Narrative review on the comparative effectiveness of robotic and open radical cystectomy for bladder cancer

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Abstract: Bladder cancer is the fourth most commonly diagnosed malignant tumor in the United States. Open radical surgery remains the gold standard of care for most patients with muscle-invasive bladder cancer and for select aggressive cases of non-invasive disease. However, radical cystectomy (RC) with lymph-node dissection has been rapidly undergoing a significant conversion from open to minimally-invasive surgery, with the argument that the latter is associated with decreased intra-operative loss, reduced pain and shorter length of hospital stay. Even though robotic surgery has been proposed to decrease morbidity and improve recovery time, it is important to recognize there is still conflicting evidence regarding crucial outcomes. We aimed to summarize current literature in order to create a narrative analysis on comparative effectiveness of robotic and open radical cystectomy (ORC) for key outcomes including oncologic outcomes, quality of life, postoperative complications, and healthcare costs. PubMed database was searched to identify both retrospective and prospective original articles on comparative studies published through January 2020. A total of 40 studies were included in the final report. The majority of the paper will discuss and interpret limitations of existing literature. Ultimately, we will also highlight possible implications of potential publication bias and summarize future directions in the management of muscle-invasive bladder cancer.

Keywords: Comparative study; bladder cancer; cystectomy; surgical procedures, robotic

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Introduction

Bladder cancer is still one of the most challenging diseases in oncology, with an estimate 80,470 new cases will be diagnosed in the US in 2019 with approximately 17,670 deaths occurring during the same period (1). Radical cystectomy (RC) with bilateral pelvic lymph node dissection (pLND) is the most common treatment option for clinically localized muscle invasive bladder cancer (MIBC) and some non-muscle invasive bladder cancers (NMIBC) (2,3). Open radical cystectomy (ORC) has long been established as an effective primary treatment alternative for patients diagnosed with non-metastatic MIBC, select cases of high-risk non-muscle invasive disease, and recurrent tumors after failed bladder sparing treatments (4-6). However, similar to the conversion from open to minimally-invasive surgery observed with radical prostatectomies and nephrectomies, uptake of robotic-assisted radical cystectomy (RARC)

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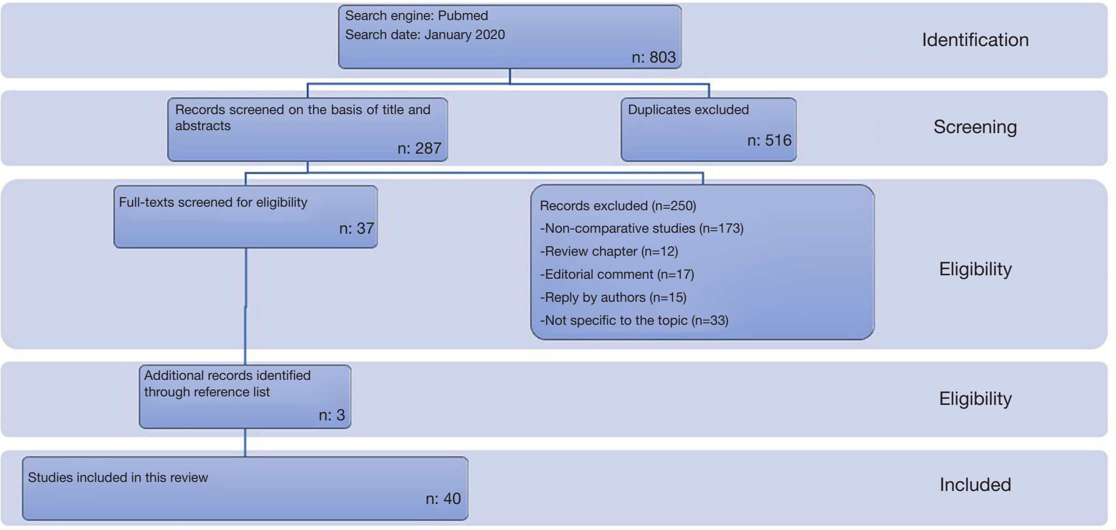

Figure 1 Flowchart of study selection.

has been steadily increasing over the last two decades (7). Initial retrospective studies showed significant advantages of RARC over ORC, while most early prospective trials failed to find considerable differences between techniques (8-10). Therefore, critically assessing outcomes and costs between techniques are essential at a time of value-based healthcare. Against this backdrop, we aimed to review the comparative effectiveness of ORC and RARC for key effects including oncologic outcomes, quality of life, postoperative complications, and healthcare costs. We will also discuss how surgical approach might influence early recovery after surgery, the potential implications of publication bias on reported robotic series, and future directions in the surgical management of bladder cancer. We present the following article in accordance with the Narrative reporting checklist (available at http://dx.doi.org/10.21037/amj-20-81) (11).

Methods

Methodology of literature search

A review of the literature was performed to create this narrative analysis. We searched the PubMed database to identify original articles on comparative analysis between RARC and ORC published through January 2020. We used a range of keywords, including the following search headings: comparative study and bladder cancer or bladder neoplasm and radical cystectomy, ORC, or robot-assisted radical cystectomy. We checked the reference lists for additional relevant manuscripts and used the "related articles" feature on PubMed to obtain further studies of interest. In order to be included in this review, studies were required to compare RARC and ORC for the treatment of localized bladder cancer either on a prospective randomized or retrospective design, include concurrent pLND (irrespective of extension), and urinary diversion (irrespective of type). Only studies reporting at least one outcome were included. Non-comparative studies and those reporting on patients with metastatic disease were excluded.

Narrative results and discussion

A total of 803 articles resulted from the initial search. After removal of duplicates, primary review, and initial screening of 287 abstracts, 37 articles with full texts comparing RARC and ORC outcomes were identified and selected. Three additional manuscripts were added after reference list review. Therefore, a total of 40 articles were included to specifically address the stated purpose. *Figure 1* contains the flowchart of study selection. A total of 34 observational [(12-31) and (32-45)], and 6 RCT (9,10,46-49) comparative studies were included in this descriptive analysis and reported on at least one complication and perioperative outcome. Most important characteristics of included studies are depicted in *Table 1*.

Oncologic outcomes

Retrospective reports on oncologic outcomes following

Table 1 Characteristics of included studies

Author/year	N of patients		Age, y*		N of surgeons	Surgeon experience	Male (%)		follow-up, mean (SD) or median (IQR)	
	RARC	ORC	RARC	ORC			RARC	ORC	RARC	ORC
Retrospective studies										
Ng 2010	83	104	70.9	67.2	1	NA	78	70	3	3
Richards 2010	35	35	65	66	Multiple	NA	86	71	NA	NA
Gondo 2012	11	15	68.9	69.7	1	NA	82	94	20.5 ± 2.42	20.5 ± 2.42
Khan 2012	48	52	66.5	65	3	NA	85	77	38.4 (NA)	38.4 (NA)
Styn 2012	50	100	66.6	65.6	6	fellowship trained in urologic oncology	NA	NA	8 (1-25)	13.5 (0-37)
Sung 2012	35	104	62.2	65.9	5	NA	88.5	81.7	3.0 (NA)	3 (NA)
Kader 2013	100	100	67	67	4	NA	72	72	3.0 (NA)	3.0 (NA)
Knox 2013	58	84	65.9	67.1	6	NA	79	70	7.5 (NA)	8 (NA)
Maes 2013	14	14	71	67.6	1	NA	78	100	NA	NA
Aboumohamed 2014	82	100	71.5	71.5	NA	NA	78	70	24 (NA)	24 (NA)
Leow 2014	2667	40980	NA	NA	NA	NA	88.8	83	3.0 (NA)	3.0 (NA)
Musch 2014	100	42	71.4	69	6	NA	76	64	3.0 (NA)	2.0 (NA)
Niegisch 2014	64	79	68	71	4	Board certified urologists	78	77	9.1 (NA)	9.1 (NA)
Koupparis 2015	102	56	68.2	66.4	2	NA	69	78	3.0/3.0	3.0/3.0
Bak 2016	42	70	70	70	NA	NA	83.3	82.9	40 (0-70)	42 (0-72)
Cusano 2016	121	92	65.9	67.8	4	NA	78.5	79.3	16.8 (6.9-31.0)	16.5 (6.6-32.4)
Gandaglia 2016	138	230	70	70.9	2	NA	83.5	83.5	40.0 (32.0-47.1)	59.1 (48.4-67.2)
Iwamoto 2016	20	40	73	72.5	Multiple	NA	70	72.5	1.0 (NA)	1.0 (NA)
Li 2016	57	267	67	65.7	6	fellowship trained in urologic oncology	84.4	75.1	12.0 (NA)	12.0 (NA)
Satkunasivam 2016	28	79	63.5	67	NA	NA			9.4 (NA)	62.1 (NA)
Winters 2016	29	58	79.2	79.6	6	NA	62	64	0.7 (IQR 0.2-1.4)	1.7 (IQR 0.3-2.9)
Kingo 2017	38	125	68.3	72.3	5	NA	82	77.6	NA	NA
Koie 2017	29	196	65	69	NA	NA	93.1	77	20.7(10.2-35.2)	68(29.2-98.6)
Muto 2017	21	28	66.8	70.3	2	over 200 ORCs each, Limited RARC experience	85.7	75	26(8-32)	17.5(7-23.5)
Sharma 2017	65	407	70.9	70.2	5	NA	96.9	73.2	1.0 (NA)	1.0 (NA)
Flamiatos 2018	100	149	NA	NA	6	NA	84	72	1.0 (NA)	1.0 (NA)
Kukreja 2018	100	96	66.2	66.2	NA	fellowship trained in urologic oncology	81	81	3.0 (NA)	3.0 (NA)

Table 1 (*continued*)

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Author/year	N of patients		Age, y*		N of surgeons	Surgeon experience	Male (%)		follow-up, mean (SD) or median (IQR)	
	RARC	ORC	RARC	ORC			RARC	ORC	RARC	ORC
Simone 2018	64	46	62.5	63.6	NA	NA	78.1	86.6	48 (NA)	48 (NA
Tan 2018	50	45	62.8	65	2	NA	76	71.1	3.0 (NA)	3.0 (NA)
Panwar 2018	24	54	57	58	3	at least 20 RARC prior to study	NA	NA	8.68 ± 4.5	12.02±3.96
Ram 2018	125	45	61.8	60.1	3	NA	87.2	88.8	NA	NA
Hanna 2018	2048	7513	69	70	NA	NA	78.8	74.1	3.0 (NA)	3.0 (NA)
Faraj 2019	203	278	73	71	NA	NA	82.3	82	81 (37-114)	56 (31-85)
Moschini 2019	767	8990	67	67	NA	NA	80	80	81 (NA)	102 (NA)
Prospective studies										
Nix 2010	21	20	67.4	69.2	NA	More than 400 ORCs + more than 75 RARCs	66	85	NA	NA
Parekh 2013	20	20	69.5	64.5	1	NA	90	80	NA	NA
Messer 2014	20	20	69.5	64.5	1	NA	90	80	12.0 (NA)	12.0 (NA)
Bochner 2015	60	58	66	65	4	More than 10 yrs, post fellowship	85	72	58.8 (46.8 - 70.8)	58.8 (46.8 - 70.8)
Khan 2016	20	20	68.6	66.6	1	More than 150 ORCs and more than 110 RARCs	85	90	12.0 (NA)	12.0 (NA)
Parekh 2018	150	152	70	67	26	More than 10 radical cystectomies	84	84	24 (NA)	24 (NA)

*, Median or mean; RARC, robotic-assisted radical cystectomy; ORC, open radical cystectomy; NA, not available; SD, standard deviation; IQR, inter-quartile range.

RARC were promising but were mostly limited due to significant patient selection bias, short term follow-up, and limited number of patients included in most series (*Table 2*). Most of these retrospective analyses focused on rate of positive margins and lymph-node yields, with nearly all studies suggesting very similar outcomes for any type (standard *vs.* extended) of dissection. Positive surgical margins (PSM) has been largely related to stage of disease, with early reports demonstrating no significant increase in risk of PSM following RARC, which could be due to the fact that this might have been the preferred approach for less advanced cancers (50,51).

Long-term follow-up and report on multiple oncologic outcomes are sparse when taking into account all comparative randomized trials published to date (9,10,46,47,49,52). Rate of PSM ranged from 3.6% to 15% and 4.8% and 10% for RARC and ORC, respectively (*Table 2*). A recent metanalysis grouping all comparative RCT did not find any significant difference between RARC and ORC on either tumor recurrence (RR 0.94, 95% CI, 0.69–1.29, P=0.81) or PSM rates (RR 1.16, 95% CI, 0.56–2.40, P=0.90) (53). Only one well conducted RCT with a median follow-up of 60 months reported on cancer-specific survival (CSS) and overall survival (OS) and did not show any differences between techniques for both outcomes at 5 years of follow-up (52). Finally, recently published results with a 3-year follow-up from the RAZOR trial did not find any difference between techniques in the cumulative incidence rates of recurrence (P=0.80), progression-free survival (68.4%, 95% CI, 60.1–75.3 and 65.4, 95% CI, 56.8–72.7 for RARC and

Table 2 Summary of oncologic outcomes

Author/year	PSM (%)		LND yield (Mean or Median*)		NAC (%)		Continent diversion (%)		DFS (%)		CSS (%)		OS (%)	
	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC
Retrospective studies														
Ng 2010	7.2	8.7	17.9	15.7	NA	NA	43.4	51	NA	NA	NA	NA	NA	NA
Richard 2010	3	9	17*	20*	2.8	8.5	14	11	NA	NA	NA	NA	NA	NA
Gondo 2012	9	20	20.7	13.8	0	0	36	40	NA	NA	NA	NA	NA	NA
Khan 2012	0	10	16	11	NA	NA	12.5	9.6	NA	NA	NA	NA	NA	NA
Styn 2012	16	11	14.3	15.2	46	42	NA	NA	NA	NA	NA	NA	NA	NA
Sung 2012	NA	NA	19.1	12.9	NA	NA	62.9	22.1	NA	NA	NA	NA	NA	NA
Kader 2013	12	11	17.7	15.7	10	10	3	17	NA	NA	NA	NA	NA	NA
Knox 2013	7	8	21.3	17.7	15	22	8.6	10.7	NA	NA	NA	NA	NA	NA
Maes 2013	21	14	11.9	9.5	NA	NA	0	0	NA	NA	NA	NA	NA	NA
Aboumohamed 2014	NA	NA	NA	NA	NA	NA	0	0	NA	NA	NA	NA	NA	NA
Leow 2014	NA	NA	NA	NA	NA	NA	8.5	6.1	NA	NA	NA	NA	NA	NA
Musch 2014	2	2	27.5	19.6	2	1	24	26	NA	NA	NA	NA	NA	NA
Niegisch 2014	6.4	10.1	20*	21*	9	3	45	49	NA	NA	NA	NA	not reached	55.2 m
Koupparis 2015	NA	NA	NA	NA	42.2	4.1	10.8	7.1	NA	NA	NA	NA	NA	NA
Bak 2016	NA	NA	NA	NA	19	17.1	31	20	NA	NA	NA	NA	NA	NA
Cusano 2016	8.3	5.6	18	11.5	28.9	19	40.8 #	30.4	NA	NA	NA	NA	NA	NA
Gandaglia 2016	8.7	13.5	12-Jan	13-Jan	19.9	0	15.2 #	62.5	54.2 (5y)	57.1 (5y)	73.5 (5y)	61.9 (5y)	59.1 (5y)	58.4 (5y)
Iwamoto 2016	0	5	21	16	NA	NA	15	23	NA	NA	NA	NA	NA	NA
Li 2016	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Satkunasivam 2016	NA	NA	NA	NA	17.9	3.8	100 #	100	NA	NA	NA	NA	NA	NA
Winters 2016	27	22	22.6	17.2	38	29	7	4	NA	NA	NA	NA	NA	NA
Kingo 2017	NA	NA	NA	17.27	34.2	20.8	100 #	100	NA	NA	NA	NA	NA	NA
Koie 2017	0	0.5	15*	18*	100	100	NA	NA	NA	NA	NA	NA	NA	NA
Muto 2017	NA	NA	11.5	11	42.9	32.1	33.3	10.7	37.4	30.9	NA	NA	40.2	34.8
Sharma 2017	10.8	12	15*	16*	21.5	39.3	15.4	26.3	NA	NA	NA	NA	NA	NA
Flamiatos 2018	NA	NA	NA	NA	23	26	16	26	NA	NA	NA	NA	NA	NA
Kukreja 2018	NA	NA	NA	NA	55	51	NA	NA	NA	NA	NA	NA	NA	NA
Simone 2018	0	0.3	33.4	30.7	25	4.7	100 #	100	79.3 (48 mos)	73.4 (48 mos)	86.4 (48 mos)	85.3 (48 mos)	82.1 (48 mos)	79.6 (48 mos)

Table 2 (*continued*)

Table 2 (*continued*)

Author/year	PSM (%)		LND yield (Mean or Median*)		NAC (%)		Continent diversion (%)		DFS (%)		CSS (%)		OS (%)	
	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC
Tan 2018	NA	NA	NA	NA	33	22.2	20 #	15.6	NA	NA	NA	NA	NA	NA
Panwar 2018	4.2	3.7	26.13	20.66	4.16	14.8	37.5	18.52	NA	NA	91.66 (16 mos)	90.74 (16 mos)	91.66 (16 mos)	77.78 (16 mos)
Ram 2018	6.4	4.4	23.6	20.82	17.6	17.8	38	28.9	NA	NA	NA	NA	NA	NA
Hanna 2018	9.3	10.7	17*	12*	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Faraj 2019	3.4	5.4	18*	12*	56.4	46	15.8	14.4	70.8 (5 y)	64.7 (5 y)	NA	NA	58.9	57.7
Moschini 2019	10	6.3	21	20	26	3.6	NA	NA	26 (3 y)	37 (3 y)	NA	NA	NA	NA
Prospective studies														
Nix 2010	0	0	19	18	NA	NA	33.3	30	NA	NA	NA	NA	NA	NA
Parekh 2013	5	5	11*	23*	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Messer 2014	5	5	NA	NA	30	35	5	10	NA	NA	NA	NA	NA	NA
Khan 2016	15	10	16.3	18.8	10	15	10	15	NA	NA	NA	NA	NA	NA
Parekh 2018	6	5	23.3	25.7	27	36	25	20	NA	NA	NA	NA	NA	NA
Bochner 2015 and 2018	3.3	5.2	NA	NA	32	45	55	60	NA	NA	NA	NA	NA	NA

RARC, robotic-assisted radical cystectomy; ORC, open radical cystectomy; NAC, neoadjuvant chemotherapy; NA, not available; LND, lymphadenectomy; # ICUD, intracorporeal urinary diversion; DFS, disease-free survival; CSS, cancer-specific survival; OS, overall survival.

ORC, respectively, P=0.60) or OS (73.9%, 95% CI, 65.5–80.5 and 68.5%, 95% CI, 59.8–75.7 for RARC and ORC, respectively, P=0.33) (54).

Perioperative parameters and complications

The majority of the studies provide little information on the specific adverse events patients experienced (*Table 3*). Several retrospective studies included ORC patients with more comorbidities and advanced stages of disease, which could likely have led to a selection bias when comparing complications between techniques (*Table 3*). There seems to be an advantage in favor of RARC over ORC when comparing the frequencies of 90d overall complications, 90d higher-grade complications (Clavien ≥3) and 90d mortality between groups within included retrospective series. However, data from most RCT point towards a different scenario when it comes to the incidence of complications between techniques (53). Adverse events occurred in 67% and 69% of patients in RARC and ORC groups, respectively in the RAZOR trial, with similar complication rates within 90 days between groups for both low and higher-grade complications (49). Moreover, a pooled analysis of 3 RCT did not show any difference in the incidence of major complications (Clavien ≥3) between RARC and ORC (RR 1.03, 95% CI, 0.75–1.49, P=0.74) (53).

RARC seems to be consistently associated with lower estimated blood loss (EBL), shorter length of stay (LOS), lower transfusion rates (TR) and longer operative times (OT) among most retrospective studies. When looking exclusively into included RCT, the same seems to be true in regard to EBL, TR, and OT. Similarly, the RAZOR trial found a significant difference in median LOS in favor of RARC compared to ORC (6 days, 5–10 versus 7 days, 6–10, P<0.02) (49). However, a recent metanalysis of 5 RCTs reported on only a marginal diminished LOS in favor of RARC compared to ORC (RR −0.63 days, 95% CI, −1.21 to −0.05, P=0.03) (53). In all, this difference in LOS might be due to recent change in post-operative pathways, as discussed in detail below.

Table 3 Comparative description of complications between RARC and ORC

Author and year	GI (%)		GU (%)		Urine leak (%)		UES (%)		Sepsis (%)		Wound infection (%)		IAI (5%)		MI (%)		DVT/PE (%)		PNA (%)	
	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC	RARC	ORC
Retrospective studies																				
Ng 2010	19.7	22.4	NA	NA	2.4	0.5	NA	NA	19.4	15.8	6.5	8	6.1	9.9	1.2	2.9	6.1	1.9	2.4	1.4
Khan 2012	20	19	NA	NA	NA	NA	NA	NA	5	8.1	10	8.1	NA	NA	0	0	NA	NA	NA	NA
Styn 2012	22	25	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sung 2012	25.7	31.8	NA	NA	8.6	0.9	NA	NA	20	7.7	2.8	16.3	0	0.9	NA	NA	NA	NA	NA	NA
Knox 2013	12	13.1	NA	NA	0	1.2	15.5	3.6	3.4	7.2	1.2	7.2	3.4	6	0	2.4	1.7	3.6	0	2.4
Musch 2014	8	33	NA	NA	NA	NA	1	0	32	43	NA	NA	2	2	1	0	3	19	NA	NA
Bak 2016	21.5	22.8	NA	NA	NA	NA	NA	NA	21	20	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cusano 2016	19.8	25	5	6.5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Iwamoto 2016	0	12.5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Kingo 2017	14	10.4	NA	NA	NA	NA	NA	NA	18	9.6	0	1.6	6	4.8	NA	NA	2	4.8	2	2.4
Koie 2017	17.2	3.6	NA	NA	NA	NA	NA	NA	6.9	11.7	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Flamiatos 2018	46	54	14	17	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Tan 2018	47.5	31.1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Panwar 2018	2	14	NA	NA	NA	NA	NA	NA	NA	NA	4	10	NA	NA	NA	NA	NA	NA	1	1
Ram 2018	9.6	13.2	NA	NA	0.8	4.44	NA	NA	2.4	6.7	8	20	5.6	2.2	3.2	0	NA	NA	NA	NA
Prospective studies																				
Nix 2010	9.5	15	NA	NA	NA	NA	NA	NA	9.9	5	NA	NA	NA	NA	NA	NA	4.8	0	NA	NA
Parekh 2013	5	5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bochner 2015	23	29	5	14	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	8.3	8.6	NA	NA
Khan 2016	45	5	NA	NA	10	15	10	0	35	15	NA	NA	5	30	10	1	10	0	10	1
Parekh 2018	27	24	NA	NA	NA	NA	9	7	45	37	9	19	5	2	2	1	6	9	5	4

RARC, robotic-assisted radical cystectomy; ORC, open radical cystectomy; GI, gastrointestinal; SBO, small-bowel obstruction; GU, genitourinary; UES, ureteroenteric stricture; IAI, Intra-abdominal infection; MI, myocardial infarction; DVT/PE, deep vein thrombosis / pulmonary embolism; PNA, pneumonia; NA, not available

Health-related quality of life (HRQOL) outcomes

The expansion of robotic cystectomy has resulted in a number of studies that have sought to assess if there is any difference between robotic and open techniques with regard to post-operative HRQOL. The studies measuring the HRQOL of RARC *vs.* ORC problematically used varying instruments at differing follow-up times, thereby making it difficult to compare the two techniques directly. Nevertheless, the five studies analyzed in this review almost universally reported no statistically significant differences between techniques. Differences that were reported were either minimal or transient in nature. One retrospective analysis of 324 patients at a single institution that evaluated HRQOL was unique in using a combination of the Bladder Cancer Index (BCI) for long term post-operative convalescence (1,3,6,12 months) and Convalescence and Recovery Evaluation (CARE) for short term follow-up (2,4,6 weeks) (30). Baseline BCI/CARE scores were comparable between RARC and ORC groups. Post-operative analysis revealed that recovery was comparable across BCI domains and that scores had nearly returned to baseline level at 1 year for all patients. Two other retrospective studies that utilized the BCI and included somewhat smaller cohorts similarly found no significant difference in HRQOL (21,31). Messer *et al.* conducted a 40 patient RCT utilizing the Functional Assessment of Cancer Therapy-Vanderbilt Index Questionnaire (FACT-VCI) at 3, 6, 9, and 12 months post-operatively (48). They reported no significant differences with regard to physical, social/family, functional, or emotional well-being between RARC and ORC cohorts, with the exception of a slightly lower score in the ORC arm for physical well-being at 6 months. Two other RCTs, one of 302 patients that utilized FACT-VCI and one of 118 patients that utilized the Quality of Life Questionnaire Core 30, also assessed the HRLQ. Assessment at baseline, 3 and 6 months post-operatively yielded no significant differences between either arm in either study (9,49). One major limitation of studies reporting on HRQOL outcomes is the absence of objective independent measures of postoperative pain and return to work outcomes. Moreover, if is often hard to account for differences in surgeon's expertise. None of these studies provided granular data on differences between type of urinary diversion. Since most of the urinary diversions were carried out using ECUD, it is easy to underestimate potential gains in QOL due to the use of a robotic approach. Finally, on a recent report on HRQOL using data form the RAZOR trial, Becerra *et al.* showed there was no statistically significant difference between the surgical approaches at any time point, even though attention should be paid to the fact that all diversions were performed extracorporeally in this prospective trial (55). Therefore, definitive comparative HRQOL data will most likely come from large prospective studies comparing RARC with ICUD to either ORC or RARC with ECUD.

Healthcare costs

Amidst an evolving health system with limited resources, comparisons of overall, direct, and cost-to-patient between RARC and ORC are of outmost importance in order to improve population health. Robotic surgery has been questioned on most retrospective studies due to concerns regarding higher costs, as demonstrated in two previous population-based retrospective studies (22,56). In the first study, even though there were no differences in 90-d major complications between RARC and ORC, and RARC had 46% decreased odds of minor complications, 77% reduced odds for blood transfusion and shorter length of stay, RARC was associated with higher median 90-d direct hospital costs (ORC: $26,681 *vs.* RARC: $31,007; P<0.01). Major driver was increased cost of supplies, not board or room costs. Importantly, when restricting the analysis to centers performing ≥19 cases a year, RARC was no longer more costly than ORC for the highest-volume surgeons (22). In the second study, inpatient costs did not differ statistically, but RARC was still associated with higher 30-d ($31,009 *vs.* $27,947) and 90-d ($36,121 *vs.* $32,521) costs, likely influenced by a greater use of home health, and less usual discharge to home among RARC patients. Notably, the latter analysis included a fairly small cohort of patients undergoing RARC, and possibly failed to include SEER Medicare patients after 2012, which most likely reflects the beginning of RARC adoption within the general population (56). Besides these early observations, more recent cost outcomes analysis on perioperative and beyond inpatient spending have showed somewhat different results (37,38,57). Interestingly, one of these more recent studies found 90-d spending to be higher for ORC compared with minimally invasive cystectomy (open $38,071 *vs.* $34,369, P<0.01) (57). In part, the discrepancies in these results may be due to the difference in the period of most recent analysis, with lesser spending driven by increased experience, better postoperative management, and disposition after RARC in more recent years. Moreover, the dollar amount charged to patients for services was significantly reduced in the robotic group in a recent cost-to-patient estimate analysis (37).

The explanation for these findings were that more patients underwent imaging studies within 30 days of ORC, and were charged more for room and board and inpatient medications due to prolonged hospitalization (37). Finally, a recent study looked into cost-effectiveness of cystectomy with urinary diversion by comparing both techniques in terms of health utilities and gains in quality-adjusted life years (QALYs) (38). In this latter analysis, even though RARC was still significantly more expensive then ORC, it was associated with increased QALYs and was the preferred approach as long as it could prevent complications and transfusions (38). Unfortunately, the urological community is still awaiting definitive answers on comparative cost analysis between RARC and ORC since most randomized trials to date have failed at delivering such results (53). However, efforts should focus on reducing intra-operative expenditures by judicious use of instruments and by becoming more efficient at decreasing intra-operative time (56-58). Hospitals should adhere to standardized processes in order to decrease LOS, optimize use of postoperative home-health resources, and prioritize discharging patients to home whenever deemed safe.

ERAS and robotic surgery

First introduced in patients undergoing colorectal surgeries, enhanced recovery after surgery (ERAS) are perioperative programs designed to optimize the perioperative care of patients undergoing major surgeries. Eras protocols applied to patients undergoing either open or robotic cystectomy have shown to positively affect rates of multiple outcomes, including a decrease in complication, readmission, transfusion rates, post-operative ileus, and LOS (59). ERAS has had a major impact on ORC outcomes as demonstrated in multiple series based on data later then 2012, with reductions in LOS, postoperative complications, morbidity, and overall health costs (60,61). However, up until recently, there was still debate regarding the benefits of ERAS implementation for patients undergoing RARC (62). Multiple series have lately reported on similar reductions in LOS when ERAS recommendations are utilized in the care of patients undergoing RARC (51,63). Similarly, a recent prospective study on non-opioid pathway for patients undergoing RARC showed reduced oral opioid use, LOS, and median time to regular diet (64). Moreover, cumulative effect of ERAS and RARC lowered 90-d readmission rates and gastrointestinal complications in a recent single-center prospective cohort study (40). A minimally invasive approach aligns itself with the core principles of ERAS, decreasing surgical trauma and stress response, and facilitating quicker patient recovery. In fact, a recent consensus of the European Association of Urology working group on ERAS after RARC has been recently published, acknowledging the benefits of multiple ERAS components in the care of patients undergoing RARC, and giving guidance specifically for this patient population (65). Compared with ORC, ERAS designed for RARC incorporates multiple elements previously described for ORC (patient education, optimization of preoperative nutrition status, thromboembolic prophylaxis, early mobilization, etc.) with special emphasis to avoidance of epidural and reduced postoperative analgesia requirements (65).

Publications bias

Comparative analysis between surgical approaches should be interpreted with caution, especially when it entails evaluating the efficacy of the da Vinci robotic platform on clinical outcomes. One important comment to make is that the most recent randomized trial comparing both techniques has not found any significant differences in overall complications or major complication rates between techniques (49). Moreover, on a recent update of results, there hasn't been any differences between techniques for progression-free survival, cumulative incidence rates of recurrence, or overall survival with a 3-year follow-up (54). Moreover, it should be pointed out that ERAS protocols had not been implemented prior to 2012, which might have flawed some retrospective studies included here, incorporating more modern RARC and relatively older ORC series.

Another important aspect to consider is the influence of industry funding of research on reported outcomes (66,67). A large well-conducted review found that funded studies were more likely to have favorable efficacy results and conclusions compared with non-sponsored ones (67). Moreover, even though authors are expected to declare pertinent financial conflicts of interest (COI) when publishing their results, a recent analysis comparing COI with industry registered payments found that it was very common for payments to go undeclared in robotic surgery manuscripts (66). This is important because accepting corporate payments have been shown to impact the chance of reporting a benefit in favor of robotic surgery (68). Financial cooperation between industry and academic institutions will continue to occur, since this partnership is important for the conduction of multiple studies. However, liability processes should be implemented in order to guarantee transparency to journal readers. Moreover, class associations and journals might want to include a statement on the dollar amount payed to authors, because this seems to drive the inclination to report more favorable results on articles submitted for publication.

Future directions

Minimally invasive and robotic urologic surgery continues to evolve and has recently added a new platform specifically designed for single-port (SP) procedures (69). The da Vinci SP allows for three articulating instruments and a camera to be inserted into the patient through a SP (70). A recent series was published to evaluate and determine the feasibility and safety of this new platform (69). Nine patients, including one simple cystectomy with intracorporeal ileal conduit diversion, were operated on at a center of excellence with no reported intraoperative complications, even though operative time was noted to be longer compared to the equivalent multi-arm approaches (69). This is particularly attractive for RC since it decreases surgical trauma and allows for intracorporeal urinary diversions. However, large-scale head-to-head comparisons between the novel and the multi-arm platforms are still needed in order to better define indications and use of this new technology.

Although most prospective comparative data between RARC and ORC have failed to demonstrate big differences in complications, the attention has now shifted to the assessment of outcomes of the different types of urinary diversion utilized after removal of the bladder (71). Particularly in regard to the extension of required ureteral dissection when performing either ICUD or ECUD, intraoperative use of indocyanine green (ICG) has been shown to improve real-time assessment of ureteral blood supply, and significantly reduced the rates of ureteroenteric strictures in a group of patients undergoing RARC with ICUD (72). This is a technology that is becoming standard on latest generations of the robot and could potentially have a positive impact on decreasing the incidence of delayed urinary complications after RARC.

Conclusions

Comparative effectiveness investigation is an important part in assessing health care delivery. In this narrative review of contemporary studies RARC was consistently found to be associated with decreased blood loss and lower transfusion rates compared with ORC. Despite multiple advantages reported for RARC in regard to LOS, mortality within 90 days, and higher-grade complications within 90 days on retrospective series, no significant differences were encountered between techniques in regard to postoperative complications, rates of recurrence and PSM, overall survival, and HRQOL outcomes in prospective studies. Further comparisons between RARC with ICUD and either ORC or RARC with ECUD, with special attention to costs and improvement in quality of care are necessary in order to better delineate future management of this common disease.

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