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Review

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Oncologic outcomes in robot-assisted radical cystectomy: Where do we stand in 2021?

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Abstract

Robot-assisted radical cystectomy is an alternative to the standard open surgical approach and has been increasingly used to surgically treat bladder cancer. Data on oncologic outcomes for the robotic approach have matured, and now intermediate and long-term oncologic outcomes are available. This review focuses on oncologic outcomes of the robotic approach with a focus on recent data and high-quality studies. Based on the current literature available, there are no consistent differences between the robotic and open approaches with respect to positive margin rates, lymph node yields, recurrence patterns, or recurrence free, cancer-specific, and overall survival. If oncologic surgical principles are adhered to, excellent oncologic outcomes are achievable with the robotic approach.

Keywords: Urinary bladder neoplasms, radical cystectomy, robotic radical cystectomy, oncologic outcomes, robotics, recurrence, survival

INTRODUCTION

Radical cystectomy and pelvic lymph node dissection is standard of care for surgically eligible patients with non-metastatic muscle-invasive bladder cancer, and is a preferred treatment for select patients with high risk of non-muscle invasive disease[1,2]. While open radical cystectomy has been the recognized gold standard for years, robot-assisted radical cystectomy (RARC) has become increasingly popular. Initially

described by Menon *et al.*[3] in 2003, utilization of RARC increased from 0.7% in 2002 to 18.5% in 2012 in the United States[4]. Advantages of the robotic approach relative to open radical cystectomy (ORC) include reduced blood loss, favorable transfusion rate and shorter length of stay[5].

Here, we review pertinent oncologic outcomes in the current RARC literature. We queried the PubMed electronic database in January 2021 for studies that report on oncologic outcomes for RARC. An emphasis was placed on randomized controlled trials, as well as contemporary comparative open approach cohorts, large single institution surgical series, multi-center initiatives and systematic reviews. A list of the major studies considered in this review is found in Table 1.

NODAL YIELD

Lower nodal yield and positive surgical margin status are independently associated with worse OS after adjustment for neoadjuvant chemotherapy and pathologic factors. In fact, nodal yields of 10-14 have been proposed as a marker of surgical quality[33]. Professional guidelines and best practice statements are less quantitatively prescriptive[1,34], as patient, clinical and pathologic factors can influence lymph node yield. In a 2015 systematic review, Yuh *et al.*[35] assessed 105 papers and found that median yield for a robotic approach was 19 lymph nodes (range: 3-55) with cumulative analyses finding no difference *vs.* ORC. Nodal yields are directly related to the surgical dissection template chosen, whether standard or extended. Among robotic surgeons, high volume surgeons and institutional volume were independently associated with performance of extended template dissections[36].

Several RCTs have found comparable nodal yields between RARC and ORC [Table 2]. Nix *et al.*[11] found mean LN yields of 19 *vs.* 18 in RARC *vs.* ORC ($P = 0.51$) using a standard dissection template. In the largest clinical trial, RAZOR investigators found similar median lymph node yields of 23.3 for RARC with 51% utilizing an extended template, and 25.7 for ORC with 55% utilizing an extended template ($P = 0.13$)[6]. Other smaller RCTs reported similar findings[8,9]. Several recent meta-analyses did not assess nodal yield[37,38].

Considering the abundance of data, adequate lymph node yields are achievable via robotic platforms, including extended and super extended templates. Maintenance of oncologic principles including performance of a meticulous dissection within pre-defined anatomic boundaries of a template appears to be more important than surgical approach.

POSITIVE MARGIN RATE

Positive surgical margin (PSM) rate is a measure of local disease burden, an independent predictor of survival, and can be a measure of surgical quality[33,39,40]. Early criticism of minimally invasive approaches was that there was risk of higher positive margin rates in locally advanced tumors, as evidenced by a single non-controlled, non-comparative retrospective study[32]. It was theorized that the lack of tactile feedback and learning curve was potential explanations[35,41].

These early criticisms have largely been refuted. A systematic review showed that PSM rate was low in pT2 disease (< 1.5%) and 0%-25% in pT3 disease or higher, without any significant difference between ORC and RARC in a cumulative analysis of 17 studies[35]. Interestingly, PSM did not appear to decrease with sequential case numbers or institutional volume[32], a finding that may reflect surgeons' willingness to take on more difficult cases with experience[35]. As a result of these early robotic data and historical open cystectomy series, acceptable PSM rates for robotic surgeons were proposed as < 3% for pT2, < 10% for pT3, < 25% for pT4 and < 7% overall[34,40].

Table 1. Selected studies evaluating oncologic outcomes after robot-assisted radical cystectomy

Ref.	Year	Comparison	Study design	Setting	Primary outcome	Pertinent secondary outcome(s)
Comparative studies, randomized						
RAZOR trial, multiple authors[6,7]	2020, 2018	ORC *vs.* RARC	RCT	Multi center	2-year PFS	TTR, PFS, OS
CORAL trial, Khan *et al.*[8]	2020	ORC *vs.* RARC *vs.* LRC	RCT	Single center	5-year RFS, CSS, OS	Surgical margin, recurrence patterns
Bochner *et al.*[9]	2018	ORC *vs.* RARC	RCT	Single center	90-day complication	RFS, CSS, OS, recurrence patterns
Parekh *et al.*[10]	2012	ORC *vs.* RARC	RCT	Single center	Surgical margin Total lymph node yield	Quality of life Functional recovery
Nix *et al.*[11]	2010	ORC *vs.* RARC	RCT	Single center	Lymph node yield	Demographics, perioperative, pathologic results, narcotic use
Comparative studies, non-randomized						
RACE study, Wijburg *et al.*[12]	2021	ORC *vs.* RARC	Prospective	Multi center	90-day complication	HRQOL, complications, clinical outcomes including surgical margin
Asil *et al.*[13]	2021	ORC *vs.* RARC	Retrospective	Multi center	Intraoperative and postoperative endpoints	Surgical margin, lymph node yield
Ip *et al.*[14]	2020	ORC *vs.* RARC	Retrospective	Single center	RFS, OS	Perioperative and pathologic outcomes
Zhang *et al.*[15]	2020	ORC *vs.* RARC	Retrospective	Single center	Perioperative outcomes, complications	Pathologic outcomes, overall survival
Faraj *et al.*[16]	2019	ORC *vs.* RARC	Retrospective	Single center	RFS, OS	Recurrence patterns, predictors of primary outcome
Moschini *et al.*[17]	2019	ORC *vs.* RARC	Retrospective	Multicenter	Surgical margin status	Predictors of surgical margin status
Simone *et al.*[18]	2018	ORC *vs.* RARC, ICUD only	Retrospective	Single center	RFS, CSS, OS	Complications, perioperative and pathologic outcomes
Hanna *et al.*[19]	2018	ORC *vs.* RARC	Retrospective	Population registry	Intraoperative and postoperative endpoints	Descriptors and predictors of robotic surgical approach
Gandagli *et al.*[20]	2016	ORC *vs.* RARC	Retrospective	Multi center	RFS, CSS, OS	Complications, perioperative and pathologic outcomes, recurrence
Tan *et al.*[21]	2016	ORC *vs.* RARC	Retrospective	Single center	RFS	Recurrence patterns, CSS, OS
Matulewicz *et al.*[22]	2016	ORC *vs.* RARC	Retrospective	Population registry	Surgical margin status, lymph node yield	Primary outcome variables as predictors of survival
Nguyen *et al.*[23]	2015	ORC *vs.* RARC	Retrospective	Single center	RFS	Recurrence patterns at 2 years
Atmaca *et al.*[24]	2015	ORC *vs.* RARC, ICUD only	Retrospective	Single center	Demographics, functional, intraoperative outcomes	Surgical margin, lymph node yield
Non-comparative studies						
IRCC, Elsayed *et al.*[25]	2021	RARC only	Retrospective	Multicenter	RFS, LRFS, DMFS, OS	Recurrence patterns, predictors of recurrent free survival
Brassetti *et al.*[26]	2020	RARC, ICUD only	Retrospective	Multicenter	RFS, CSS, OS	Surgical margin, lymph node yield, predictors of survival
IRCC, Hussein *et al.*[27]	2019	RARC only	Retrospective	Multicenter	10-year RFS, CSS, OS	Surgical margin, lymph node yield, predictors of survival

IRCC, Hussein *et al.*[28]	2017	RARC only	Retrospective	Multicenter	Incidence of early oncologic failure (any disease relapse < 3 mo s/p RARC)	Recurrence patterns, adherence to oncologic principles, predictors of early oncologic failure
ERUS, Collins *et al.*[29]	2017	RARC, ICUD only	Retrospective	Multicenter	RFS	Recurrence patterns
IRCC, Raza *et al.*[30]	2015	RARC only	Retrospective	Multicenter	5-year RFS, CSS, OS	Surgical margin, lymph node yield, predictors of survival
IRCC, Hellenthal *et al.*[31]	2011	RARC only	Retrospective	Multicenter	Proportion of RARC w/lymphadenectomy performed	Lymph node yield, predictors of lymphadenectomy performance
IRCC, Hellenthal *et al.*[32]	2010	RARC only	Retrospective	Multicenter	Surgical margin status	Predictors of surgical margin status

RAZOR: Randomized open *vs.* robotic cystectomy; ORC: open radical cystectomy; RARC: robotic assisted radical cystectomy; RCT: randomized controlled trial; TTR: time to recurrence; RFS: recurrence free survival; PFS: progression free survival; CSS: cancer specific survival; OS: overall survival; CORAL: controlled three-arm trial of Open, Robotic, and laparoscopic radical cystectomy; RACE: radical cystectomy evaluation; HRQOL: health-related quality of life; IRCC: International Robotic Cystectomy consortium; LRFS: local recurrence free survival; DMFS: distant metastasis free survival; ICUD: intracorporeal urinary diversion; ERUS: European Association of Urology Robotic Urology Section; LRC: laparoscopic radical cystectomy.

Since then, multiple RCTs and retrospective comparative studies offer additional insight that robotic cystectomy can meet these standards of surgical quality. The RAZOR trial showed overall PSM rates of 5% (ORC) *vs.* 6% (RARC), $P = 0.6$ without any difference in pathologic stage between the groups. Of those with PSMs, 7/9 (78%) in RARC and 5/7 (71%) in ORC were T3 or above[6]. Two smaller RCTs also found no difference in PSM rate between open and robotic approaches[8,9]. A meta-analysis compiling 541 patients from RCTs showed no difference in PSM rates between RARC and ORC (RR = 1.2; 95%CI: 0.6-2.4)[37]. Additionally, one non-randomized comparative study found significantly increased PSM rate for ORC (18%) *vs.* RARC (6%) in an inversed probability weighted population despite similar pathologic staging, though when further specified by site of positive margin these results were not significantly different[12]. Multiple other non-randomized comparative studies have not found significant differences in PSM rate by approach[13-17,19,20,22-24].

Collectively, the above data suggest favorable PSM rates are achievable via the robotic platform and are in alignment with standards of surgical quality set forth by best practices statements[34]. Regardless of surgical approach, the largest determinant of PSM rates is local disease stage.

RECURRENCE PATTERNS

Recurrence of bladder cancer after radical cystectomy is dependent on tumor and nodal stage, and ranges from 20% to 30% in pT2 disease, 40% for pT3, > 50% for pT4 and approximately 70% in pN1 disease or greater[42]. Other independent predictors of tumor recurrence include lymphovascular invasion and positive soft tissue margins[43]. Recurrences generally occur within the first 2-3 years and predict worse overall survival (OS)[44].

Recurrence is generally classified as local, often referring to the cystectomy bed and within the pelvic lymph node template, or distant. Atypical patterns in MIS generally refer to peritoneal carcinomatosis, abdominal wall/port site metastases and extra pelvic lymph node recurrences, which have been described but are rare. In fact, a systematic review of 1094 studies found only 5 that reported port site metastasis[45]. Proposed contributors of atypical recurrence patterns in MIS include depressive local immunologic factors and/or enhanced tumor dissemination related to pneumoperitoneum, breach of oncologic operative principles,

Table 2. Oncologic outcomes from selected studies after robot-assisted radical cystectomy

Ref. and study acronym	Year	Surgical approach	Cases, (*n*)	PSM, *n* (%)	Lymph node yield, mean (SD) or median (IQR or range)	RFS	CSS	OS
Comparative studies, randomized								
RAZOR trial, multiple authors[6,7]	2020, 2018	ORC	152	7 (5)	25.7 (SD 14.5)	65%, 3 yr	nr	69%, 3 yr
		RARC	150	9 (6)	23.3 (SD 12.5)	68%, 3 yr	nr	74%, 3 yr
CORAL trial, Khan *et al.*[8]	2020	ORC	20	2 (10)	18.5 (IQR 14-25)	60%, 5 yr	64%, 5 yr	55%, 5 yr
		RARC	20	3 (15)	14.5 (IQR 11-21)	58%, 5 yr	68%, 5 yr	65%, 5 yr
		LRC	19	1 (5)	15.5 (IQR 12-22)	71%, 5 yr	69%, 5 yr	61%, 5 yr
Bochner *et al.*[9]	2018	ORC	58	3 (5)	29 (IQR 22-38)	59%, 5 yr	80%, 5 yr#	65%, 5 yr#
		RARC	60	2 (3)	31 (IQR 23-37)	64%, 5 yr	75%, 5 yr#	65%, 5 yr#
Parekh *et al.*[10]	2012	ORC	20	1 (5)	23 (IQR 15-28)	nr	nr	nr
		RARC	20	1 (5)	11 (IQR 9-22)	nr	nr	nr
Nix *et al.*[11]	2010	ORC	20	0 (0)	18 (range 8-30)	nr	nr	nr
		RARC	21	0 (0)	19 (range 12-30)	nr	nr	nr
Comparative studies, non-randomized								
RACE study, Wijburg *et al.*[12]	2021	ORC	168	nr (18)*	13 (IQR 9-18)	75%, 1 yr	nr	nr
		RARC	180	nr (6)	15 (IQR 11-21)	76%, 1 yr	nr	nr
Asil *et al.*[13]	2021	ORC	31	1 (3)	22 (nr)	nr	nr	nr
		RARC	61	9 (15)	Range 22-25	nr	nr	nr
Ip *et al.*[14]	2020	ORC	159	23 (14)	20 (SD 14)*	75%, 5 yr#	nr	65%, 5 yr#
		RARC	73	8 (11)	12 (SD 8)	80 %, 5 yr#	nr	70%, 5 yr#
Zhang *et al.*[15]	2020	ORC	272	22 (8)	nr	nr	nr	55%, 5 yr
		RARC	676	34 (5)	nr	nr	nr	58%, 5 yr
Faraj *et al.*[16]	2019	ORC	278	15 (5)	12 (IQR 9-18)*	63%, 10 yr	nr	46%, 10 yr
		RARC	203	7 (3)	18 (IQR 14-24)	70%, 10 yr	nr	40%, 10 yr
Moschini *et al.*[17]	2019	ORC	1666	160 (10)	16 (10-24)	nr	nr	nr
		RARC	870	112 (13)	18 (12-25)	nr	nr	nr
Simone *et al.*[18]	2018	RARC, ICUD only	64	0 (0)	33.4 (SD 12.3)	79%, 4 yr	85%, 4 yr	82%, 4 yr
		ORC	46	0 (0)	31.3 (SD 14.6)	73%, 4 yr	86%, 4 yr	80%, 4 yr
Hanna *et al.*[19]	2018	ORC	7513	(10.7)	12 (IQR 7-20)*	nr	nr	nr
		RARC	2048	(9.3)	17 (IQR 10-25)	nr	nr	nr
Gandagli *et al.*[20]	2016	ORC	230	31 (13)	13 (IQR 9-17)	57%, 5 yr	62%, 5 yr	58%, 5 yr
		RARC	138	12 (9)	12 (IQR 8-17)	54%, 5 yr	74%, 5 yr	59%, 5 yr
Tan *et al.*[21]	2016	ORC	90	17 (19)*	12.6 (SD 10.9)	70%, 2 yr	81%, 2 yr	74%, 2 yr

		RARC	94	6 (8)	14.9 (SD 10.0)	79%, 2 yr	84%, 2 yr	84%, 2 yr
Matulewicz *et al.*[22]	2016	ORC	9639	(13)	11 (IQR 5-19)*	nr	nr	nr
		RARC	2397	(11)	16 (IQR 9-25)	nr	nr	nr
Nguyen *et al.*[23]	2015	ORC	120	15 (13)*	20 (IQR 11-27)	60%, 5 yr#	nr	nr
		RARC	263	16 (6)	21 (IQR 13-28)	70%, 5 yr#	nr	nr
Atmaca *et al.*[24]	2015	ORC	42	1 (2)	17 (SD 13.5)	nr	nr	nr
		RARC, ICUD only	32	2 (6)	25 (SD 9.7)	nr	nr	nr
Non-comparative studies								
IRCC, Elsayed *et al.*[25]	2021	RARC only	2107	nr	nr	66%, 5 yr	nr	60%, 5 yr
Brassetti *et al.*[26]	2020	RARC, ICUD only	113	9 (8)	36 (IQR 28-45)	58%, 5 yr	61%, 5 yr	54%, 5 yr
IRCC, Hussein *et al.*[27]	2019	RARC only	446	30 (7)	14 (IQR 9-22)	59%, 10 yr	65%, 10 yr	35%, 10 yr
ERUS, Collins *et al.*[29]	2017	RARC, ICUD only	717	34 (4)	18 (IQR 13-25)	75%, 2 yr		
IRCC, Raza *et al.*[30]	2015	RARC only	702	55 (8)	16 (IQR 10-24)	67%, 5 yr	75%, 5 yr	50%, 5 yr
IRCC, Hellenthal, *et al.*[31]	2011	RARC only	527	nr	17.8 (range 0-68)	nr	nr	nr
IRCC, Hellenthal, *et al.*[32]	2010	RARC only	513	35 (6.8)	nr	nr	nr	nr

#Visual estimate based on Kaplan Meier curves provided in paper (specific numbers not provided by reference in text). *$P < 0.05$. PSM: Positive surgical margin; SD: standard deviation; IQR: interquartile range; RFS: recurrence free survival; CSS: cancer-specific survival; OS: overall survival; ORC: open radical cystectomy; RARC: robotic assisted radical cystectomy; LRC: laparoscopic radical cystectomy; nr: not reported; ICUD: intracorporeal urinary diversion; RAZOR: randomized open *vs.* robotic cystectomy; CORAL: controlled three-arm trial of open, robotic, and laparoscopic radical cystectomy; RACE: radical cystectomy evaluation; IRCC: International Robotic Cystectomy Consortium; ERUS: European Association of Urology Robotic Urology Section.

or variant lymphatic dissemination related to robotic technique[23].

Nguyen *et al.*[23] reported atypical patterns of recurrence in a non-randomized single center comparative study of ORC *vs.* RARC, including higher incidence of peritoneal carcinomatosis (21% *vs.* 8%) and extra pelvic lymph node (23% *vs.* 15%) [Table 3]. However, the denominator of these estimated proportions was distant recurrences and not overall recurrence, as is typically reported. It was additionally notable that distant recurrences were not significantly different between the two approaches, and the authors noted that selection bias may have contributed to these findings. The same group published a follow up study consisting of 310 patients and found that predictors of distant recurrences, peritoneal carcinomatosis and extra pelvic lymph node metastases did not significantly differ and concluded that tumor biology is likely the chief influencer of atypical recurrence, not surgical approach[46]. Bochner *et al.*[9] later found that there was variation in location of recurrence and that RARC resulted in greater numbers of recurrences in the abdomen and pelvis. However, this only achieved significance when pooled and stratification of abdominal recurrences as separate from distant and local recurrences is controversial and of unclear clinical significance[47]. Notably, the study was not powered to determine differences in patterns of recurrence.

Table 3. Recurrence patterns from selected studies

Ref.	Year	Surgical approach	Cases (*n*)	Local recurrence[a], *n* (%)	Distant recurrence[b], *n* (%)	Atypical recurrence[c]			Significantly different?	Comments
						Peritoneal carcinomatosis, *n* (%)	Abdominal wall/port site, *n* (%)	Extra pelvic lymph nodes, *n* (%)		
Comparative studies, randomized										
RAZOR trial, multiple authors[6,7]	2020, 2018	ORC	152	3 (2.0)	25 (16.4)	1 (0.7)	1 (0.7)	9 (5.9)	No	Largest RCT to date
		RARC	150	6 (4.0)	22 (14.7)	2 (1.3)	0	9 (6.0)		
CORAL trial, Khan *et al.*[8]	2020	ORC	20	3 (15.0)	nr	nr	nr	nr	No	Small sample size. Distant recurrences reported in aggregate only, not shown here
		RARC	20	3 (15.0)	nr	nr	nr	nr		
		LRC	19	3 (15.7)	nr	nr	nr	nr		
Bochner *et al.*[9]	2018	ORC	58	5 (8.6)	27 (46.6)	2 (3.4)	0	10 (17.2)	No[d]	Not powered to detect differences in recurrence patterns
		RARC	60	17 (28.3)	20 (33.0)	2 (3.3)	5 (8.3)	5 (8.3)		
Comparative studies, non-randomized										
Faraj *et al.*[16]	2019	ORC	278	19 (7)	64 (23)	5 (1.8)	0	11 (4.0)	No	Large single institutional study
		RARC	203	12 (6)	40 (20)	4 (2.0)	0	4 (2.0)		
Tan *et al.*[21]	2016	ORC	90	17 (19)	25 (28)	3 (3)	1 (1)	2 (2)	No	Intracorporeal diversions in all robotic cases
		RARC	94	11 (12)	8 (9)	2 (2)	1 (1)	3 (3)		
Nguyen *et al.*[23]	2015	ORC	79	15/65 (23)	26/73 (36)	2/26 (8)	nr	4/26 (15)	Yes	Denominator is distant recurrence, as listed in the reference
		RARC	158	24/136 (18)	43/147 (29)	9/43 (21)	nr	10/43 (23)		
Non-comparative studies										
IRCC, Elsayed *et al.*[25]	2021	RARC only	2107	241 (11)	382 (18)	26 (1.2)	25 (1.2)	109 (5.2)	n/a	RARC not associated with different patterns or higher recurrence relative to historic ORC series
IRCC, Hussein *et al.*[27]	2019	RARC only	446	69 (15)	97 (22)	6 (1)	5 (1)	21 (5)	n/a	Analysis restricted to patients with > 10 years follow up
Collins *et al.*[29]	2017	RARC, ICUD only	717	78 (10.7)	128 (17.8)	5 (0.7)	2 (0.3)	47 (6.6)	n/a	Totally intracorporeal urinary diversion cohort

[a]Local recurrence defined as any recurrence in the cystectomy bed or lymph node dissection template. [b]Distant recurrence defined as any recurrence which is not local or atypical. [c]Though sometimes reported in the referenced studies as a subset of distant recurrences, atypical recurrences reported here are mutually exclusive of local and distant recurrence. [d]"The difference in local recurrence rates did not meet conventional levels of significance (sHR = 0.36; 95%CI: 0.11-1.12, *P* = 0.077). Similarly, the difference in the rate of abdominal recurrence did not reach statistical significance (sHR = 0.38; 95%CI:0.07-1.96; *P* = 0.2). However, when the pelvic and abdominal recurrences were combined into a single group representing local/regional recurrence, the ORC group showed significantly less local/regional recurrence compared to RARC (sHR = 0.34; 95%CI: 0.12-0.93; *P* = 0.035)". RAZOR: randomized open *vs.* robotic cystectomy; ORC: open radical cystectomy; RARC: robotic assisted radical cystectomy; RCT: randomized controlled trial; CORAL: controlled three-arm trial of open, robotic, and laparoscopic radical cystectomy; IRCC: International Robotic Cystectomy Consortium; ICUD: intracorporeal urinary diversion; nr: not reported.

Multiple studies have since demonstrated that recurrence patterns do not differ by surgical approach. The RAZOR trial found no significant difference between ORC and RARC in recurrence patterns and showed low overall local recurrence rates (2% *vs.* 4%). Rare atypical recurrences were also observed in the ORC arm and did not differ between approaches[7]. A large non-randomized single center comparative study from Mayo Clinic in Arizona showed similar rates of local, distant and rare atypical recurrences[16]. An institutional report of ~180 cases, 90 of which were robotic with intracorporeal diversion, showed a low rate of atypical recurrences with no difference between surgical approaches[21]. An IRCC study of 2107 pts showed slightly higher local recurrence (11%, citing a greater percentage of extravesical disease and variant histology in their cohort) with atypical recurrence patterns similar to ORC series and those of the RAZOR trial[7,25]. A separate IRCC analysis found that tumor factors rather than those related to surgical approach were predictive of early recurrence after cystectomy and also showed that surgeons in their cohort reported a very low rate of divergence from oncologic principles[28]. Lastly, a large multi-institutional robotic cystectomy and totally intracorporeal urinary diversion cohort from the EAU Robotic Urology Section Scientific Working Group found that early recurrence rates and patterns appeared comparable to open series[29].

If oncologic principles are followed, these aggregate data suggest that atypical recurrence is exceedingly rare and are more likely reflective of tumor biology than surgical approach.

SURVIVAL OUTCOMES

The primary measure of treatment efficacy in radical cystectomy is survival, including recurrence-free, cancer-specific and overall survival[1]. Though reported here for reference, we would discourage direct comparison across studies as there is significant heterogeneity with respect to cancer variables (e.g., receipt of neoadjuvant chemotherapy, disease stage, and tumor histopathology), patient demographic and clinical characteristics, surgeon and institutional factors including intra-operative practices and post-operative follow up protocols, adjuvant therapies and length of follow up. This heterogeneity is reflected by a 2015 systematic review of mostly retrospective studies which demonstrated a wide range of 5-year survival estimates of DFS, CSS and OS between 53%-74%, 66%-80% and 39%-66%, respectively[35].

Several contemporary comparative studies do offer additional limited insight, though we are only aware of 3 RCTs that report survival outcomes. RAZOR is the largest RCT reporting survival outcomes at approximately 150 patients in each arm and reports 3 year outcomes[7]. RARC was similar compared with ORC in RFS (68% *vs.* 65%, $P = 0.6$) and OS (74% *vs.* 69%, $P = 0.3$). Bochner *et al.*[9] found that a median follow up of 4.9 years, no differences were observed in recurrence [hazard ratio (HR) = 1.27; 95%CI: 0.69-2.36; $P = 0.4$], cancer-specific survival ($P = 0.4$), or overall survival ($P = 0.8$). However, the authors cautioned that their study was not powered to assess survival outcomes. A meta-analysis with pooled data from these two studies found that RARC and ORC may result in similar time to recurrence (HR = 1.1; 95%CI: 0.8-1.4), but the evidence of certainty was low[37]. More recently, the CORAL study reported 5-year RFS, CSS, OS as well and found no differences in surgical approaches comparing open *vs.* robotic *vs.* laparoscopic approaches[8]. However, their study was limited by low sample size as only 20 patients were included in each arm and included high-risk non-muscle invasive bladder cancer.

Though lacking the rigor of a controlled trial, long-term oncologic outcomes from several robotic cohorts have recently become available. Faraj *et al.*[16] reported their 10 year survival outcomes in a single institution retrospective comparative study and found that RFS and OS were similar between ORC and RARC approaches (63% *vs.* 70%, $P = 0.14$ and 46% *vs.* 40%, $P = 0.47$ respectively). The cohorts were similar in cancer characteristics, patient demographics and clinical factors as well as intra operative practices.

Retrospective non-comparative results from the IRCC on patients with long-term follow up show RFS, CSS and OS at 10 years were 59%, 65% and 35%, consistent with historical ORC and MIS cohorts[27]. Not surprisingly, in multivariable models, they found that survival was associated with age, positive margins, tumor/nodal stage, and adjuvant treatments. Similar results are described in a multicenter study among RARC patients with totally intracorporeal urinary diversion[26]. A single institutional comparative study also showed similar survival in a totally intracorporeal urinary diversion robotic cohort when compared with ORC[18].

Matured, long-term survival data from randomized controlled studies, including RAZOR, are further anticipated. Early and intermediate survival outcomes between RARC and ORC appear to be similar. Since no consistent difference in PSM rates or recurrence patterns have been found in the literature, we expect long-term survival differences to be driven largely by factors related to disease aggressiveness including stage and need for adjuvant therapies, rather than surgical approach.

FUTURE PERSPECTIVES

Nearly 20 years after the robotic approach to radical cystectomy was described[3]. RARC remains an effective and minimally invasive option for patients undergoing cystectomy that can achieve oncologic outcomes that are comparable to the gold standard open approach. Evidence-based consensus and best practices on RARC are available[34].

There are no absolute contraindications to the robotic approach, but an early learning curve is recognized and several challenging case scenarios (e.g., large bulky tumors, history of pelvic radiation) should be preferentially managed by experienced robotic surgeons. RARC can be safely utilized in the octogenarian[48], and oncologic outcomes are excellent in sex-sparing techniques in the female patient[49] as well as male patient[50]. Excellent pathologic outcomes have been described for aggressive histopathological variants which are known to present with higher tumor stage[51]. The usage of the robotic approach to cystectomy will continue to increase as urologic surgeons become more experienced and comfortable with the platform and education becomes more commonplace in residency training programs[4].

Though the current evidence is well-supported, it is limited by the lack of large, randomized controlled trials. We eagerly anticipate more mature, high-quality data comparing oncologic outcomes of open and robotic cystectomy. Robot-assisted radical cystectomy with intracorporeal urinary diversion *vs.* open radical cystectomy (iROC) is a multicenter prospective RCT in England randomizing 320 patients to iRARC or ORC. Accrual finished in February 2020, and oncologic outcomes of interest include atypical recurrence patterns, survival, as well as outcomes related to surgeon fatigue, cost-effectiveness and patient quality of life[52].

CONCLUSION

Surgical quality indicators, including lymph node yield and positive surgical margin rate, are comparable between ORC and RARC. Despite an early case series of atypical recurrence patterns, contemporary comparative studies, including the largest randomized controlled trial, as well as a multi-institutional retrospective robotic cohort of > 2000 consecutive patients, show this is a rare occurrence and not associated with surgical approach. Survival outcomes appear to be similar as well, including long term survival from several comparative and non-comparative reports. Ultimately, surgeon comfort with the selected approach and adherence to oncologic principles is more important than the approach itself.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data acquisition and interpretation: Miller BL, Lau CS, Pachorek M, Yuh B, Sam AP

Performed data acquisition, as well as provided administrative, technical, and material support: Miller BL, Lau CS, Pachorek M

Availability of data and materials

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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