The current status of robot-assisted cystectomy

Stavros Ioannis Tyritzis^{1,2*}, Justin W. Collins^{1,2}, Nils Peter Wiklund^{1,2}

¹Department of Molecular Medicine and Surgery, Section of Urology, Karolinska Institute, Stockholm, Sweden, ²Center for Minimally Invasive Urological Surgery, Athens Medical Center, Athens, Greece *E-mail: styritzis@gmail.com

ABSTRACT

Robot-assistance is being increasingly used for radical cystectomy (RC). Fifteen years of surgical evolution might be considered a short period for a radical procedure to be established as the treatment of choice, but robot assisted radical cystectomy (RARC) is showing promising results when compared with the current gold standard, open RC (ORC). In this review, we describe the current status of RARC and continue the discussion on the on-going RARC versus ORC debate.

INTRODUCTION

Bladder cancer is a lethal disease. A global overview of 2012 showed an incidence of 430,000 cases and a death toll of more than 160,000 cases.^[1] The highest mortality rates were seen in Europe, around eight deaths per 100,000 patients.^[1] Despite these numbers, the oncological efficacy of any available treatment for bladder cancer has not significantly improved the surivival rates over the past 30 years.^[2] RC is a surgical procedure with high postoperative complication rates and there is need for minimizing surgical morbidity. In addition, RC should aim to provide good functional outcomes. The challenge for bladder cancer surgeons is to extirpate the disease and deliver an acceptable postoperative quality of life. In this effort, minimally invasive surgery, and especially robot-assisted RC (RARC) has emerged as an alternative to open surgery.

RARC has been adopted globally, and its use has increased more than 25-fold, from 0.7% to 18.5% in 2012.^[3] Recent data from high-volume centers and registries are reporting promising results. In this review, we discuss the current knowledge on RARC, namely its oncological efficacy, functional outcomes,

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and safety. Moreover, we will discuss the available evidence comparing RARC versus open RC (ORC).

COMPLICATIONS

Even the most experienced high-volume institutions exhibit high rates of overall complications of RC reaching up to 64%,^[4] while the rates of Clavien >3 complications can be as high as 41%.^[5] These figures reflect the necessity of centralization of RC in dedicated centers. Another critical factor is to optimize the surgical and clinical pathway of a patient undergoing RC. The use of enhanced recovery protocols (ERP) with RARC utilizing totally intracorporeal techniques for urinary diversion aim to improve patient recovery compared to traditional perioperative management.^[6] ERPs have been shown to reduce the length of stay by 1–2 days, while minimizing postoperative ileus, complications, and risk for readmission at 30 days.^[7] The ERP concept was introduced by the open colorectal surgeons^[8] more than 30 years ago. An effort has been made for ERP to be adopted globally, especially by robotic surgeons, but it remains underutilized,^[6] this despite the fact that minimally invasive surgery is included as one of the 22 elements of an ERP for RC.^[9]

Concerning the totally intracorporeal technique, results published by the international RC consortium (IRCC),

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have shown that shifting to the intracorporeal technique is safe and advantageous.^[10] In a multi-center, retrospective study of 167 patients undergoing RARC with intracorporeal diversion (ileal conduit: 106; neobladder: 61), and 768 patients undergoing RARC with extracorporeal diversion (ileal conduit: 570; neobladder: 198), the intracorporeal patients had a lower risk of postoperative complication at 90 days postoperatively. (32%) (odds ratio: 0.68; 95% confidence interval, 0.50–0.94; P = 0.02).^[10] In addition, gastrointestinal and infectious complications were significantly lower in pateints in whom an intracorporeal approach was used.^[10] The obvious advantages of the totally intracorporeal technique are the protection of bowel inside the abdomen, no hypothermia or loss of fluids through osmosis, less bleeding, no need for extensive ureteral dissection, which may lead to ureteral strictures, and minimal surgical trauma.^[11]

The lack of ERP and underutilization of the intracorporeal approach might jeopardize an accurate interpretation of the results of RC studies. Several studies including published randomized control trials (RCTs), are limited by these factors. In these studies, significant heterogeneity also exists in the types of urinary diversion used.

Table 1 shows a chronological evolution of the results of RARC, by looking at two time-periods.(Early period (2008–2012) and late period (2012–2017)).^[12-35] All the included studies may overlap and may also include periods of surgeons' learning curve. The fact that in the late period, we see more "mature" studies, does not result in significant improvements in the perioperative or oncological outcomes.

Apart from individual RARC series, we have identified 12 systematic analyses^[26,27,29,36-42] and two meta-analyses of the 4 published RCTs^[43,44] since 2013. Table 2 summarises which approach to RC performs significantly better in important surgical and oncological parameters. Apart from operation time, blood loss, positive surgical margins, and survival, other parameters remain debatable with some showing a trend toward RARC's superiority. As an example, as regards overall complications, five studies favor RARC^[36,38-40,45] and six studies state that both procedures are equal.^[29,37,41,43,44,46] As for the length of stay, seven studies are in favor of RARC^[36-41,45] and three report equal results,^[43,44,46] and as for lymph node yields, three studies show an advantage of RARC^[36,39,41] and eight indicate equivalence between the two.^[26,27,29,38,42-45] It is however clear that RARC performs as expected; as a minimally invasive procedure, providing

Author	Year	Patients (n)	Follow-up (months)	Complication rates (%)	Mortality (%)	PSM (%)	LNY (%)	OS (%)	CSS (%)	DFS (%)
				RARC early peri	od					
Dasgupta <i>et al</i> . ^[12]	2008	20	23	10	0	0	16	95	NR	90
Pruthi et al.[13]	2010	100	13	36	NR	0	19	NR	NR	NR
Hayn <i>et al.</i> ^[14]	2010	496	NR	NR	NR	7	18	NR	NR	NR
Jonsson <i>et al</i> . ^[15]	2011	45	25	39-33 (early-late)	2.2	2.2	19	NR	84	86
Hayn <i>et al.</i> ^[16]	2011	156	9	51.9	5.8	NR	NR	NR	NR	NR
Goh <i>et al</i> . ^[17]	2012	24	3	29.2-10 (early-late)	0	0	55	NR	NR	NR
Smith et al.[18]	2012	227	NR	30	0	2.2	18	NR	NR	NR
Yuh <i>et al.</i> ^[19]	2012	241	NR	35	4.1	NR	NR	NR	NR	NR
				RARC late perio	bd					
Collins et al.[20]	2014	113	25	47.8 (17 clavien ≥3)	0.9	5.3	20.7	80.3	81.1	NR
Azzouni et al.[21]	2013	100	>3	81.1 (19 clavien ≥3)	1	4	24	NR	NR	NR
Niegish <i>et al.</i> ^[22]	2014	64	9.1	36 (clavien ≥3)	3.1	6.4	20	65	NR	75
Raza et al.[23]	2014	99	43	NR	NR	8	20.7	42.4	67.8	52.5
Yuh <i>et al</i> . ^[24]	2014	162	52	82.1 (37 clavien ≥3)	NR	4.3	28	54	80	74
Sim <i>et al</i> . ^[25]	2015	101	27.5	64.3 (36.6 clavien ≥3)	0	8.9	20.6	80.2	69.8	NR
Yuh et al.[26]	2015	638	NR	NR	NR	5.6	19.3	39-66	53-74	66-80
Raza et al.[27]	2015	702	67	NR	NR	8	16	67	75	50
Asimakopoulos et al.[28]	2016	40	26.5	30-32.5 (early-late)	0	2.5	19	NR	NR	NR
Gandaglia <i>et al.</i> ^[29]	2016	155	42	NR	NR	9	11	65.2	73.5	53.7
Pyun <i>et al.</i> ^[30]	2016	70	NR	46.9 (20.3 clavien ≥3)	NR	0	26.7	NR	NR	NR
Simone et al.[31]	2016	45	24	44.4 (17.8 clavien ≥3)	0	0	35	82.4	82.3	72.5
Kim <i>et al.</i> ^[32]	2016	58	28.8	NR	3.4	3.4	18	77	80	75
Bak <i>et al</i> . ^[33]	2016	42	40	64.3 (26.2 clavien ≥3)	0	NR	NR	75	NR	75
Tan <i>et al</i> . ^[34]	2017	134	3	54.5 (14.9 clavien ≥3)	2.2	7.5	15.3	NR	NR	NR
DiLizia et al.[35]	2017	76	36	47 (12 clavien ≥3)	0	5	16	85.7	NR	NR

OS=Overall survival, CSS=Cancer-specific survival, DFS=Disease-free survival, NR=Not reported, RARC=Robot-assisted radical cystectomy, PSM=Positive surgical margins, LNY=Lymph node yield

Table 2: Robot-assisted (robot-assisted radical cystectomy) versus open radical cystectomy performance in major surgical and oncological variables based on systematic analyses and meta-analysis of published studies

Performs better	References								
ORC	[29,36-40,43-45]								
Equal? (trend	[29,36-41,43-46]								
for RARC's									
advantage)									
RARC	[29,36,38-40,43-46]								
RARC	[29,36-41,43-46]								
Equal	[26,27,29,36,38-39,42-45]								
Equal	[26,27,29,36,38-39,42-45]								
Equal	[26,27,29,38,41,45]								
	Performs better ORC Equal? (trend for RARC's advantage) RARC RARC Equal Equal								

 $\mathsf{ORC}{=}\mathsf{Open}$ radical cystectomy, $\mathsf{RARC}{=}\mathsf{Robot}{-}\mathsf{assisted}$ radical cystectomy, $\mathsf{LNY}{=}\mathsf{Lymph}$ node yield

less blood loss and transfusions, less length of stay (LOS) and probably less overall complications, although the latter aspect is not yet verified. In the recently announced results of RAZOR study, which is a 1:1 prospective, randomized, noninferiority trial comparing RARC to ORC, the intraoperative and postoperative transfusion rates as well as mean blood loss were significantly lower for RARC (42% versus 91% and 277.5 cc versus 558.8 cc, respectively).^[47] It is noteworthy that in the same study, no other difference was recorded in postoperative complications. RARC had 58% and ORC had 56% overall complications with similar results in minor and major complications. Clavien 3–5 complications were 18.7% for RARC and 17.6% for ORC.^[47]

Blood loss and transfusion are considered as minor complications, by the Clavien-Dindo classification system, but it seems that they have a significantly negative impact on the oncological outcome. A possible explanation lies in the induced immunosuppression and the association of blood compatibility with infections.

Six retrospective studies comprising more than 7000 patients reported that transfusion during RC was associated with increased overall mortality, cancer-specific mortality and disease recurrence (hazard ratios: 1.19 (95% confidence interval [CI]: 1.11–1.27, P<0.00001), 1.17 (95% CI: 1.06–1.30, P = 0.002, 1.14 (95% CI: 1.03–1.27), respectively).^[48] Similarly, Abel et al. reported that intraoperative, and not postoperative transfusion, was linked to worse survival and a higher possibility for recurrence.^[49] Whereas, Buchner et al. recorded a negative effect of transfusion in a cohort of 722 patients after 26-month follow-up irrespective its timing^[50] and after adjusting for cancer stage. In the same fashion, Siemens et al. reported the negative impact of blood transfusions, by showing that it also increases LOS and re-admission rates.^[51] On the other hand, a two-center retrospective study of 1060 patients, did not concur with the above reports.^[52]

When looking at the four published prospective randomized trials and the recent meta-analysis by Tan et al., we see several variables, which limit us from drawing "conclusive findings."[44] These differences consist of patient and tumor characteristics, the level of surgical experience, the surgical volume, the clinical pathway used, the types of urinary diversion (neobladder or ileal conduits), and the application of the extra- or intracorporeal approach. The small number of patients, the short follow-up and the nonmulticenter character of many of the published articles add further to their limitations. The conclusion is that RARC is better compared to open surgery regarding blood loss and wound complications and worse in operative time.^[44] RARC and ORC performed equally in postoperative complications, positive surgical margins (PSM), resected lymph nodes and LOS.

The Memorial Sloan Kettering Cancer Center has published the largest RCT to date.^[53] However, in this study, there are also apparent limitations: It is a single-center trial and low-powered (58 ORC-60 RARC). All RARCs were performed extracorporeally, almost 50% of the patients in both arms received a neobladder, and most notably, the study was designed to detect a statistical difference of 20% in Clavien grade 2–5 complications. The authors acknowledged the fact that if the difference was set to 10% or 15%, the outcome might have been different. The same limitations are seen in the other three RCTs. Thus, we have to await the results from the RAZOR study, which will be the largest noninferiority RCT with more than 320 patients, from 15 institutions.^[54]

SURVIVAL OUTCOME MEASURES

Table 3 summarizes the oncological end-points from traditional ORC series from high-volume centers, as well as RARC versus ORC series, including the 4 RCTs and meta-analyses.^[41,44,54-79] An overall conclusion that can be drawn from the above studies, further supported by the fact that long-term data are now available, is that RARC is equivalent to ORC in terms of oncological efficacy.

Concerning lymph node dissection, which is a crucial part of the procedure from an oncological viewpoint, it has been shown that RARC can achieve the same or even better lymph node yields than ORC. Li *et al.* have reviewed nine comparative RARC versus ORC studies with 874 patients,^[36] concluding that RARC removed at least two nodes more than ORC (WMD: 2.25; 95% CI, 0.57–3.94; P = 0.009). Four systematic analyses, between 2013 and 2017 were in agreement with the above results. On the other hand, the RCTs and their meta-analysis did not show any difference.

Another critical oncological variable is PSM. The first meta-analysis confirmed that PSM have a statistically significant negative effect on the survival outcomes.^[80]

The systematic reviews and the meta-analysis of the RCTs show that RARC and ORC have comparable margin rates. A systematic review for RARC estimated a 5.6% (0%–26%) positive surgical margin rate.^[26] However, when adjusted for surgeon experience, the margin rates ranged between 4% and 9%. pT2 and pT3-4 disease are associated with

positive margins in 1%–1.5% and 0%–25%, respectively. The IRCC database (n = 939) showed an 8% positive margin rate.^[27] Similar margin rates are seen in ORC studies from high-volume centers (4.2%–8.6%) [Table 3]. In the newly announced results of the RAZOR study, overall margin rates were similar for RARC and ORC, but RARC had

Surgery type	Author	Year	Patients (n)	Follow-up (months)	Complication rates (%)	Mortality (%)	PSM (%)	LNY (%)	OS (%)	CSS (%)	DFS (%)
ORC	Hautmann <i>et al.</i> [55]	2011	1100	38	NR	3.2-5.2	NR	18	57.9	69.5	71.2
	Hautmann + Studer <i>et al</i> . ^[56]	2006	2289	34	21.5-30	NR	NR	NR	NR	NR	NR
	Herr <i>et al.</i> ^[57]	2004	1091	NR	NR	NR	6.5	12.5	NR	NR	NR
	Stein <i>et al.</i> [58]	2001	1054	122	28	3	NR	NR	66	68	NR
	Madersbacher <i>et al.</i> ^[59]	2003	507	31	NR	NR	NR	NR	59	62	NR
	Ghoneim et al.[60]	2008	2720	43	NR	2.6	NR	NR	NR	NR	55
	Yafi <i>et al.</i> ^[61]	2011	2287	29	NR	3.2	8.6	9	48	57	67
	Dotan et al.[62]	2007	1589	120	NR	NR	4.2	11	NR	NR	71
	Konety et al.[63]	2003	1923	63.5	NR	NR	NR	NR	NR	NR	NR
	Lowrance et al.[64]	2008	553	NR	38-7.4 (early-late)	1.7	NR	NR	NR	NR	NR
RARC versus ORC	Wang <i>et al</i> . ^[65]	2008	54	NR	21 versus 24	0 versus 0	6.1 versus 14.3	17 versus 20	NR	NR	NR
	Nix <i>et al</i> . ^{[66]*}	2010	41	NR	33 versus 50	0 versus 5	0 versus 0	19 versus 18	NR	NR	NR
	Ng <i>et al</i> . ^[67]	2010	187	NR	41 versus 58.7	0 versus 5.8	6 versus 9	16 versus 15	NR	NR	NR
	Gondo <i>et al.</i> ^[68]	2012	26	NR	54.5 versus 73.3	NR	9.1 versus 20	20.7 versus 13.8	NR	NR	NR
	Parekh ^[69] *	2013	47	NR	25 versus 25 (clavien >2)	NR	5 versus 5	11 versus 23	NR	NR	NR
	Khan <i>et al</i> . ^[70]	2012	100	38.4	42 versus 71	0 versus 2	0 versus 10	16 versus 11	NR	NR	79 versus 69
	Sung et al.[71]	2012	139	NR	22 versus 77	1 versus 3	NR	NR	NR	NR	NR
	Styn <i>et al.</i> ^[72]	2012	150	13.5 versus 8	66 versus 22	0 versus 3	32 versus 10	14.3 versus 15.2	NR	NR	NR
	Richards <i>et al</i> . ^[73]	2012	70	NR	10 versus 35	0 versus 5	5 versus 10	17 versus 15	NR	NR	NR
	Knox <i>et al</i> . ^[74]	2013	142	NR	43 versus 64	1 versus 2	7 versus 8	21.3 versus 17.7	NR	NR	NR
	Kader <i>et al</i> . ^[75]	2013	200	NR	35 versus 57	1 versus 0	12 versus 11	17.7 versus 15.7	NR	NR	NR
	Maes <i>et al.</i> ^[76]	2013	28	NR	21 versus 14	NR	10.7 versus 7.1	11.9 versus 9.5	NR	NR	NR
	Musch <i>et al.</i> ^[77]	2014	142	NR	59 versus 93	2 versus 5	2 versus 1	27.5 versus 19.6	NR	NR	NR
	Nepple et al. ^[78]	2013	65	12.2	NR	NR	2 versus2	17.0 versus 15.5	63 versus 68*	75 versus 63*	67 versus 58*

Table 3: Summary of large open radical cystectomy series and comparative studies of robot-assisted radical cystectomy

Contd...

Table 3: Contd... Author Patients Follow-up Complication Mortality (%) PSM (%) LNY (%) Surgery Year **OS** (%) CSS (%) **DFS** (%) type (n) (months) rates (%) Bochner et al.[53]* 2015 118 3 62 versus 66 0 versus 1.7 3.3 25.7 NR NR NR versus versus 5.2 24.5 Khan et al.[79]* 2016 40 12 55 versus 70 0 versus 0 15 16.3 NR NR NR versus versus 10 18.8 Tan *et al*.[44] 2016 184 33.8 NR NR 8.2 14.9 83.8 78.8 84.4 versus versus versus versus versus 19.3 73.5 69.5 80.9 12.6 Hu et al.[41] 2016 1317 44 8.0 NR NR 7 versus HR NR HR 1.1 versus 9.8 1.14 3 (clavien >2)

*At 2 years. PSM=Positive surgical margins, LNY=Lymph node yield, OS=Overall survival, CSS=Cancer-specific survival, DFS=Disease-free survival, NR=Not reported, ORC=Open radical cystectomy, RARC=Robot-assisted radical cystectomy

a higher positive bladder margin rate (11% versus 5%, P = 0.05).^[47]

When looking at survival end-points, the results of RARC are promising and appear equivalent to the results of ORC. A systematic review of the oncological outcomes of RARC, using the IRCC dataset^[26] reported that 5-year disease-free survival, cancer-specific survival (CSS), and overall survival (OS) rates ranged between 53%–74%, 66%–80%, and 39%–66%, respectively. There was no statistically significant difference bwteen ORC and RARC. The results of the RAZOR study confirmed the oncological equivalence of the two approaches, considering that the noninferiority design had the 2-year progression-free survival as the end-point.^[47] However, significant heterogeneity and overlapping between the included studies creates issues in the interpretation of the results.

The IRCC provided an updated analysis of the oncological outcomes of RARC.^[27] In a median follow-up of 44 months, the 5-year recurrence-free survival (RFS), CSS, and OS were 67%, 75%, and 50%, respectively. While acknowledging that 38% of the cohort (n = 702) had advanced disease (pT3-4) and 21% were lymph-node positive, the published survival rates are encouraging.

Snow-Lisy *et al.* reported outcomes for both RARC and laparoscopic RC patients with the current longest published follow-up of 12 years.^[81] The 5-year CSS rate was 70% for this cohort.

In the Karolinska Institute series of 113 consecutive totally intracorporeal RARC, with a median follow-up of 25 months, cancer-specific survival was 81% at 3 years and 67% at 5 years.^[82]

Tan *et al.* published one of the few studies comparing ORC to RARC with totally intracorporeal urinary diversion.^[83] In this study, a total of 184 patients, equally distributed,

with 33.8 months of follow-up, found no difference in the recurrence-free survival and the recurrence sites.

There has been debate as to whether RARC negatively impacts early recurrence patterns due to inadequate resection or pneumoperitoneum; so far, there is no good evidence to support this viewpoint. A comparison of extracorporeal RARC versus ORC concluded that RARC exhibited different recurrence patterns, suggestive of higher rates of extrapelvic and peritoneal carcinomatosis.^[84] However, the study was shown to have no statistical evidence to support these views.^[85] Recurrence following RC often occurs early, with >80% of recurrences occurring within the first 2 years.^[86] The ERUS Scientific Working Group reported on early recurrence patterns among 717 patients who underwent RARC with intracorporeal urinary diversion. RFS at 3, 12, and 24 months was 95.9%, 80.2%, and 74.6%, respectively. Distant recurrences most frequently occurred in the bones, lungs, and liver, and pelvic lymph nodes were the most common site of local recurrence. This multi-center series identified five patients (0.7%) with peritoneal carcinomatosis and two patients (0.3%) with metastasis at the port site (wound site) concluding that "unusual" recurrence patterns were not identified and that recurrence patterns appear similar to those in ORC series.^[86]

The oncological equivalence of RARC and ORC approaches further highlights the urgent necessity for improved neoadjuvant and adjuvant chemotherapeutic regimens, which aim to augment the efficacy of surgery and improve patient survival outcomes.

FUNCTIONAL OUTCOMES

Continence and potency are the most important quality indicators for the neobladder patients. Unfortunately, there is a lack of data, which makes the comparison for RARC and ORC problematic. Looking at ORCs performance from the 2012 EAU International Consultation on Bladder Cancer, reviewing cases between 1970 and 2012, day-time and night-time continence was achieved in 85%–90% and 60%–80%, respectively.^[4] Tyritzis *et al.* published the Karolinska Institute series which included functional outcomes from 70 RARCs with neobladder diversion.^[87] Nineteen males (90.5%) and two out of three (66.7%) females were continent (0–1 pad/day) at 12 months. Sixteen patients that received a nerve-sparing RARC were potent with or without medication at 12 months. In Table 4, the published RARC studies of neobladders with functional outcomes are shown.^[17,28,31,87-91]

Since many techniques for the creation of neobladders have been described, urodynamic data would be an interesting indicator of functional continence outcomes. Satkunasivam *et al.* compared RARC with intracorporeal neobladder with ORC, stating that the RARC neobladder had similar urodynamic characteristics, but with inferior daytime continence.^[91] Patient urinary bother scores were similar between the two procedures. The limitations of this study include its retrospective nature, its low power in patient numbers (28 RARC, 79 ORC) and a short follow-up for RARC (9.4 months) compared to the 62.1 months for ORC.^[91]

COST COMPARISON

Cost analysis can be a challenging task due to differences between the individual health-systems, public insurance

Table 4: Functional outcomes of studies of robot-assistedradical cystectomy with neobladder diversion									
Author	Patients (n)	Daytime continence (%)	Nighttime continence (%)	Potency (%)					
Akbulut <i>et al</i> . ^[88]	7	85.7	71.4	55					
Goh <i>et al</i> .[17]	8	75	NA	NA					
Canda et al.[89]	17	64.7	17.6	9.1					
Tyritzis et al.[87]	70	90.5	75.4	81.2					
Simone et al. ^[31]	45	74	55	NA					
Tan <i>et al</i> . ^[90]	20	95	65	NA					
Asimakopoulos <i>et al.</i> ^[28]	40	100	72	72					
Satkunasivam <i>et al.</i> ^[91]	28	41.6*	37.5*	NA					

*Definition of continence is almost dry to slightly wet.

NA=Not available

systems, and other parameters. In addition, indirect costs are not taken into account, as these are reflected by readmissions and the high acquisition and maintenance fees of the robot, limits further our ability to make a precise evaluation. Table 5 provides a summary of the available cost studies to date.

Lee *et al.* estimated that the costs of RARC with ileal conduits, cutaneous continent diversion and neobladders were \$20,659, \$22,102, and \$22,685, respectively, compared to \$25,505, \$22,697 and \$20,719 for ORC.^[92] The dominant cost driver in the study was hospital stay, showing that RARC could be less expensive than ORC with a reduced hospital stay. Similarly, Leow *et al.* concluded that RARC could become cost-efficient if the operation time was <6 h and the hospital stay <1 week.^[37] This was the first study that calculated all 90-day direct costs, including supplies. In this study, RARC had less major postoperative complications, which decreased the overall costs.^[37]

Another study based on the surveillance, epidemiology, and end results program-Medicare linked data concluded that RARC was more expensive when looking at perioperative, 30- and 90-day costs.^[41] The statistically significant difference ranged between \$3000 and 4000 (\$24051 [interquartile range (IQR) \$15332-\$32078] vs. \$21 637 [IQR \$12567-\$32 460], P = 0.08). Finally, the most recent cost analysis by Bansal and associates suggested that RARC was more expensive than ORC by 18.9%. The key cost drivers were operative time, hospitalization time, and annual surgical volume.^[97] None of the current publications on cost have taken into account the time for patients to get back to "normal activities," following discharge from the hospital. The need for home-care is an important cost and the impact of minimally invasive surgery on this aspect of health economics has to date been under-investigated.

An update on health economics for muscle-invasive bladder cancer showed that the economic burden would be decreased if the surgical complications could be reduced and if neoadjuvant chemotherapy could be utilized more since it improves the quality of life and survival of the patients.^[98]

Author	Year	Patie	nts (<i>n</i>)	Direc	t cost	Indirect cost		Total cost	
		RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC
Lee et al.[92]	2011	١	1A	Worse	Better	Better	Worse	Better	Worse
Smith et al.[93]	2010	20	20	Worse	Better	Ν	A	Ν	A
Martin et al. ^[94]	2011	19	14	Worse	Better	Ν	A	NA	
Yu et al. ^[95]	2012	224	1444	Worse	Better	Ν	A	NA	
Mmeje et al. ^[96]	2013	١	1A	Worse	Better	Better	Worse	NA	
Leow et al.[37]	2015	2101	34,672	Worse	Better	Ν	A	N	A
Bochner et al.[53]	2015	64	58	Worse	Better	Ν	A	N	A
Hu et al.[41]	2016	439	7308	Worse	Better	Ν	A	N	A

ORC=Open radical cystectomy, RARC=Robot-assisted radical cystectomy, NA=Not available

CONCLUSION

RC is one of the most challenging and morbid surgical procedures, in which the surgeon has to provide the best outcome in terms of oncological control, complications, and functional outcomes. Experience of the surgeon and the center, has shown to positively impact outcomes. However, the procedure itself might not be enough for cure, since we are dealing with an aggressive cancer. Survival may be improved in the future by optimal neoadjuvant or adjuvant chemotherapy protocols. Apart from extirpating completely the disease, the complications of surgery need to be reduced. The current evidence indicates that RARC achieves better results in terms of blood loss, transfusion rates and hospital stay with an equivalent oncological outcome compared to ORC. On the other hand, the cost of RARC is a significant drawback. Future RCTs are awaited along with the further refinement of surgical technique and peri-operative patient management.

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