described before and follows in more detail.<sup>3</sup> The first step is to suture the urethral remnant to the assigned 1 cm opening on the antimesenteric border of the wall of the ileal segment to be segregated. An estimated 10 cm segment on the right and a 40 cm segment on the left side of urethro-ileal anastomosis were assigned. The distal 20 cm ileal segment is left attached to the caecum. Laparoscopic intestinal staplers are introduced from the 15 mm trocar on the left abdomen and are placed perpendicular across the intestinal wall, with inclusion of the adjacent 2 cm of mesointestinum. The proximal and distal ends of the ileum are put together and a side-to-side ileoileostomy is accomplished with the use of two more laparoscopic intestinal staplers. The proximal 10 cm segment of the afferent loop is spared. The antimesenteric border of the remaining ileal segment is incised. Asymmetric closure of the posterior wall is performed. To facilitate and reinforce this closure, the medial aspects of the opened ileal segments are sutured together. A completed posterior wall anastomosis - running from the upper-right to the lower-left and leaving 10 cm segments on each side of the urethra located in the middle - is accomplished. Thereafter, anterior wall anastomosis is performed, leaving the proximal redundant wall that will be closed at the very end of the

surgery, following the insertion of ureteral stents. A Wallace-type uretero-ureteral anastomosis is made. Then, we excise the stapler line at the proximal end of the afferent loop. The posterior wall is anastomosed halfway between the ileal wall and the medial edge of the uretero-ureteral anastomosis. A feeding tube is inserted through the urethra, advanced within the lumen of the ileal segment, and held close to the anastomosed ends of the ureters. Then, JJ stents are passed through the feeding tube over a guidewire to the uretero-intestinal anastomosis site and fed up to the ureters and renal pelves. The guidewires are then removed and both ends of the JJ stents are allowed to coil. For a Studer pouch, the distal tips of the stents are tied to the tip of a 22°F urethral catheter outside the body that will then be passed through the urethra into the pouch over a guidewire. With this manoeuvre the urethral catheter and JJ stents tied to it are removed together 21 days after surgery following cystography. Lastly, the redundant ileal wall of the pouch is closed on itself.<sup>3</sup> Figures 4 and 5 show robotic construction of an intracorporeal Studer pouch. In our initial 27 cases, there were 25 males and 2 females. Mean patient age was 61.4 years (range 43-80) and mean body mass index (BMI) was 25.5 kg/m<sup>2</sup> (range 19.3-32.8). Overall, eight patients (29.6%) received neoadjuvant chemotherapy.

Schumacher et al.<sup>27</sup> reported the mean operative time and the mean blood loss as 476±96 minutes (325-760) and 677±477 mL (200-2,200) in RARC and intracorporeal Studer pouch reconstruction (n=36) and ileum conduit formation (n=9) patients, respectively. Goh et al.<sup>28</sup> performed RARC and intracorporeal Studer pouch reconstruction (n=8) and ileal conduit formation (n=7) overall in 15 patients. The mean operation time was 7.5 hours in both groups. The mean estimated blood loss was 225 mL and 200 mL in Studer pouch and ileal conduit group, respectively.

### **OPEN VERSUS ROBOTIC APPROACH**

A number of studies have compared open versus robotic RC. Most of the published studies are retrospective series, therefore, a selection bias is inevitable that precludes drawing strict conclusions on this issue. Two prospective and randomised clinical trials compared open versus robotic RC procedures.<sup>13,14</sup> In both of these studies, around 20 patients were included in

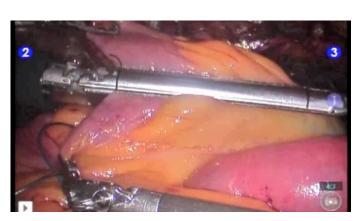


Figure 4: Laparoscopic bowel stapler is seen introduced from the 15 mm port located on the left abdomen approximately 2 cm above the anterior superior iliac spine to divide the ileum for Studer pouch reconstruction.

Obtained from Prof Balbay and Dr Canda's own robotic surgical procedure.

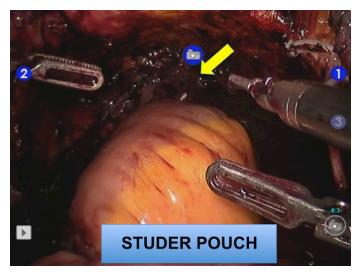


Figure 5: Completed intracorporeal Studer pouch with internalised bilateral DJ stents. Arrow points out the anastomosis between the urethra and the pouch.

Obtained from Prof Balbay and Dr Canda's own robotic surgical procedure.

the study arms. The estimated blood loss was detected to be significantly lower in the robotic group in both studies.<sup>13,14</sup> Additionally, quicker return of bowel functions and lower use of inpatient narcotics were detected in the robotic arm in one of the studies.<sup>14</sup>

Wang et al.<sup>29</sup> conducted a prospective but nonrandomised study in order to compare open (n=21) versus robotic (n=33) approaches. Significantly decreased blood loss, transfusion requirement, hospital stay, and time to resumption of regular diet were detected in the robotic group.<sup>25</sup> Complications oncologic and perioperative outcomes of open versus robotic RC in 200 patients with extracorporeal urinary diversion were compared retrospectively in another study.<sup>16</sup> The robotic group was found to have the advantages of a significantly shorter mean operative time, significantly lower mean estimated blood loss and mean hospital stay, and significantly fewer overall and major complications.<sup>16</sup>

Styn et al.<sup>17</sup> reviewed a total of 50 RARC and 100 open RC cases with similar demographic parameters. The robotic group was found to be associated with a significantly decreased median estimated blood loss and 30-day transfusion rate. However, the operative time was longer in the robotic group. RARC was found to be an independent predictor of fewer overall and major complications at postoperative 30 and 90 days by Ng et al.<sup>15</sup> On the other hand, other studies also did not find any significant differences between open and robotic approaches in terms of complications.<sup>13,14,16,17,29</sup> Schumacher et al.,<sup>27</sup> from The Karolinska Institute, published surgeryrelated complications of RARC with intracorporeal urinary diversion in 45 patients. Overall, fewer complications were observed between the groups over time, with a significant decrease in late versus early complications.<sup>27</sup>

Very recently, the IRCC reported an analysis of intracorporeal versus extracorporeal urinary diversion following RARC for bladder cancer. Overall, 18 international centres, with 935 patients, were included. Of those patients, 167 underwent intracorporeal urinary diversion (ileal conduit: 106; neobladder: 61) and 768 underwent extracorporeal urinary diversion (ileal conduit: 570; neobladder: 198). No significant differences were detected in terms of patient age, gender, BMI, American Society of Anesthesiologists (ASA) scores, and the rate of prior abdominal surgery between the groups. The mean operation time was detected to be similar in both groups. Although not significant, the duration of hospital stay was longer in the intracorporeal urinary diversion group (9 days versus 8 days, p=0.086). Reoperation

rates during the perioperative period (0-30 days) were similar. No significant difference was detected during the 90-day complication rates between the groups. However, a better trend in favour of intracorporeal urinary diversion groups was detected (41% versus 49%, p=0.05). An important finding of this study was that gastrointestinal complications were significantly lower in the intracorporeal group ( $p \le 0.001$ ). In addition, patients who underwent intracorporeal urinary diversion were regarded as having a of experiencing postoperative lower risk complications at 90 days of surgery (p=0.02).<sup>30</sup>

### CONCLUSIONS

Currently, the most effective local treatment of muscle-invasive bladder cancer and noninvasive, high-grade bladder tumours that recur or progress despite intravesical therapies is open RC, extended pelvic LN dissection with urinary diversion. Performing these complex procedures utilising pure laparoscopy is very difficult. However, a surgical robot enables the surgeon to perform complex procedures much more easily due to having the advantages of 3D and magnified image capability, higher grades of wristed hand movements, and decreased hand tremor, and also due to the fourth robotic arm, which enables additional assistance and tissue retraction, leading to a shorter learning curve.

According to the published literature comparing open and robotic RC, some authors have published similar outcomes in terms of operative time, mean LN yield, PSM rate, and complication rates between the groups, whereas some others have reported decreased estimated blood loss, transfusion rate, complications, length of hospital stay, wound problems, time to flatus, and time to regular diet in the postoperative period in robotic group.

Totally intracorporeal RARC with urinary diversions are technically feasible procedures with good intermediate-term oncologic results, acceptable morbidities, excellent short-term surgical and pathological outcomes, and satisfactory functional results.

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