Robot–assisted radical cystectomy and intracorporeal urinary diversion – safe and reproducible?

Allen Sim¹, Mevlana Derya Balbay², Tilman Todenhöfer¹, Stefan Aufderklamm¹, Omar Halalsheh³, Johannes Mischinger¹, Johannes Böttge¹, Steffen Rausch³, Simone Bier³, Arnulf Stenzl¹, Georgios Gakis¹, Christian Schwentner¹*, Abdullah Erdem Canda³*

¹Department of Urology, Eberhard–Karls University Tuebingen, Germany
²Department of Urology, Memorial Şişli Hospital, Istanbul, Turkey
³Department of Urology, Yildirim Beyazit University, School of Medicine, Ankara Ataturk Training & Research Hospital, Ankara, Turkey

*CS and EC are shared senior authors of this manuscript

Introduction

Robot–assisted radical cystectomy (RARC) plus intracorporeal urinary diversion is feasible. Few centers worldwide demonstrated comparable functional and oncologic outcomes. We reported a large series of RARC and intracorporeal diversion to assess its feasibility and reproducibility.

Material and methods

We identified 101 RARCs in 82 men and 19 women (mean age 68.3 years) from October 2009 to October 2014. The patients underwent RARC and pelvic lymphadenectomy followed by intracorporeal urinary diversion (ileal conduit/ neobladder). Out of the 101 patients, 28 (27.7%) received intracorporeal ileal conduits and 73 (72.3%) intracorporeal neobladders. Studer pouch was performed in all the patients who underwent intracorporeal neobladder formation. Perioperative, functional and oncologic results including CSS and OS are reported.

Results

Mean operative time was 402.3 minutes (205–690) and blood loss was 345.3 ml (50–1000). The mean hospital stay was 17.1 days (5–62). All the surgeries were completed with no open conversion. Minor complications (Grade I and II) were reported in 27.7% of patients while major complications (grade III and above) were reported in 36.6% of patients. The mean nodal yield was 20.6 (0–46). Positive ureteric margins were found in 8.9% of patients. The average follow–up was 27.5 months (1–52). Daytime continence could be achieved in 89.2% of patients who underwent intracorporeal neobladder formation. Perioperative, functional and oncologic results including CSS and OS are reported.

Conclusions

RARC with intracorporeal diversion is safe and reproducible in ‘non–pioneer’ tertiary centers with robotic expertise having acceptable operative time and complications as well as comparable functional and oncologic outcomes.

Key Words: radical cystectomy ◆ neobladder ◆ ileal conduit ◆ intracorporeal diversion ◆ robot–assisted laparoscopy

INTRODUCTION

Radical cystectomy (RC) with pelvic lymph node dissection is considered to be the gold standard treatment of muscle–invasive bladder cancer (BC). In some cases of high–grade non–muscle invasive disease which is refractory to BCG therapy, radical cystectomy is also a viable option. In the majority of cases, the most popular choice of diversion is either an ileal conduit or an orthotopic neobladder. Recently, however, minimally invasive radical cystectomy techniques have been gaining popularity and nowadays in most cases robot–assisted technique is used. Robot–assisted radical cystectomy (RARC) has been shown to be equivalent to open radical cystectomy in terms of oncological and functional outcomes, while
superior when it comes to the perioperative outcomes such as shorter hospital stay and blood loss [1–5]. It has been shown that robotic techniques have comparable oncologic outcomes in terms of nodal yield and positive margin rates compared to the open technique [2, 5]. However, robotic cystectomy and intracorporeal urinary diversion is technically challenging. Therefore, many surgeons are still adopting the hybrid approach when performing the cystectomy using robotic assistance and completing the urinary diversions extracorporeally to shorten the operating time. Wiklund and associates have pioneered the technique of intracorporeal urinary diversion creating both neobladders and ileal conduits completely intracorporeally [6]. The technique is to be credited as an almost identical replication of open surgical principles. Recently, the group reported their oncologic and functional outcomes of their RARC cohort showing comparable results to open series [7]. Equally, Desai and Gill presented remarkable outcomes using a modification of the aforementioned technique [8]. These reports have further consolidated that RARC and intracorporeal diversion are technically feasible with good outcomes. However, these observations are limited to very few pioneering centers worldwide and it remains unknown whether RARC and intracorporeal urinary diversions are reproducible by other tertiary centers with robotic expertise. Particularly, intracorporeal neobladder formation is regarded a technically challenging and potentially time-consuming surgery with steep learning curves [9, 10]. Herein, we present a homogenous series of patients who underwent RARC and subsequent intracorporeal urinary diversion in the form of ileal conduit and neobladder. We aim to demonstrate that RARC with intracorporeal urinary diversion is safely reproducible and teachable given adequate robotic experience. To our knowledge, this is one of the largest series of RARC with intracorporeal urinary diversion to date.

MATERIAL AND METHODS

We retrospectively identified 101 patients who underwent RARC and intracorporeal urinary diversion in two academic centers from October 2009 to October 2014. Institutional review board approval (# 081/2014R) was obtained before starting data collection and analysis. A total of 300 radical cystectomies were performed in the two centers during the same period. One surgeon from each center performed the RARC with intracorporeal diversions, each experienced in open cystectomy and robotic prostatectomy. A dedicated robotic team comprising of a senior resident and nurse practitioner participated routinely in all the cases. The indications for RARC were muscle–invasive transitional carcinoma (TCC) and high–grade non– muscle invasive disease refractory to intravesical BCG treatment. Both men and women were included in the analysis. Other exclusion criteria were non–TCC histology, coagulopathy, pre–existing incontinence for patients undergoing neobladder, cerebrovascular disease and severe pulmonary dysfunction rendering robotic surgery impossible. In our series, patients with previous intra–abdominal surgeries or radiotherapy were not excluded. Data analysis comprised of perioperative variables (operating time, blood loss, hospital stay), standardized complication reporting using the Clavien–Dindo system [11], pathology reporting and functional as well as oncologic outcomes. Furthermore, 3–year cancer specific survival (CSS) and overall survival (OS) were reported.

Surgical technique

RARC was done using a three–arm da Vinci S–system (Intuitive Surgical, Sunnyvale, California). The optical trocar was placed 2 cm above the umbilicus while a 0 degree telescope was used in all cases. The two remaining robotic trocars were placed a handbreadth lateral to the umbilicus and two more 12 mm assisting trocars were inserted 5 cm above the anterior superior iliac spine. Finally, a 5 mm trocar was placed in the right upper abdomen. RARC was then performed in a steep Trendelenburg position. Nerve sparing in both men and women was attempted whenever oncologically permitted. In females, nerve sparing was achieved by careful preservation of a tissues lateral to vagina to avoid damage to autonomic nerves. Extended pelvic node dissection included the external, the internal as well as the common iliac nodes, the obturator fossa and the presacral area. The bladder specimen and the lymph nodes were put into impermeable retrieval bags until removal at the end. Both ureters were clipped early and the left ureter was transposed below the sigmoid mesocolon. They were then tagged to the right lateral abdominal wall until reimplantation. The robot was undocked and the operating table was flattened. We will include detailed description of the surgical steps involved in intracorporeal urinary diversions.

Intracorporeal neobladder

The robot was redocked and a 50 cm loop of terminal ileum was isolated approximately 20 cm proximal to the ileocecal valve. It is crucial to ensure that the most dependent part can reach down to pelvis easily to ensure a tension–free urethro–ileal anasto-
An opening was then made at the most dependent portion and a urethral-ileal anastomosis was performed using a running suture according to the Van Velthoven technique [12]. The ileal loop was next discontinued using a 60 mm Endo-GIA stapler (Covidien). Bowel continuity was then restored using an Endo-GIA stapler by performing a functional end-to-end anastomosis. The isolated loop was consequently opened according to previously described techniques from Wiklund et al. [6]. The posterior plate was then reconstructed using a 3/0 absorbable suture in a running fashion. The neobladder was then asymmetrically folded into a spherical reservoir applying the same suture. A 20 Fr Foley catheter was then advanced into the reservoir and its water-tightness was tested accordingly. Then the ureters were conjoined using the Wallace technique with a 4/0 absorbable suture. Single-J stents were placed over guide wire and the ends were advanced through the wall of the reservoir. Both ureters were then anastomosed to the afferent limb using a 4/0 absorbable suture. Stents were advanced to the skin through the 12 mm trocar.

### Intracorporeal ileal conduit

In the patients who underwent intracorporeal ileal conduit, 15 cm of the terminal ileum 20 cm away from the ileocaecal valve was isolated. The uretero-ileal anastomosis was performed as described above. The single J stents were brought out through the distal end of ileal conduit. The distal end of ileal conduit was then brought out to the right abdominal wall and matured. Specimens were ultimately retrieved through a separate incision (Specimen delivered via the vagina in women). The incisions were closed in layers after placement of 2 surgical drains.

### Statistical analysis

Data are descriptively reported using mean and range. The 3 year cancer-specific survival and overall survival were assessed using the Kaplan–Meier estimator.

### RESULTS

In total, 101 RARCs with intracorporeal urinary diversion were identified in 82 men and 19 women. Out of which, 73 patients (57 male, 16 female) underwent intracorporeal neobladder; and 28 patients (25 male, 3 female) underwent intracorporeal ileal conduit. The mean age was 68.3 years (41–88). The mean body mass index (BMI) was 26.5 kg/m² (19–34).

In those patients who underwent intracorporeal neobladder, the Studer pouch was performed. Neoadjuvant chemotherapy was administered in 13 patients (12.9%) with presumably advanced stage (Table 1). The preoperative stage and grade of disease is also included in the table. All procedures were completed without open conversion (Table 2). The mean operating time was 402.3 minutes (205–690) and blood loss was 345.3 ml (50–1000) while the mean diversion

### Table 1. Patient’s characteristics

|                          | All patients (n=101) | Ileal conduit (n=28) | Neobladder (n=73) |
|--------------------------|----------------------|---------------------|-------------------|
| Males (%)                | 82 (81.2)            | 25 (89.3)           | 57 (78.0)         |
| Females (%)              | 19 (18.8)            | 3 (10.7)            | 16 (22.0)         |
| Age, years, mean (range) | 68.3 (41–88)         | 76.1 (62–88)        | 62.1 (41–80)      |
| BMI, mean (range)        | 26.5 (19–34)         | 27.5 (20–32)        | 25.6 (19–34)      |

### Table 2. Perioperative and postoperative outcome

|                          | All patients (n=101) | Ileal conduit (n=28) | Neobladder (n=73) |
|--------------------------|----------------------|---------------------|-------------------|
| Operating time, min, mean (range) | 402.3 (205–690) | 350.3 (205–510) | 452.5 (280–690) |
| Diversion time, min, mean (range) | 156.6 (85–300) | 133.4 (85–210) | 178.4 (110–300) |
| Blood loss, ml, mean (range) | 345.3 (50–1000) | 346.9 (100–1000) | 347.5 (50–800) |
| Conversion (%)         | 0 (0)                | 0 (0)               | 0 (0)             |
| Hospital stay, day, Mean (range) | 17.1 (5–62) | 17.6 (5–40) | 16.5 (12–62) |
| Nerve sparing, bilateral (%): |                          |                     |                   |
| Males (%)               | 52/82 (63.4)         | 0/25 (0)            | 52/57 (91.2)      |
| Females (%)             | 15/19 (78.9)         | 0/3 (0)             | 15/16 (93.8)      |
| Complications (Clavien): |                          |                     |                   |
| I                       | 12 (11.9)            | 4 (14.3)            | 8 (10.9)          |
| II                      | 16 (15.8)            | 2 (7.1)             | 14 (19.2)         |
| III                     | 28 (27.7)            | 5 (17.9)            | 22 (30.1)         |
| IV                      | 9 (8.9)              | 1 (3.6)             | 8 (10.9)          |
| V                       | 0 (0)                | 0 (0)               | 0 (0)             |
time was 156.6 minutes (85–300). The mean hospital stay was 17.1 days (5–62). Bilateral nerve sparing was performed in all females and in 52 out of 82 men (63.4%). The postoperative tumor stage was CIS in 7 patients (6.9%), pT0 in 11 patients (10.9%), pT1 in 6 patients (5.9%), pT2 in 33 patients (32.7%), pT3 in 31 patients (30.7%), pT4 in 13 patients (12.8%) and all of them were high grade disease. Node positive disease was found in 23 patients (22.8%). The mean nodal yield was 20.6 nodes (0–46). Out of all the patients, 8.9% had positive ureteric margins despite having negative intra–operative frozen section. Concomitant prostate cancer was found in 29 men (35.3%). The Gleason score was 3+3 in 18 patients (62.1%), 3+4 in 6 patients (20.7%) and 4+3 in 3 patients (10.3%) and Gleason 8 disease was found in 2 patients (6.9%) (Table 3). A total of 3 men (10.3%) had positive prostatic margins (2 men from ileal conduit arm and one patient from the neobladder arm). There was no preoperative PSA performed, as it was not part of routine preoperative investigations. However, to date there has not been any biochemical recurrence.

### Complications

The perioperative complications were grade I in 12 patients (11.9%), grade II in 16 patients (15.8%), grade III in 28 patients (27.7%) and grade IV in 9 patients (8.9%). There were no grade V complications reported. There were no complications associated with patient positioning (Table 2). Minor (Clavien I&II) and major (Clavien ≥III) complication rates were 27.7% and 36.6% respectively. Early surgery–related complications (<30 days) occurred in 50.5% of patients with 6 patients requiring reoperation. Out of which, three patients had prolonged ileus, one patient had post–operative hemorrhage, one patient had small bowel anastomosis dehiscence and one patient had small bowel sealed perforation treated with small bowel resection. Late surgery–related complications (>30 days) were seen in 13.9% of patients. There was no statistical difference between the complication rates of neobladder and ileal conduit patients.

### Oncologic outcomes

The average follow–up was 27.5 months (1–52). During the follow–ups, one patient (1.0%) who underwent intracorporeal neobladder had developed local recurrence. Metastatic disease developed in 25 patients (24.8%) and all of them received chemotherapy. 17 patients have died due to metastatic disease during the follow–up period, whereas 9 patients died from other non cancer–related disease. The 3–year cancer specific survival (CSS) and overall survival (OS) was 80.2% and 69.8% respectively (Table 4).

### Functional outcomes

The continence and sexual outcomes were assessed in patients 12 months after surgery. A nurse interviewed the patient regarding the continence outcomes during the clinic visits. Continence is defined as usage of less than 1 pad a day and IIEF–5 score was used to assess the potency of patients. Daytime continence could be achieved in 89.2%, while

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**Table 3. Pathology characteristics**

|                           | All patients (n=101) | Ileal conduit (n=28) | Neobladder (n=73) |
|---------------------------|---------------------|---------------------|------------------|
| Post–operative pT–stage (%) |                     |                     |                  |
| CIS                       | 7 (6.9)             | 1 (3.6)             | 6 (8.2)          |
| T0                       | 11 (10.9)           | 3 (10.7)            | 8 (11.0)         |
| T1                       | 6 (5.9)             | 0 (0)               | 6 (8.2)          |
| T2                       | 33 (32.7)           | 9 (32.1)            | 24 (32.9)        |
| T3                       | 31 (30.7)           | 8 (28.6)            | 23 (31.5)        |
| T4                       | 13 (12.8)           | 7 (25.0)            | 6 (8.2)          |
| Post–operative grade (%)  |                     |                     |                  |
| Low grade                | 0 (0)               | 0 (0)               | 0 (0)            |
| High grade               | 90 (100)            | 25 (100)            | 65 (100)         |
| pN stage (%)             |                     |                     |                  |
| N0                       | 78 (77.2)           | 22 (78.6)           | 56 (76.7)        |
| N+                       | 23 (22.8)           | 6 (21.4)            | 17 (23.3)        |
| Lymph node count, mean (range) | 20.6 (0–46)       | 16.8 (0–36)         | 23.3 (8–46)      |
| Positive margins, %      | 8.9                 | 14.3                | 6.8              |
| Concomitant prostate cancer (%) |                  |                     |                  |
| Gleason score (%)         | 29 (35.3)           | 13 (52.0)           | 16 (28.1)        |
| Gleason 6                 | 18 (62.1)           | 7 (53.8)            | 11 (68.8)        |
| Gleason 7a (Gleason 3+4)  | 6 (20.7)            | 2 (15.4)            | 4 (25.0)         |
| Gleason 7b (Gleason 4+3)  | 3 (10.3)            | 2 (15.4)            | 1 (6.2)          |
| Gleason 8                 | 2 (6.9)             | 2 (15.4)            | 0 (0)            |
| Positive margins (Prostate) | 10.3%               | 15.4%               | 6.3%             |

**Table 4. Early (<30 days) and late (>30 days) surgical complications**

|                      | Overall, n=101 | Ileal conduit, n=28 | Neobladder, n=73 |
|----------------------|---------------|---------------------|------------------|
|                      | Early | Late | Early | Late | Early | Late |
| Clavien              |        |      |        |      |        |      |
| Grade 1              | 11    | 1    | 4      | 0    | 7      | 1    |
| Grade 2              | 16    | 0    | 2      | 0    | 14     | 0    |
| Grade 3              | 18    | 10   | 3      | 2    | 15     | 8    |
| Grade 4              | 6     | 3    | 1      | 0    | 5      | 3    |
| Grade 5              | 0     | 0    | 0      | 0    | 0      | 0    |
| Total, %             | 50.5  | 13.9 | 35.7   | 7.1  | 56.2   | 16.4 |
complete nighttime continence was noted in 67.6% of patients who underwent intracorporeal neobladder. Erectile dysfunction was reported in 63.5% of men (Table 5).

**DISCUSSION**

RARC has been gaining popularity as a viable alternative to open radical cystectomy for patients with bladder carcinoma. However, it is still not as widely adopted as robotic radical prostatectomy for various reasons. Initial criticism was focused on the lack of oncologic outcome data. Recent reports have confirmed the long-term safety and efficacy of laparoscopic RC as well as of RARC [5]. Equivalent oncologic outcomes have been shown by using surrogate parameters such as nodal yield and margin status. Secondly, RARC especially intracorporeal diversion has always been considered a very lengthy procedure with the potential risk of complications associated with the steep Trendelenburg position. This may be true for the initial series; however, contemporary data has indicated competitive surgical times [9] and other studies have also shown that operating time and patient’s length of stay continues to improve with the learning curve [10]. Thirdly, RARC and extracorporeal urinary diversion has been deemed a cumbersome procedure consisting of a robotic part and an open extracorporeal part for urinary diversion. Many have hence questioned the point of performing RARC with extracorporeal diversion as this potentially takes away the advantages of minimally invasive surgery such as smaller wound incision and reduced bowel exposure. Wiklund and colleagues have pioneered the technique of intracorporeal neobladder formation following RARC. They followed the principles of open surgery in creating a Studer neobladder including proper folding [13]. Their approach has evolved over time leading to technical modifications and a reduction of complications and operative times. In a cumulative analysis of 70 patients with a median follow-up of 30.3 months, they found negative margins in 98.6%. Relevant complications occurred in 31.4% at 30 d and 18.6% at >30 d. At 90 d, the overall complication rate was 58.5%. The recurrence-free, cancer-specific, and overall survival at 24 months was 80.7%, 88.9%, and 88.9%. Daytime continence and satisfactory sexual function or potency at 12 months ranged between 70% and 90% in both men and women. These results are well in line with contemporary open series [7]. A retrospective comparison to open diversion in the framework of the International Robotic Cystectomy Consortium including 935 patients further confirmed the safety of intracorporeal diversion by showing lower risk of postoperative complication including gastrointestinal complications in these patients [14]. Notably, only 61 patients had undergone intracorporeal neobladder formation in this comparative study. In the U.S., similar approaches have been described. Although shorter follow-up with fewer patients, comparable results have been reported [8]. Herein, we present our cumulative experience with RARC and intracorporeal urinary diversion performed in two tertiary referral centers with robotic expertise. Surgery has been done according to previously published techniques and principles. This is a representation of a real life experience of RARC and intracorporeal urinary diversion outside of the pioneering centers. Many findings by the pioneer groups have been corroborated and their results have been widely replicated. Hence, RARC and intracorporeal urinary diversion may be safely implemented into clinical routine whenever adequate robotic experience is available. To the best of our knowledge, our report describes the largest series of RARC and intracorporeal diversion apart from the Karolinska group. Importantly, we have streamlined the approach with well-defined and reproducible steps. Obviously, our surgical times in the initial cases were long due to the learning curve. However, over time average operative time spent could be reduced to less than 6 hours. This is in line with what has been shown by various studies that robotic cystectomy and intracorporeal urinary diversion can be done safely with a structured approach in a high volume center [9, 15]. From our experience, another important element to a successful RARC with intracorporeal urinary diversion that provides patient with good oncological, functional and perioperative outcomes is a dedicated robotic team. RARC with intracorporeal diversion is extremely complex and can be intimidating for any

### Table 5. Functional and oncologic outcomes

|                          | All patients (n=101) | Ileal conduit (n=28) | Neobladder (n=73) |
|--------------------------|----------------------|----------------------|-------------------|
| Follow up, mo, mean (range) | 27.5 (1–52)          | 22.5 (3–52)          | 32.4 (1–52)       |
| Continence, %            |                      |                      |                   |
| Daytime                  | NA                   | NA                   | 89.2              |
| Nighttime                | NA                   | NA                   | 67.6              |
| Erectile Dysfunction (%) | 63.5                 | 100                  | 48.0              |
| Recurrences (%)          | 1 (1.0)              | 0 (0)                | 1 (1.4)           |
| Distant metastasis (%)   | 25 (24.8)            | 9 (32.1)             | 16 (21.9)         |
| Cancer Specific Survival, % (CSS) | 80.2              | 70.8                  | 84.0              |
| Overall survival, % (OS) | 69.8                 | 67.0                  | 71.0              |
young robotic surgeon. It helps to have a dedicated robotic team as familiarization is important not just for the surgeon, but also for the bedside assistants, scrub team as well as the theatre staff. In our practice, a dedicated team comprised of a senior resident and nurse practitioner participates routinely in all the cases. Teamwork from all the members of the team involved is crucial to ensure a smooth sailing surgery to minimize complications, conversion rate and shorten the operating time.

The potential advantages of intracorporeal urinary diversions include tension-free urethro–ileal anastomosis, smaller skin incision for delivery of specimen and, decreased bowel manipulation and exposure to external environment. All these factors can ultimately contribute the better outcomes in terms of better perioperative outcomes and lower risk of postoperative complications [1–5, 14].

Our results have shown the safety and reproducibility of this complex technique with comparable operating times, perioperative complications, functional and oncologic outcomes with the pioneer centers. In terms of hospital stay, our series showed a longer hospital stay compared to the contemporary series; this could be partly attributed to our subsidy system whereby the patients have to stay for 1 week to receive full subsidies. However, we face the similar limitations faced by previous authors such as retrospective nature, limited number of patients and follow up durations. However, current results seem to favor robotic cystectomy with intracorporeal urinary diversion; a conclusion which can only be established eventually with a randomized study of adequate power.

**CONCLUSIONS**

With the advancement of technology and refinement of surgical technique, it is a matter of time before more will embark on robotic cystectomy and intracorporeal urinary diversions. A standardized technique with a dedicated robotic team in a high volume center makes robotic intracorporeal urinary diversion a feasible and reproducible technique.

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