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15

Robot-Assisted Radical Cystectomy as a Treatment Modality for Patients with Muscle-Invasive Bladder Cancer

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1. Introduction

Over the last two decades open radical cystectomy and urinary diversion have become a widely accepted form of treatment in both men and women with transitional cell carcinoma of the bladder. In the mid-1980s orthotopic urinary diversion with anastomosis to the urethra became an oncologically and functionally acceptable option in appropriately selected male patients. With better understanding of the anatomy and of the continence mechanism, orthotopic urinary diversion was subsequently performed in the early 1990s in female patients[1].

Until today open radical cystectomy is still considered the gold standard treatment for patients with muscle-invasive transitional cell carcinoma of the bladder [2, 3]. This is based on the following observations: First, the best long-term survival rates and lowest local recurrence rates have been reported after radical cystectomy [4 5]. Second, the morbidity and mortality of radical cystectomy have significantly improved during the last decades, and good functional results in patients with orthotopic urinary diversions have been achieved [6 7]. Third, radical cystectomy and pelvic lymph node dissection provides the most accurate tumor staging, thus helps selecting patients for adjuvant treatment protocols [8 9].

Radical cystectomy performed through a laparoscopic approach was first described in 1992 [10]. Since then, laparoscopic radical cystectomy has been reported in over 500 patients and current results suggest that this approach may cause less blood loss, decreased postoperative pain and faster recovery compared to open surgery [11 12]. However, due to the technical difficulty (two-dimensional laparoscopic view, counterintuitive motion, poor ergonomics, and nonwristed instrumentation), the steep learning curve and the lack of long-term oncological results, this treatment has not been adopted by mainstream urology.

The introduction of robot assisted surgery for pelvic laparoscopy, especially in performing radical prostatectomy, has changed the possibilities of performing complicated operations in the small pelvis. Three-dimensional vision with ten-fold magnification and the dexterity provided by the endo-wrist (six degrees of freedom) allows the surgeon to operate the tips of the laparoscopic instruments like an open surgeon [13]. Thus, the surgeon will benefit from a faster learning curve as compared to conventional laparoscopy. Further, these advantages have allowed surgeons to translate standard open surgical procedures to a minimally invasive approach, especially its potential in operating in a narrow pelvis as well as for the reconstruction of the urinary tract.

With the beginning of robot-assisted pelvic surgery a decade ago, radical cystectomy and reconstruction of the urinary tract is currently possible. However, until today, results on robot-assisted radical cystectomy (RARC) are mainly reported from a few centers worldwide. Further, results on RARC with intracorporeal urinary diversion are sparse, as most surgeons perform the reconstructive part outside the abdomen due to technical difficulties and longer operative time.

2. Robot-assisted radical cystectomy

The history of robot-assisted radical cystectomy started with Beecken et al. who was the first to perform a RARC with intracorporeal formation of an ileal orthotopic bladder substitute in 2002 [14]. Operating time was 8.5 hours and blood loss 200ml. At five months post-operatively the oncological and functional result of the reservoir were considered excellent. Menon et al. reported the first series of RARC in 17 patients in 2003 [15]. In their series, an ileal conduit was performed in three patients, a W-pouch in ten, a double chimney in two, and a T-pouch in two cases. Mean operating time for radical cystectomy was 140 min and 120–168 min for the different urinary diversions, which were all performed extracorporeally. Mean blood loss was less than 150 mL, and surgical margins were negative in all cases.

Since then, several case series have been published, however, most RARC series comprise less than 100 cases per center [table 1]. Additionally, our current knowledge on RARC is mainly based on reports from less than twenty different surgical centers worldwide. In order to provide a better overview on the value of RARC, data from a mix of 15 academic and private centers from the USA and Europe are prospectively collected and the results reported by the International Robotic Cystectomy Consortium (IRCC) [16] [17] [18]. Despite increasing evidence that RARC seems as effective as open radical cystectomy, it is still too premature to draw any firm conclusions about the status of RARC.

3. Patient selection

Which patients are suitable for RARC using a minimal invasive approach? As patients planned for radical cystectomy are in general older and have a higher prevalence of smoking-related co-morbidities, pulmonary diseases may cause intraoperative problems. Some of these patients may even not be suitable for robot-assisted interventions because of the need for CO_2 insufflation and the steep Trendelenburg position. The cardiac and respiratory systems are especially vulnerable to the extreme and lengthy head-down position. However, in order to minimize these risks, a 25° Trendelenburg position during radical cystectomy and lymph node dissection is possible without affecting the surgical quality [19]. For the urinary diversion the Trendelenburg position can further be decreased to 15°, thus minimizing potential pulmonary complications.

A question mark regarding contra-indications in selecting patients for RARC remains. Presence of bulky disease, locally advanced disease, or enlarged lymph nodes have been considered relative contra-indications [20] [21]. Khan et al. reported specific surgery-related complications at RARC [22]. They found that patients with multiples intravesical therapies, such as mitomycin or BCG, are more likely to have adhesions between the bladder and the

Author (reference)	No. of pts.	Type of urinary diversion:	extracorporeal intracorporeal	Conversion to open surgery	Mean operative time (min)	Mean perioperative blood loss (ml)	Mean post op. hospital stay (days)	Positive margins (bladder)	No. of lymph nodes removed	Follow-up (months)
Beecken et al, 2003 [14]	1	Orthotopic neobladder	intracorporeal	no	510	200	n. a.	neg.	n. a.	n. a.
Menon et al, 2003 [15]	17	Cystectomy Ileal conduit (3) Orthotopic neobladder (14)	extracorporeal	1 pt	140 260 308	150	n. a.	neg.	x (4 – 27)	n. a.
Hemal et al, 2004 [	24	Ileal conduit (4) Orthotopic neobladder (20)	extracorporeal	no	228 - 348	100 - 300	4 - 5	neg.	3 - 27	n.a.
Galich et al, 2006 [33]	13	Ileal conduit (6) Orthotopic neobladder (5) Indiana pouch (2)	extracorporeal	no	697 (240 – 828)	500 (100 – 1000)	8 (4 – 23)	neg.	n. a.	n. a.
Rhee et al, 2006 [30]	7	Ileal conduit	extracorporeal	no	638 (592 – 684)	479	11 (6 – 16)	neg.	n. a.	n. a.
Abraham et al, 2007 [54]	14	Cystectomy Ileal conduit	extracorporeal	no	410 (340 – 545)	212 (50 – 500)	6 (4 – 7)	1 pt (pT4)	22.3 (13 – 42)	n. a.
Mottrie et al, 2007 [56]	27	Ileal conduit (19) Orthotopic neobladder (8)	extracorporeal	no	340 (150 – 450)	301 (50 – 550)	n. a.	neg.	23 (6 – 37)	10.2
Lowentritt et al, 2008 [38]	4/20#	Ileal conduit (4)	extracorporeal	no	350 (340 – 410)	300 (250 – 500)	5 (3 – 8)	neg.	12 (9 – 16)	n. a.
Murphy et al, 2008 [31]	23	Ileal conduit (19) Orthotopic neobladder (4)	extracorporeal	no	397 (314 – 480)	278 (49 – 507)	12 (8 – 15)	neg.	16 (7 – 25)	17 (4 – 40)
Wang et al, 2008 [32]	32	Ileal conduit (17) Orthotopic neobladder (12) Indiana pouch (3)	extracorporeal	no	390 (210 – 570)	400 (100 – 1200)	5 (4 – 18)	2 pts (pT3 N1)	17 (6 – 32)	n. a.
Woods et al, 2008 [34]	27	Ileal conduit (?) Orthotopic neobladder (?)	extracorporeal	no	400 (225 – 660)	277 (50 – 700)	n. a.	2 pts. (pT4)	12 (7 – 20)	n. a.
Hemal et al, 2008 [55]	6	Ileal conduit (5) Orthotopic neobladder (1)	extracorporeal	no	330	200 (150 – 1000)	9.2	no	12 (4 – 19)	n. a.

n. a. not available, # report on 4 female pts., ≠one case without urinary diversion, renal failure, ǂ results from pts. < 70years vs. ≥ 70 years)

Author (reference)	No. of pts.	Type of urinary diversion:	extracorporeal intracorporeal	Conversion to open surgery	Mean operative time (min)	Mean perioperative blood loss (ml)	Mean post op. hospital stay (days)	Positive margins (bladder)	No. of lymph nodes removed	Follow-up (months)
Yuh et al, 2008 [40]	54	n. a.	extracorporeal	2 pts.	n. a.	557	9.1	0 pts. (pT0- pT2) 7 pts. (pT3-pT4)	20 (SD 12) pT0 - pT2 15 (SD 7) pT3 - pT4	n. a.
Gamboa et al, 2009 [57]	41	Ileal conduit (24) Orthotopic neobladder (17)	intracorporeal	no	498 (320 – 805)	254 (50 – 700)	8 (5 -37).	2 pts. (pT4)	25 (4 – 68).	n. a.
Kauffman et al, 2009 [39]	79	Ileal conduit (46) Orthotopic neobladder (33)	extracorporeal	n. a.	378	460	5	6 pts.	18.4	n. a.
Schumacher et al, 2009 [63]	18	Ileal conduit (5) Orthotopic neobladder (13)	intracorporeal	3 pts.	501 (382 – 750)	525 (200 – 2200)	12 (6 – 79)	1 pt. (pT4)	20 (10 – 42)	25 (4 – 58)
Richards et al, 2010 [65]	35	Ileal conduit (30) Orthotopic neobladder (5)	extracorporeal	no	530 (458 – 593)	350 (250 – 600)	7 (6 – 9)	1 pt.	16 (11 – 24)	n.a.
Guru et al, 2010 [52]	26	Ileal conduit (13) Ileal conduit (13)	intracorporeal extracorporeal	no	391 387	315 454	8.8 (5 – 23) 8.5 (6 – 14)	1 pt. (pT4)	25 26	n. a.
Pruthi et al, 2010 [68]	100≠	Ileal conduit (61) Orthotopic neobladder (38)	extracorporeal (94) intracorporeal (5)	no	276	271	4.9	neg.	19 (8 - 40)	18.4 (5 - 44)
Lavery et al, 2010 [66]	15	n. a.		no	423 (300 – 506)	160 (50 – 500)	3.4 (3 – 7)	neg.	41.8 (18 – 67)	3
Coward et al, 2011≢[22]	99	Ileal conduit (60) Orthotopic neobladder (39)	extracorporeal	no	288 vs. 264	289 vs. 249	4.7 vs. 5.0	neg.	19.5 (8 – 40) 18.1 (10 – 37)	n. a.
Khan et al, 2011 [45]	50	Ileal conduit (45) Orthotopic neobladder (5)	extracorporeal	no	361 (240 – 600)	340 (100 1150)	10 (5 – 24)	1 pt. (pT4)	17 (11 – 28)	3
Manoharan et al, 2011 [67]	14	Orthotopic neobladder (14)	extracorporeal	no	310 (± 220)	360 (± 48)	8.5	neg.	12 (± 3)	n. a.
Cha et al, 2011 [72]	85	Ileal conduit Orthotopic neobladder	extracorporeal	no	n. a.	n. a.	n. a.	5.9%	19	18
Schumacher et al, 2011 [35]	45	Ileal conduit (9) Orthotopic neobladder (36)	intracorporeal	3 pts.	477 (325 – 760)	550 (200 – 2200)	9 (4 – 78)	1 pt. (pT4)	22.5 (10 – 52)	24 (3 – 77)

Table 1. Contemporary reports/series of robotic-assisted laparoscopic radical cystectomy (RARC) and urinary diversion for TCC of the bladder.

surrounding structures, especially the rectum, rendering dissection difficult. Thus, careful dissection is required in developing the rectovesical plane to avoid injury of the rectum. Prior abdominal surgery, radiotherapy or neoadjuvant chemotherapy may be relative-contraindications for RARC, as these factors can significantly increase the degree of technical difficulty [22 23].

Patient selection makes a direct comparison between open radical cystectomy series and smaller RARC series difficult. Results from open high-volume centers indicate that approximately two-thirds of patients at radical cystectomy have organ-confined disease, whereas one-third has non-organ-confined disease [24 25 26 27 28 29]. In general, the percentage of patients with non-organ-confined disease undergoing RARC is substantially lower than figures reported from major series from open radical cystectomy [table 2] [30 31 32 21, 33-40].

Recent multi-institutional results from the International Robotic Cystectomy Consortium (IRCC) of 527 patients treated with RARC show similar figures regarding the numbers of patients with organ-confined (65%) vs. non-organ-confined (35%) disease, as with open radical cystectomy series [18]. However, data on neoadjuvant chemotherapy were not reported in this series.

4. Surgery-related complications

Although the number of RARC cases reported in the literature is relatively small, the intraoperative complication rate seems comparable to open radical cystectomy series. Nix et al. found in a prospective randomized trial of robotic (n = 21) versus open (n = 20) radical cystectomy no difference in the absolute number of complications (p = 0.279) [41]. Less blood loss was observed in the robotic group (mean 258 mL) compared to the open group (mean 575 mL). Similarly, Wang et al. reported no difference regarding intraoperative complications in their prospective trial between robotic (n = 33) and open radical cystectomy (n = 21) [32]. Again, less blood loss was noted with RARC (mean 400 mL, range 100–1200 mL) compared to open radical cystectomy (mean 750 mL, range 250–2500 mL). Galich et al., in a comparative analysis of early postoperative outcomes following robotic (n = 13) and open (n = 24) radical cystectomy, found no difference between groups regarding surgery-related complications and blood loss [33]. Kauffman et al. collected data on 79 consecutive patients treated with RARC and extracorporeal urinary diversion [42]. In their series, high-grade complications (Clavien III–V) occurred in 16 patients (21%) during the first 3 months postoperatively. Urinary obstruction, intra-abdominal abscess, uro-enteric fistulas, and gastrointestinal bleeding were the most common high-grade complications. The high percentage of overall urinary obstruction (8%) despite extracorporeal urinary diversion without robotic assistance is of concern [42]. Khan et al. reported an 8% ureteric stricture rate, with 6% strictures occurring on the left side in their series of 50 RARC cases [22]. Results from open radical cystectomy series report an uretero-intestinal stricture rate of less than 3% [5]. Performing the anastomosis between the ureters and the urinary diversion outside the abdomen through a small abdominal incision may only be possible with relatively long ureters, thus increasing the risk for ischemic complications. Resection of the ureters at the level where they cross over the common iliac artery minimizes the risk of strictures at the uretero-intestinal anastomosis due to ischemia [43].

Different parameters may affect outcome and risk for surgery-related complications such as age, higher ASA score or previous surgery. Butt et al. did not find a significant association between age, BMI, ASA score and complication rate in their series of 66 RARC cases [44].

Author (reference)	No. of pts.	Age (years)	Organ-confined tumors ≤ pT2 (%)	Non-organ-confined tumors > pT2 (%)	Node positive disease (%)	Positive margins (%)	Follow-up (months)
Open radical cystectomy:							
Stein et al, 2001 [24]	1054	66 (range 22 - 93)	669 (64%)	385 (36%)	246 (23%)	1%	122 (range 0 - 336)*
Manoharan et al, 2009 [28]	432	69 (SD ± 9)	262 (60.5%)	170 (39.5%)	90 (21%)	5%	38 (range 1 - 172)
Dotan et al, 2007 [29]	1589	n. a.	858 (54%)	727 (46%)	288 (24%)	4.2%	up to 15 years
Hautmann et al, 2006 [26]	788	65 (SD ± 10)	528 (67%)	260 (33%)	143 (18%)	< 1%	54 (range 0.1 - 223)
Robot-assisted radical cystectomy:							
Galich et al, 2006 [33]	13	70 (range 38 - 88)	7 (54%)	6 (46%)	2 (15%)	0%	n. a.
Rhee et al, 2006 [30]	7	60 (SD ± 9)	6 (86%)	1(14%)	2 (28%)	0%	n. a.
Guru et al, 2008 [36]	58/ 67≠	67 (range 36 - 90)	29 (50%)	29 (50%)	17 (29%)	6 (10.3%)	n. a.
Wang et al, 2008 [32]	32	70 (range 41 - 84)	23 (72%)	9 (28%)	6 (19%)	2 (6%)	n. a.
Murphy et al, 2008 [31]	23	65 (SD ± 9.4)	17 (74%)	6 (26%)	2 (8.7%)	0%	17 (range 4 - 40)
Dasgupta et al, 2008 [37]	20	66 (range 36 - 77)	15 (75%)	5 (25%)	2 (10%)	0%	23 (range 7 - 44)
Lowentritt et al, 2008 [38]	4/ 20#	69.5 (SD ± 10.5)	1 (25%)	3 (75%)	1 (25%)	0%	n. a.
Woods et al, 2008 [34]	27	67 (range 49 - 80)	n. a.	n. a.	9 (33%)	2 (7.4%)	n. a.
Yuh et al, 2008 [40]	54	67	19 (35%)	35 (65%)	n. a.	7 (13%)	n. a.
Kauffman et al, 2009 [39]	79	71 (SD ± 11)	47 (59%)	32 (41%)	12 (15%)	6 (7.6%)	26.4
Pruthi et al, 2010 [68]	100	65.5 (range 33 - 86)	87 (87%)	13 (13%)	20 (20%)	0%	18.4 (range 5 - 44)
Schumacher et al, 2011 [35]	45	60.6 (range 37 – 79)	35 (77.8%)	10 (22.2%)	9 (20%)	1 (2.2%)	24 (range 3 – 77)

n. a. not available; * 91% of pts with FU > 3 years; # results on 4 female cases; ≠58 pats eligible for analysis

Table 2. Patient characteristic of contemporary robotic-assisted radical cystectomy (RARC) and open radical cystectomy series for TCC of the bladder.

Similar, Coward et al. did not find worse outcomes in terms of complications when comparing older patients (≥ 70 years) with higher ASA scores vs. younger patients (< 70 years) treated with RARC [45].

Schumacher et al. assessed the surgery-related complications at RARC with total intracorporeal urinary diversion during their learning curve [35]. A total of 45 patients were pooled in 3 consecutive groups of 15 cases each to evaluate the complications according to the Clavien classification [46]. Overall, fewer complications were observed between the groups over time, with a significant decrease in late versus early complications (P = 0.005 and P = 0.058). However, the early Clavien grade III complications remained significant (27%) and did not decline with time; thus indicating the complexity of the intracorporeal urinary diversion. Khan et al., assessed early surgery-related complications using also the Clavien Classification [22]. Early complications were observed in 34% of patients. Clavien grade IIIa/b complications were seen in 29% of their patients. Both series have somehow a lower complication rate compared to the 64% complication rate from a large series of 1142 open radical cystectomy patients from the Memorial-Sloan-Kettering Cancer Center (MSKCC) [47]. The higher percentage of non-organ-confined tumors in the open series from MSKCC may be one factor to explain this difference in favor of the robotic approach.

Hayn et al., from the IRCC assessed whether previous robotic surgical experience affects on the implementation and execution of robot-assisted radical cystectomy [17]. They found that previous robot-assisted radical prostatectomy (RARP) case volume might affect the operative time, blood loss, and lymph node yield at RARC. In addition, surgeons with increased RARP experience operated on patients with more advanced tumors. Previous RARP experience, however, did not appear to affect the surgical margin status.

5. Lymphadenectomy

Pelvic lymphadenectomy at radical cystectomy is the standard treatment for patients with muscle-invasive bladder cancer. Radical cystectomy series report that approximately 25% of patients initially staged T1–T4 N0 M0 who undergo lymphadenectomy have lymph node metastases; and the absolute number of positive nodes removed affects survival [9 48].

It has been stated that, as a guideline, removal of >20 nodes per patient should be the aim [48]. Others have reported an improved cancer-specific survival rate of 65% when ≥ 16 nodes were retrieved compared to 51% when < 16 nodes were retrieved [49]. Whereas some experts do recommend that at least 10 nodes should be removed at pelvic lymph node dissection [50 51]. While assessing the lymph node counts obtained after lymph node dissection at radical cystectomy from various institutional series, huge differences in node count are noted. Median node count has been reported to vary from 8 to 80, and is also affected by the extent of a pelvic lymphadenectomy [9 24 52 53 47 48 54 55 56 57 58]. Interindividual variances, sending separate or en-bloc nodal packages, and the pathologic work-up of the specimens may explain differences in reporting on the number of nodes removed/detected by the pathologist [58 59]. Other factors such as the commitment of the surgeon in performing a lymph node dissection or selecting patients for more or less extensive lymphadenectomy may explain differences in nodal count [60].

Controversy still persists regarding the boundaries and terminology used in lymph node dissection. Mills et al. describe a *standard* lymph node dissection that includes removal of nodal tissue up to and including the common iliac bifurcation, including the internal iliac vessels, presacral area, obturator fossa, external iliac vessels, and distal part of the common iliac artery [61]. In order to avoid injury to the hypogastric nerves, nodes medial to the ureter (proximal half of the common iliac artery, aortic bifurcation) are not removed. In contrast, Stein et al. define an *extended* lymph node dissection as including all nodal tissue in the boundaries of: the aortic bifurcation and common iliac vessels (proximally); the genitofemoral nerve (laterally); the circumflex iliac vein and lymph node of Cloquet (distally); the hypogastric vessels (posteriorly), including the obturator fossa, pre-sciatic nodes bilaterally; and the presacral lymph nodes anterior to the sacral promontory [62].

Data on lymph node yield and oncological outcome in RARC series are still limited, however, node counts are similar to open radical cystectomy series [21 31 35 34 36 63]. Earlier reports from various RARC series describe mostly the boundaries of a *limited* (obturator fossa only) or *standard* template with less than a median of 20 nodes removed [63]. A recent report by Pruthi et al. performing an *extended* lymph node dissection, described a median node yield of 28 nodes (range 12–39) [64]. Schumacher et al. found similar node counts in their series of 45 patients with a mean of 22.5 nodes (range 10 - 52) removed [35]. Applying a template up to the aortic bifurcation resulted in a mean of 32 nodes removed. Richards et al. compared lymph node counts from 35 open radical cystectomy cases to their first 35 RARC cases [65]. Median total lymph node yield was similar between groups, with 15 nodes (range 11 - 22) in the open cystectomy group compared to 16 nodes (range 11 - 24) in the RARC group. Lavery et al, reported in their first 15 RARC cases undergoing an extended pelvic lymphadenectomy up to the aortic bifurcation a mean nodal yield of 41.8 nodes (range 18 - 67) [66]. Kauffmann et al. applying a similar template at RARC found a mean of 19.1 nodes (range 0 - 56) removed [42]. Evaluating the number of nodes removed from different institutions, the IRCC reported that at RARC 82.9% underwent a pelvic lymphadenectomy, which resulted in a mean of 17.8 nodes (range 0 - 68) removed [18]. According to these reports, it seems that robotic lymphadenectomy applying an *extended* lymph node dissection template, if indicated, up to the aortic bifurcation is technically feasible with intraoperative morbidity similar to open series [63].

6. Urinary diversion

The first case of RARC with intracorporeal urinary diversion was performed by Beecken et al. in 2002 [14]. Operative time was 8.5 hours, and therefore attention was turned towards extracorporeal urinary diversion in order to decrease operative times. Menon et al. were the first to describe their technique of extracorporeal diversion, using a 5–8 cm mid-line incision [15]. Until today, the majority of urinary diversions in conjunction with RARC are done extracorporeally [table 1] [67]. However, standardization of the intracorporeal procedure and decreasing operative times might turn the interest towards this approach [19 68]. We have previously reported our results in a series of 18 patients treated with RARC and totally intracorporeal urinary diversion, later, results in 45 patients were published [19 35]. Mean operative time was 476 min (range 325–760) and mean blood loss 669 mL (range 200–2200) [35]. Whether there is an advantage of performing the complete procedure intracorporeally or not is less clear. At least in female patients, the specimen can be removed through an incision via the vaginal wall, thus avoiding a mid-line incision. The technical difficulties in performing the urinary diversion totally intracorporeally have so far prevented its wide-spread adoption. Results reported by Schumacher and co-workers indicate at least at the beginning of their learning curve increased surgery-related complications using an intracorporeal urinary diversion approach [35]. Rehman et al. reported on 9 patients treated with RARC and totally intracorporeal confection of an ileal conduit [69]. One postoperative iatrogenous necrosis of the ileal conduit, probably caused by retraction of the organ bag occurred.

7. Oncologic outcome

To objectively assess oncological outcomes in patients treated either with open radical cystectomy or RARC for bladder cancer one needs to focus on: long-term cancer control, surgical quality (positive margins), tumor spillage, and port site metastasis.

Today, the highest long-term survival rates were reported for open radical cystectomy with an extended lymph node dissection. Stein et al. reported 5-year and 10-year recurrence-free survival rates of 68% and 60%, respectively, among 1,054 patients treated with radical cystectomy and extended lymph node dissection with curative intent [24]. For lymph node-negative, organ-confined disease, 5-year and 10-year recurrence-free survival rates were 85% and 82%. Similar results have been reported from other high-volume centers performing open radical cystectomy [25 26 27 28 29].

Whether the same cancer control rates equivalent to results from open radical cystectomy series can be achieved with RARC is still unknown; to date there are no long-term data available [70]. Median time to any recurrence after radical cystectomy is approximately 12 months, whereas 86% of recurrences occur within 3 years [24]. The mean follow-up in the current RARC series ranged from 3 to 77 months [tables 1 and 2]. However, in all of these RARC series median follow-up is short (<24 months), and reported survival data in which all patients have passed at least a 12 months follow-up do not exist.

The surgical quality at radical cystectomy independent of the surgical approach is essential for optimal local cancer control. Thus, negative margins must be achieved to avoid local tumor recurrence, which ultimately results in the death of the patient. Positive surgical margins have been reported to be 5% or less in high-volume open radical cystectomy series [25 26 27 28 29]. The incidence of positive margins at RARC ranged from 0% to 13% [21 30 31 32 34 36 37 38 39 40 71 72]. Guru et al, reported a 10.3% positive margin rate at RARC, whereas Yuh et al. found 13% positive margins in their patients [36 40]. Whether this high positive margin rate is attributable to the learning curve in these series is not clear. Data from the IRCC showed an overall 7% positive margin rate in their pooled 496 patients [17]. For patients with pathologic stage ≤ T3, 3.7% had a positive margin, whereas for patients with pathologic stage T3 or T4, 16% had a positive margin. The authors found with increasing surgical experience at RARC an improvement of their positive margin rate [17].

Port site metastasis in urological malignancies are of concern; they do occur, albeit infrequently. The etiology of port site metastasis is unknown. Port site metastasis has been reported after RARC and laparoscopic radical cystectomy for bladder cancer [73 74].

8. Post-operative recovery

Perioperative pathophysiology and care suggest that a multitude of factors contribute to postoperative morbidity, length of hospital stay, and convalescence in patients undergoing surgery [75]. Radical cystectomy is still associated with significant perioperative morbidity—this despite the implementation of accelerated postoperative recovery programs, or so-called "fast-track" surgery [76]. Comparison between historical cystectomy series and recent studies regarding post-operative recovery are difficult, as the concept of "fast-track" surgery has only been adopted by the urologic community during the last decade.

In order to reduce perioperative morbidity at cystectomy, Pruthi and co-workers have implemented and continuously improved the perioperative management in their 362 patients [77]. Reported findings from the last 100 (open and RARC) of these 362 cystectomy cases showed favorable return of bowel function (mean time to flatus 2.2 days, and mean time to bowel movements 2.9 days), the majority of patients being discharged after a mean of 5 days. Readmission was observed in 12% of patients, and the most common reasons for readmission were urinary tract infection (3%), gastrointestinal disorders (2%), and deep venous thrombosis (2%). The same group has published a randomized trial and assessed perioperative outcomes in patients treated with open versus robotic radical cystectomy [41]. Patients undergoing robotic cystectomy had longer operative times (4.2 versus 3.5 hours; $p < 0.001$) and less blood loss (258 versus 575 mL; $p < 0.001$) than did patients with open cystectomy. Further, patients in the robotic group demonstrated a faster return of bowel activity (median time to flatus 2.3 days versus 3.2 days, and time to bowel movement 3.2 days versus 4.3 days). Hospital stay did not differ between groups (robotic 5.1 days, open 6.0 days; $p = 0.239$). Patients in the robotic group required significantly less analgesia than did patients with the open approach ($p = 0.019$). Similar results have been reported by Ng et al., comparing 104 open cystectomy with 83 RARC cases [78]. The robotic group demonstrated decreased blood loss (460 mL versus 1172 mL; $p < 0.0001$) and shorter length of hospital stay (5.5 days versus 8 days; $p < 0.0001$) than did the open cystectomy group. Wang et al., comparing open radical cystectomy with RARC patients, reported reduced blood loss, faster return to regular diet, and shorter hospital stay in the robotic group [32]. One may argue that fewer non-organ-confined tumors (28%) in the RARC group may have influenced their results compared to 57% non-organ-confined tumors in the open group. A recent study by Coward et al. found similar results regarding time to flatus (median 2 days) and time to bowel movements (median 3 days) after RARC in their series [45].

Despite the presumed advantages of less postoperative pain, faster return of bowel movements, shorter hospital stay, and overall quicker recovery over open surgery, the exact role of laparoscopy in improving perioperative outcomes remains unclear.

9. Quality of life

Quality of life (QoL) and postoperative recovery after surgery are important factors with direct financial implications for the health care system. Karvinen et al. reported on the effect of exercise and QoL in survivors of bladder cancer [79]. Findings from their study indicate that exercise is positively associated with QoL and the ability to perform physical activity results in increased QoL. If patients are able to return more quickly to preoperative levels with minimally invasive surgery, i.e. robotic surgery, they might be able to initiate exercise sooner, which in turn improves their QoL.

Yuh et al. evaluated QoL in a small single-center study after RARC [20]. Despite some inheriting limitations of the study design, QoL appeared to return to base-line by 3 months after RARC, and improved further at 6 months. The authors postulated that short-term improvement in QoL might also have positive implications regarding initiating adjuvant treatment protocols in these patients. Further studies are required to assess the physical and psychological implications of robotic surgery on QoL in patients undergoing radical cystectomy.

Functional results have been reported after open nerve-sparing radical cystectomy and orthotopic bladder substitution, however, reports from RARC series assessing continence and potency rates are sparse [7 80].

10. Costs

The introduction of new and costly technologies into daily clinical practice has been criticized, especially during periods of economic uncertainty. With the introduction of expensive robotic technology cost-effectiveness has become more important. For robot-assisted radical prostatectomy some studies have shown volume-dependant cost advantages [81 82]. Less information on cost-analysis is available for RARCS.

Smith et al., from North Carolina, US, performed a cost analysis at their institution between robotic and open radical cystectomy [83]. The financial costs of robotic and open radical cystectomy were categorized into operating room and hospital components, and further divided into fixed and variable costs for each. Variable costs were related to several factors, such as length of hospital stay. For each procedure the means of 20 cases were used to perform a comparative cost analysis. Based on their results, robotic cystectomy is associated with an overall higher financial cost of $1,640.

Martin et al. performed a detailed cost-analysis for open radical cystectomy vs. RARC cases [84]. They found that the most critical parameters for increased costs were operative time and hospital stay, which favored the robotic approach at their institution. Further, they stated that the real cost advantages are mostly seen when indirect costs are considered, such as treatment of perioperative complications or readmission rates due to complications.

Costs are difficult to measure and comprise other factors than just the perioperative period. Thus, earlier return to normal activity and reduced sick-leave might be important factors justifying these additional costs offered by the robotic approach.

11. Conclusions

Based on the current literature RARC is evolving rapidly as an alternative technique to open surgery in patients requiring radical cystectomy and urinary diversion. Lymph node yield and perioperative outcomes are similar to open radical cystectomy series; however, long-term oncological results are unknown. Several small prospective or randomized single-center trials showed comparable results between RARC and open cystectomy. However, the surgical procedure is technically demanding, especially when performing the urinary diversion totally intracorporeal. It is advisable to concentrate this type of surgery to high-volume centers where robotic expertise and technology is available.

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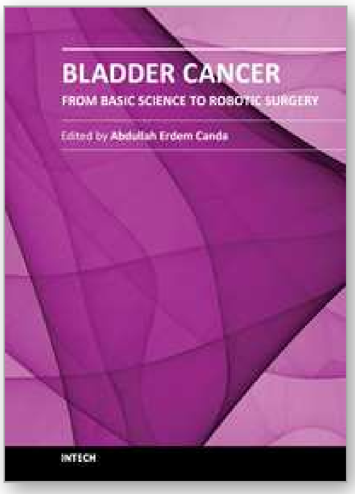

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This book is an invaluable source of knowledge on bladder cancer biology, epidemiology, biomarkers, prognostic factors, and clinical presentation and diagnosis. It is also rich with plenty of up-to-date information, in a well-organized and easy to use format, focusing on the treatment of bladder cancer including surgery, chemotherapy, radiation therapy, immunotherapy, and vaccine therapy. These chapters, written by the experts in their fields, include many interesting, demonstrative and colorful pictures, figures, illustrations and tables. Due to its practicality, this book is recommended reading to anyone interested in bladder cancer.

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