

REVIEW

Open Access



Robot-assisted radical cystectomy vs open radical cystectomy in patients with bladder cancer: a systematic review and meta-analysis of randomized controlled trials

Hongquan Liu^{1†}, Zhongbao Zhou^{2†}, Huibao Yao¹, Qiancheng Mao¹, Yongli Chu³, Yuanshan Cui^{1*} and Jitao Wu^{1*}

Abstract

Purpose Even though there isn't enough clinical evidence to demonstrate that robot-assisted radical cystectomy (RARC) is preferable to open radical cystectomy (ORC), RARC has become a widely used alternative. We performed the present study of RARC vs ORC with a focus on oncologic, pathological, perioperative, and complication-related outcomes and health-related quality of life (QOL).

Methods We conducted a literature review up to August 2022. The search included PubMed, EMBASE and Cochrane controlled trials register databases. We classified the studies according to version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). The data was assessed by Review Manager 5.4.0.

Results 8 RCTs comparing 1024 patients were analyzed in our study. RARC was related to lower estimated blood loss (weighted mean difference (WMD): -328.2; 95% CI -463.49—-192.92; $p < 0.00001$), lower blood transfusion rates (OR: 0.45; 95% CI 0.32 – 0.65; $p < 0.0001$) but longer operation time (WMD: 84.21; 95% CI 46.20 -121.72; $p < 0.0001$). And we found no significant difference in terms of positive surgical margins ($P=0.97$), lymph node yield ($P=0.30$) and length of stay ($P=0.99$). Moreover, no significant difference was found between the two groups in terms of survival outcomes, pathological outcomes, postoperative complication outcomes and health-related QOL.

Conclusion Based on the present evidence, we demonstrated that RARC and ORC have similar cancer control results. RARC is related to less blood loss and lower transfusion rate. We found no difference in postoperative complications and health-related QOL between robotic and open approaches. RARC procedures could be used as an alternate treatment for bladder cancer patients. Additional RCTs with long-term follow-up are needed to validate this observation.

Keywords Bladder cancer, Robot-assisted radical cystectomy, Open radical cystectomy, Randomized controlled trial, Meta-analysis

[†]Hongquan Liu and Zhongbao Zhou contributed equally to this work as co-first authors.

*Correspondence:

Yuanshan Cui
doctorcuiys@163.com
Jitao Wu
wjturology@163.com

Full list of author information is available at the end of the article



Introduction

With more than half a million new cases annually, bladder cancer has become one of the ten most prevalent kinds of cancer in the world [1, 2]. Open radical cystectomy (ORC) is still the advised surgical procedure for patients with muscle-invasive bladder cancer and those with very high-risk non-muscle-invasive bladder cancer [3]. The value of ORC, however, has been limited because of the drawbacks of a high morbidity and mortality, such as urinary tract infection, urinary leak, renal failure, ileus and thromboembolic complications. More than 60% of patients receiving ORC undoubtedly have at least one perioperative problem, and 20% have a high-grade complication after their procedure [4, 5]. Radical cystectomy has been performed using minimally invasive surgical techniques over the past two decades [6]. Menon et al. reported the first robot-assisted radical cystectomy (RARC) twenty years ago [7], which has become common technology around the world, especially in many high-volume locations. Initially, a tiny incision was made in the abdominal wall to execute urinary diversion by extracorporeal procedure. The development of intracorporeal urinary diversion (ICUD) has, however, been made possible by technological adjustments made to RARC. [8]. From 2005 to 2016, the use of ICUD grew from 9 to 97% of urinary diversion surgeries [9].

Several studies have indicated that compared with ORC, RARC has fewer perioperative complications, shorter length of stay and lower estimated blood loss [10–12]. Nevertheless, very few studies have revealed the long-term oncological results, and the majority of investigations are retrospective. Randomized controlled trials (RCTs) remain crucial for establishing how RARC and ORC compare to one another. Recently, a sizable quantity of fresh data from RCTs emerged that included long-term oncological outcomes, adding new evidence to the theme [13–16].

To assess the oncologic, pathological, perioperative, postoperative complications outcomes as well as health-related quality of life (QOL), for RCTs comparing RARC with ORC, we carried out this meta-analysis to update the current evidence base.

Materials and methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement [17] was followed when conducting this study. As no primary personal information will be gathered, no extra ethical approval is necessary.

Literature search

The research was registered on PROSPERO (CRD42023396105). Two reviewers independently

searched MEDLINE (2009 to August 2022), EMBASE (1995 to August 2022), and the Cochrane Controlled Trials Register databases for appropriate RCTs comparing RARC with ORC. Moreover, references from retrieved studies were searched. The following keywords were applied, such as “bladder cancer”, “cystectomy”, “robot”, “robotic”, “da Vinci”, “ORC”, “RARC”, and “randomized controlled trials”.

Inclusion criteria and selection of studies

Studies were included if they conformed to the following criteria: (1) comparison of ORC with RARC; (2) the study provided analyzable data of interest: overall survival (OS), recurrence-free survival (RFS), oncologic efficacy (positive margin status [PSM], lymph node yield, sites of recurrence) and perioperative outcomes (estimated blood loss [EBL], blood transfusion rates, operating room time [ORT], length of stay [LOS]), postoperative complications and health-related QOL assessment; (3) The article's whole text was accessible. We included either the more current or higher-quality patient-cohort article when there were equivalent papers. If the same group performed numerous experiments on a similar set of participants, we included each study. A flowchart of the study selection process is presented in Fig. 1.

Risk of bias assessment

Using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) [18], we classified the included studies. These studies were classified into three degrees: low risk of bias, some concerns, or high risk of bias. The writers came to an agreement on certain points where they disagreed.

Data extraction

We extracted the required data: (1) the first author's name and the published time of the article; (2) the region of each RCT; (3) study design; (4) treatment and sample size; (5) age, sex, body mass index (BMI) and American Society of Anesthesiologists (ASA) score; (6) tumor stage and urinary diversion type; (7) overall survival (OS) rate, recurrence-free survival (RFS) rate and sites of recurrence; (8) PSM and lymph node yield; (9) blood transfusion rates, ORT, EBL and LOS; (10) the date of postoperative complications and health-related QOL assessment.

Statistical analysis

This study used Review Manager Version 5.4 (Cochrane Collaboration, London, UK) to evaluate comparable data. Continuous results were estimated using weighted mean difference (WMD) with 95% confidence intervals (CIs). Besides, the odds ratio (OR) was used to estimate

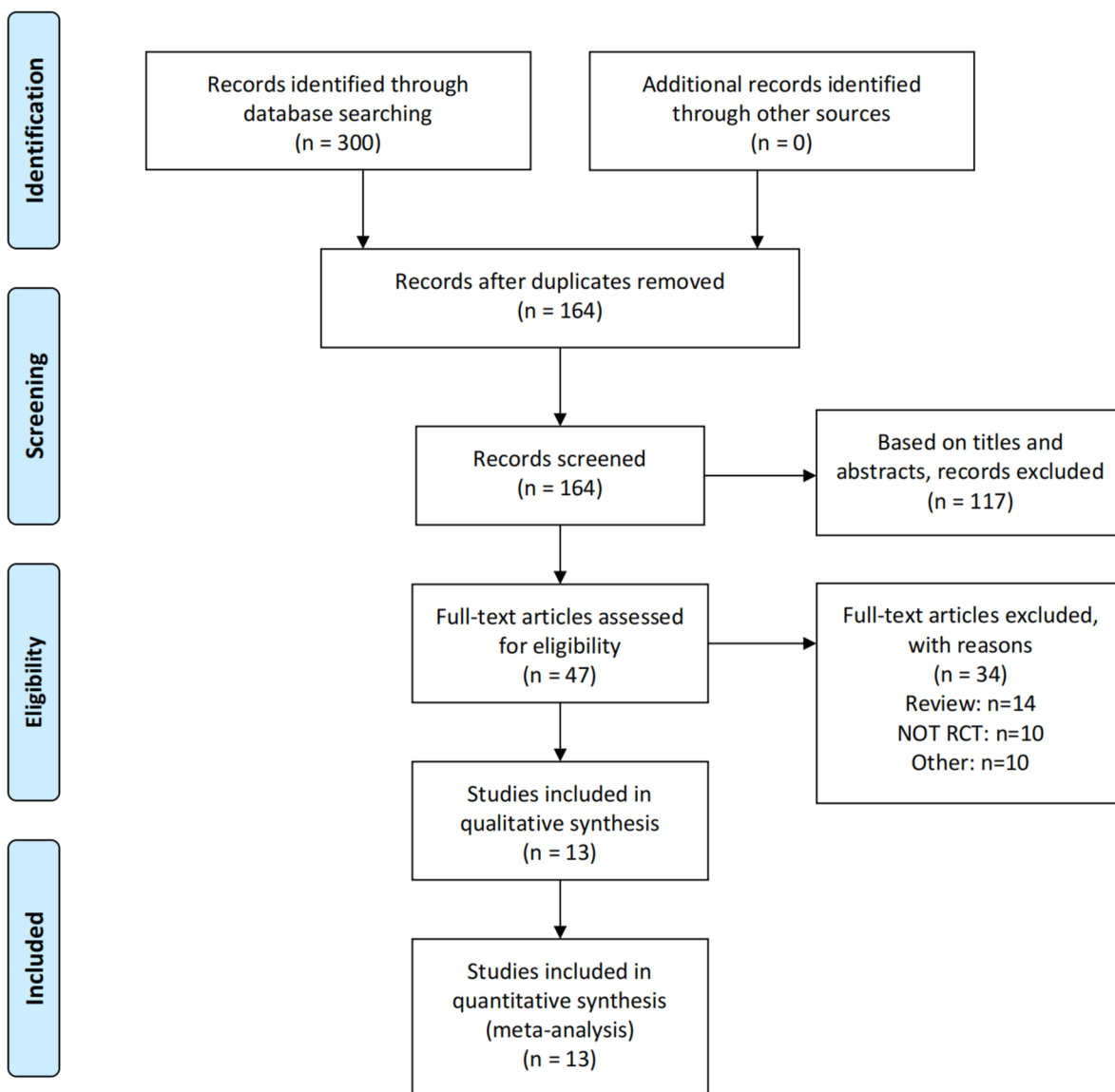


Fig. 1 A flow diagram of the study selection. RCT: randomized controlled trial

dichotomous variables. We used 95% CIs to express all outcomes, and statistical significance was set as $p < 0.05$. The degree of heterogeneity was calculated by Cochrane’s Q test and I^2 test. If there was significant inconsistency ($I^2 > 50\%$ or $p < 0.10$), we chose a random effect model for meta-analysis; if not, a fixed effect model was applied.

Results

Study characteristics

Overall, 300 potentially relevant articles were found by our initial literature search; 136 duplicates were removed. Furthermore, 117 and 34 publications were

excluded after evaluating the title/abstract and reading the full-text, respectively. And 13 studies (8 RCTs) [4, 14–16, 19–27] involving 1024 participants were studied in the meta-analysis. The basic features of the included RCTs are listed in Table 1.

Risk of bias

Each study included in the meta-analysis was RCT. According to RoB 2 [18], the majority of the listed RCTs were categorized as “low risk of bias” or “some concerns”. The bias of quality assessment is shown in Fig. 2.

Table 1 Characteristics of the included studies

Study	Region	Group	Number of patients	Age, years (median or mean)	Sex (M/F)	BMI (mean or median)	ASA score (mean or median)	Tumor stage (T1 or lower) /T2/T3/T4	Diversion type ileal conduit/ Neobladder/ continent cutaneous	Rate of neobladder (%)
Catto et al., 2022 [14]	UK	RARC/ORC	161/156	69.3/68.7	128/33; 122/34	NA	NA	71/30/NA/NA 70/34/NA/NA	142/NA/NA; 140/NA/NA	NA
Vejgaard et al., 2022 [20]	Denmark	RARC/ORC	25/25	70/67	18/7; 20/5	27.3/26.9	2.1/2.2	9/13/3/NA 6/15/4/NA	25/0/0; 25/0/0	0/0
Maiborn et al., 2022 [16]	Denmark	RARC/ORC	25/25	70/67	18/7; 20/5	27.3/26.9	2.1/2.2	9/13/3/NA 6/15/4/NA	25/0/0; 25/0/0	0/0
Mastroianni et al., 2022 [15]	Italy	RARC/ORC	58/58	64/66	44/14; 40/18	26/26	2.19/2.07	11/45/2/0; 12/44/2/0	NA/46/0; NA/42/NA	79/72
Khan et al., 2020 [21]	UK	RARC/ORC	20/20	68/68	17/3; 18/2	27.50/26.99	1.85/1.85	11/3/6/0; 14/0/4/2	18/2/0; 17/3/0	10/15
Venkatramani et al., 2020 [22]	USA	RARC/ORC	150/152	70/67	126/24; 128/24	27.8/28.2	NA	48/82/6/4; 51/81/16/4	113/36/1; 122/30/0	24/20
Bochner et al., 2018 [23]	USA	RARC/ORC	60/58	66/65	51/9; 42/16	27.9/29	2.73/2.84	35/8/12/5; 32/7/15/4	27/33/0; 23/32/3	55/55
Parekh et al., 2018 [4]	USA	RARC/ORC	150/152	70/67	126/24; 128/24	27.8/28.2	NA	48/82/6/4; 51/81/16/4	113/36/1; 122/30/0	24/20
Khan et al., 2016 [24]	UK	RARC/ORC	20/20	68.6/66.6	17/3; 18/2	27.5/27.4	1.85/1.85	11/3/6/0; 14/0/4/2	18/2/0; 17/3/0	10/15
Bochner et al., 2015 [25]	USA	RARC/ORC	60/58	66/65	51/9; 42/16	27.9/29	2.73/2.84	35/8/12/5; 32/7/15/4	27/33/0; 23/32/3	55/55
Messer et al., 2014 [26]	USA	RARC/ORC	20/20	69.5/64.5	18/2; 16/4	27.6/28.3	3.0/3.0	7/3/3/7; 12/1/2/5	19/1/0; 18/2/0	5/10
Parekh et al., 2013 [27]	USA	RARC/ORC	20/20	69.5/64.5	18/2; 16/4	27.6/28.3	3.0/3.0	7/3/3/7; 12/1/2/5	19/1/0; 18/2/0	5/10
Nix et al., 2010 [19]	USA	RARC/ORC	21/20	67.4/69.2	14/7; 17/3	27.5/28.4	2.71/2.70	6/12/3/0; 5/14/1/0	14/7/0; 14/6/0	33/30

BMI/Body mass index, ASA American Society of Anesthesiologists physical status classification, RARC Robot-assisted radical cystectomy, ORC Open radical cystectomy, NA Not available



Fig. 2 Quality assessment of each study

Oncologic outcomes

The oncologic outcomes evaluated in this meta-analysis included overall survival, recurrence-free survival and recurrence patterns.

Overall survival

Four RCTs assessed OS between RARC and ORC. As seen in Fig. 3, the OS analysis in bladder cancer suggested no significant difference in survival rates between the two approaches at 3-mon (OR: 0.57; 95% CI 0.20 – 1.64; $P=0.30$), 6-mon (OR: 0.57; 95% CI 0.29 – 1.11; $P=0.10$), 1-year (OR: 0.72; 95% CI 0.45 – 1.16; $P=0.18$), 3-year (OR: 0.89, 95% CI 0.63—1.25; $P=0.51$) and 5-year (OR: 1.15, 95% CI 0.59—2.26; $P=0.68$) follow-up. This result indicated that when compared with the ORC, the RARC group had equivalent effectiveness when it came to overall survival.

Recurrence-free survival

In order to determine recurrence-free survival, four RCTs were examined. There was little significant difference between the two approaches for the 3-month (OR:

0.43, 95% CI 0.17—1.10; $P=0.08$), 6-mon (OR: 0.58, 95% CI 0.32—1.03; $P=0.06$), 1-year (OR: 0.89, 95% CI 0.60—1.33; $P=0.58$), 3-year (OR: 0.97, 95% CI 0.70—1.34; $P=0.86$) and 5-year (OR: 0.82, 95% CI 0.43—1.56; $P=0.54$) recurrence-free survival as shown in Fig. 4, which indicated that individuals who experienced RARC or ORC had similar recurrence-free survival.

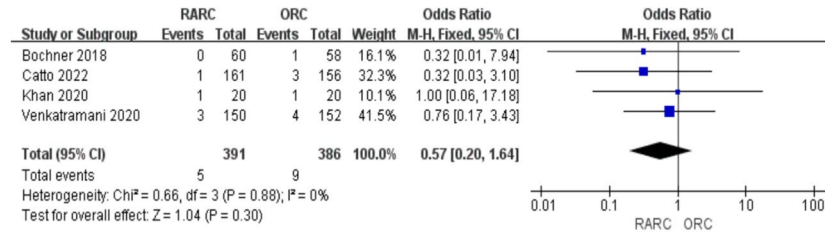
Recurrence patterns

Three RCTs were analyzed in terms of reported local (pelvic) and abdominal/distant recurrence data. Among the studies, no high risk of heterogeneity was found, so a fixed effects model was selected. As shown in Fig. 5a, we found neither RARC nor ORC was related to a substantially greater chance of a local or abdominal/distant recurrence. Nevertheless, regarding recurrence patterns, a significant difference was found between the two approaches (test for subgroup differences, $P=0.03$).

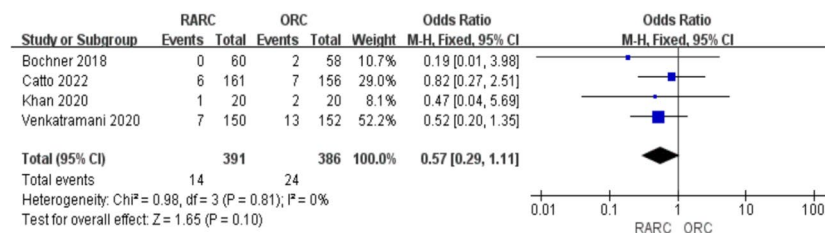
(See figure on next page.)

Fig. 3 Forest plots showing (a) 3-month overall survival, (b) 6-month overall survival, (c) 1-year overall survival, (d) 3-year overall survival, and (e) 5-year overall survival in RARC group and ORC group. MH mantel–haenszel, CI confidence interval, df degrees of freedom

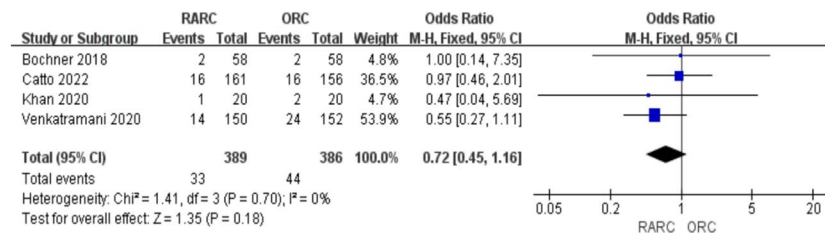
a 3-mon overall survival



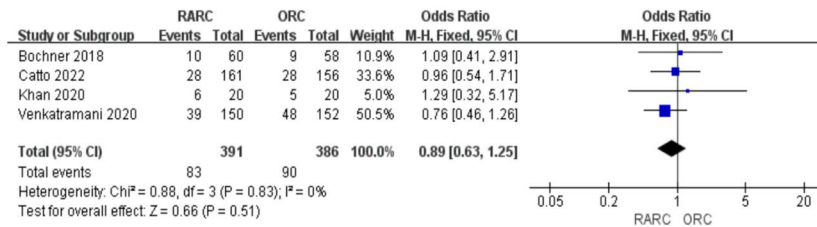
b 6-mon overall survival



c 1-year overall survival



d 3-year overall survival



e 5-year overall survival

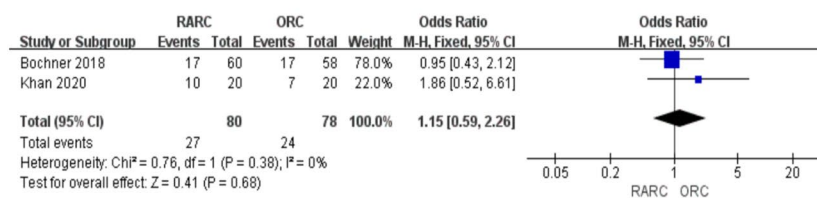


Fig. 3 (See legend on previous page.)

Pathological outcomes

Six investigations including 867 participants reported PSM rates. The heterogeneity test suggested $I^2=0\%$, so we used a fixed effect model. No difference in PSM was found (OR: 0.99; 95% CI 0.57–1.72; $P=0.97$ Fig. 5b). Likewise, no significant difference was found in terms of lymph node yield (WMD: -1.77; 95% CI -5.10 -1.57; $P=0.30$ Fig. 5c).

Perioperative outcomes

Intraoperative outcomes: operative time, EBL and blood transfusion rate

Operative time High heterogeneity was identified between studies ($I^2=94\%$), so we conducted the analysis using a random effect model. As shown in Fig. 6a, the forest plots indicated that RARC was related to longer operative time (WMD: 84.21; 95% CI 46.70 -121.72; $p<0.0001$ Fig. 6a).

Estimated blood loss Eight investigations showed the EBL [4, 14–16, 19, 24, 25, 27]. A random effect model was applied according to the findings of the heterogeneity test ($I^2=99\%$). Data from 1024 patients revealed that the EBL of RARC group was much lower than that of the ORC group. (WMD: -328.2; 95% CI -463.49—-192.92; $p<0.00001$ Fig. 6b).

Blood transfusion rate No high risk of heterogeneity was found, so we used a fixed effects model. Blood transfusion rates were found to be lower in RARC (OR: 0.45; 95% CI 0.32 – 0.65; $p<0.0001$ Fig. 6c).

Analysis of postoperative complications

We evaluated postoperative complications within 30 days and 90 days following surgery. As for the postoperative complication grades of RARC and ORC within 30 days after surgery, the analysis did not identify any significant difference: any Clavien–Dindo grade (OR: 0.71; 95% CI 0.39 – 1.29; $P=0.26$ Fig. 7a), Clavien–Dindo grade I–II (OR: 1.17; 95% CI 0.54 – 2.55; $P=0.69$ Fig. 7b), Clavien–Dindo grade III–IV (OR: 1.09; 95% CI 0.48 – 2.46; $P=0.84$ Fig. 7c). Likewise, we observed no significant difference regarding postoperative complication within 90 days between both groups: any Clavien–Dindo grade (OR: 0.84; 95% CI

0.63 – 1.12; $P=0.24$ Fig. 7d), Clavien–Dindo grade I–II (OR: 0.91; 95% CI 0.68 – 1.21; $P=0.50$ Fig. 7e), Clavien–Dindo grade III–IV (OR: 0.92; 95% CI 0.66 – 1.29; $P=0.64$ Fig. 7f).

Length of stay

We adopted a random effects model because of high heterogeneity ($I^2=98\%$). Evaluation of combined data from seven trials found no significant difference in LOS between the two groups (WMD: -0.01; 95% CI -1.25—1.24; $P=0.99$ Fig. 8).

Postoperative health-related QOL outcomes

Although six RCTs reported postoperative health-related QOL (Table 2), different quality-of-life assessment tools were used. As a result, it might not be possible to conduct a pooled analysis of data. The FACT-VCI was adopted by Messer et al. [26] to assess changes in health-related QOL scores between the two approaches at baseline, 3, 6, 9 and 12 months following surgery in 40 patients. In order to compare health-related QOL at baseline, 3 and 6 months after surgery, Bochner et al. [25] and Parekh et al. [4] adopted the QLQ-C30 and FACT-VCI, respectively, while after a mean of 8 months after surgery, Khan et al. [24] completed the FACT-BI. Vejgaard et al. [20] evaluated health-related QOL at baseline and 3 months after surgery using QLQ-C30. According to all research, health-related QOL of the two groups did not significantly differ from one another. Nevertheless, in a new trial, Catto et al. [14] used several measures in 317 participants to evaluate health-related QOL and concluded those who underwent robotic surgery showed better QOL vs open surgery at 5 weeks (difference in EQ-5D-5L scores, -0.07 [95% CI, -0.11 to -0.03]; $P=0.003$) and less disability at 5 weeks (WHODAS 2.0 scores, 0.48 [95% CI, 0.15–0.73]; $P=0.003$) and at 12 weeks (difference in WHODAS 2.0 scores, 0.38 [95% CI, 0.09–0.68]; $P=0.01$). By 26 weeks, there was little difference in terms of QOL and disability scores.

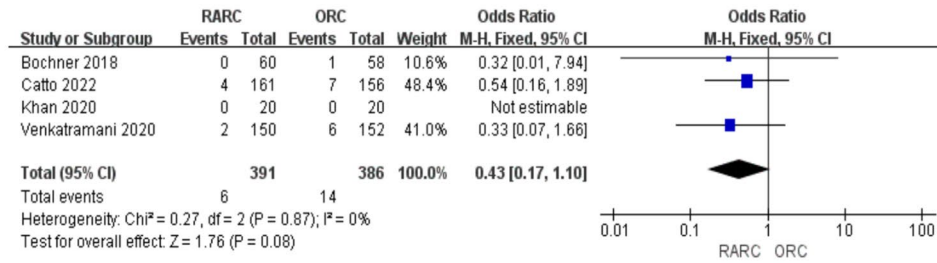
Discussion

Bladder cancer poses significant cumulative morbidity because of the advanced age and substantial smoking prevalence. Due to the intricacy of the procedure and

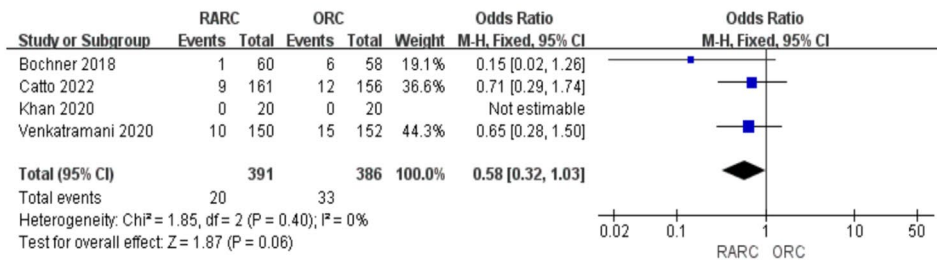
(See figure on next page.)

Fig. 4 Forest plots showing (a) 3-month recurrence-free survival, (b) 6-month recurrence-free survival, (c) 1-year recurrence-free survival, (d) 3-year recurrence-free survival, and (e) 5-year recurrence-free survival in RARC group and ORC group. MH mantel–haenszel, CI confidence interval, df degrees of freedom

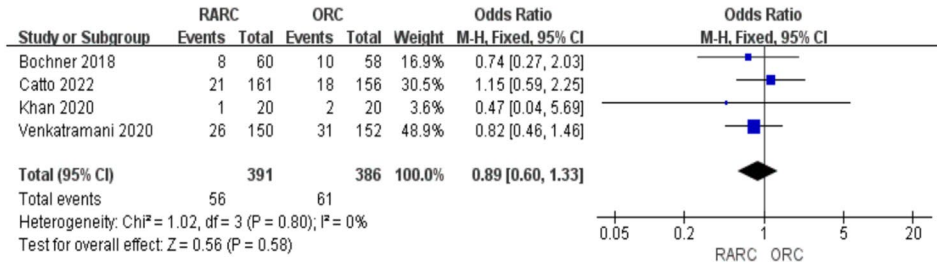
a 3-mon recurrence-free survival



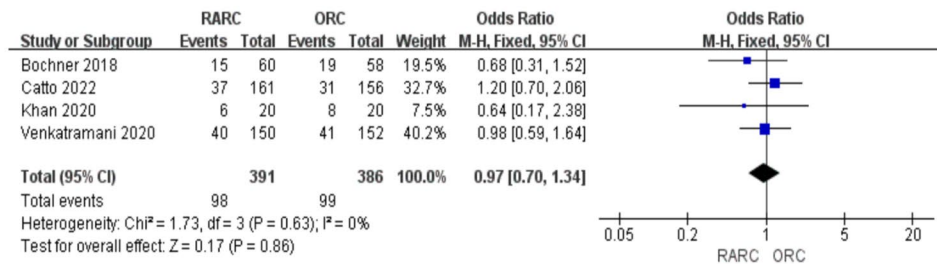
b 6-mon recurrence-free survival



c 1-year recurrence-free survival



d 3-year recurrence-free survival



e 5-year recurrence-free survival

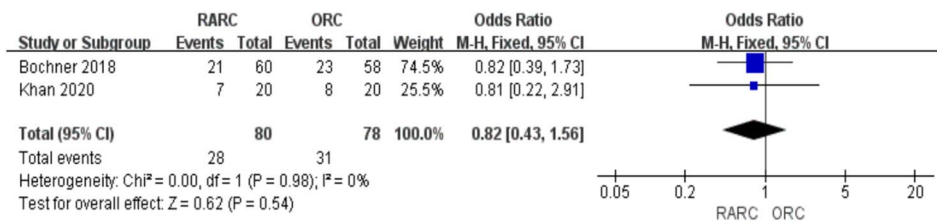
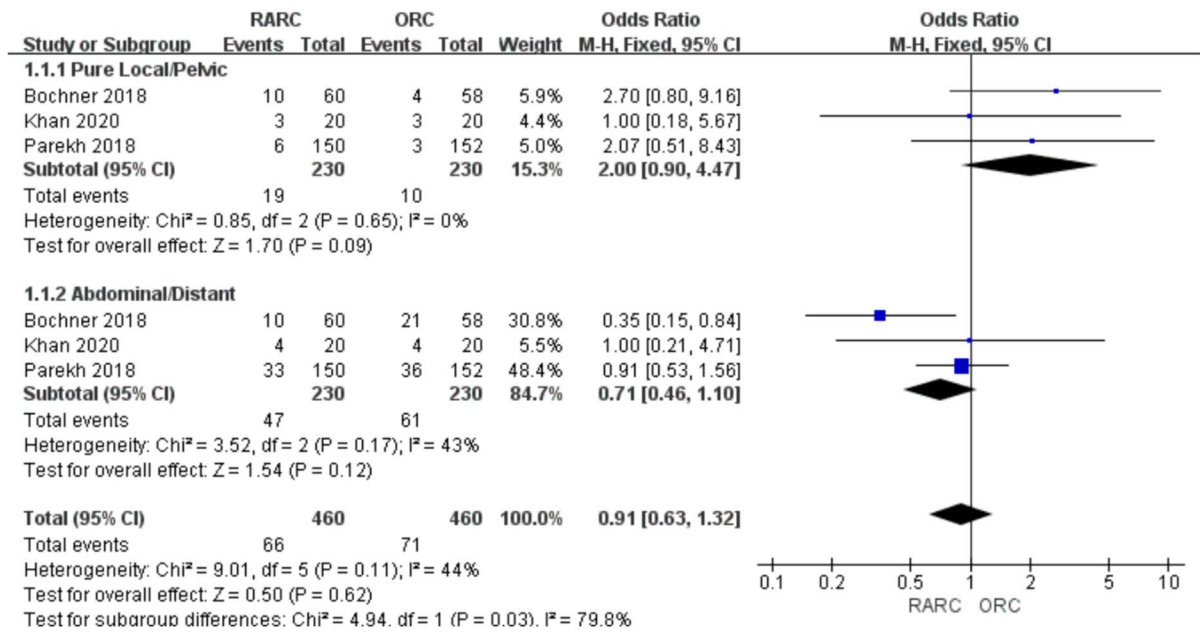
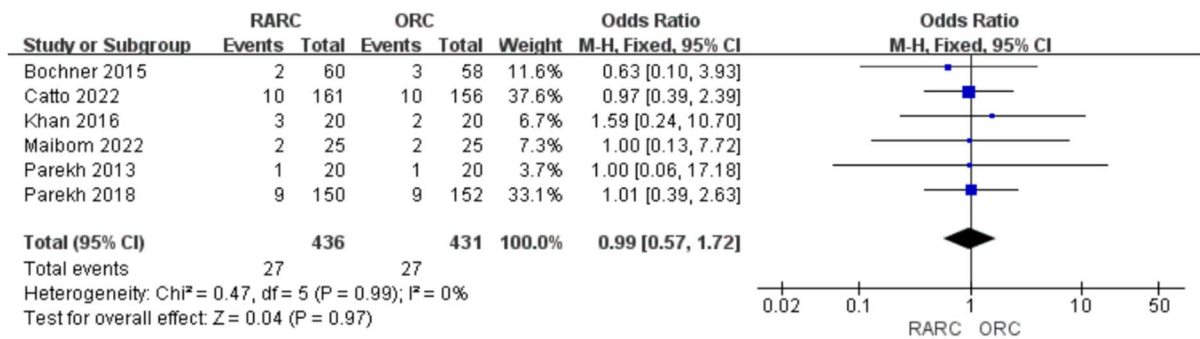


Fig. 4 (See legend on previous page.)

a Recurrence patterns



b Positive margin status



c Lymph node yield

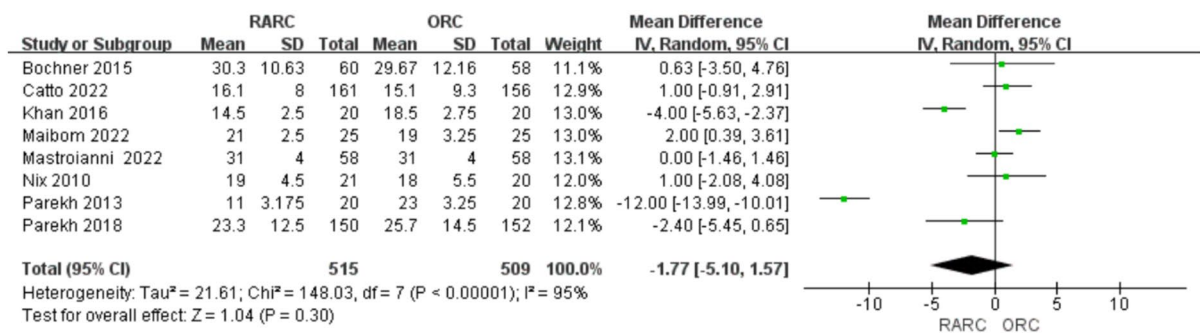
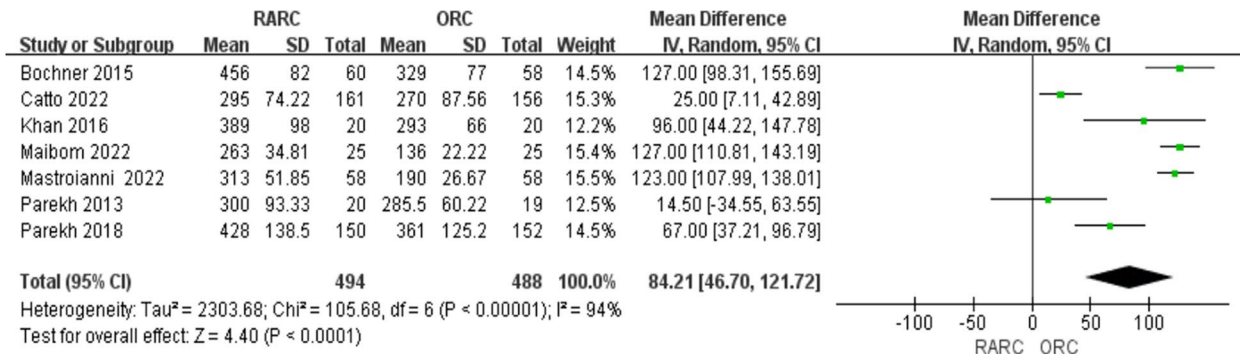
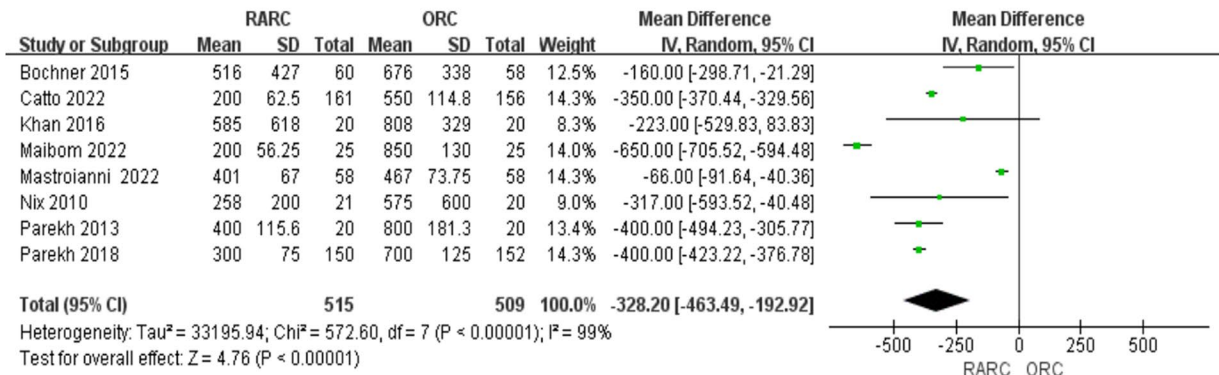


Fig. 5 Forest plots showing (a) recurrence patterns, (b) positive margin status, and (c) lymph node yield

a Operative time



b Estimated blood loss



c Blood transfusion rate

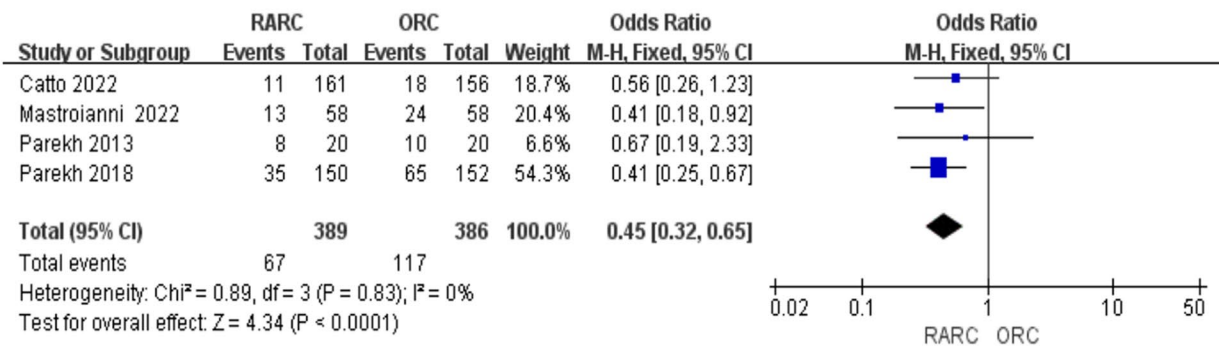
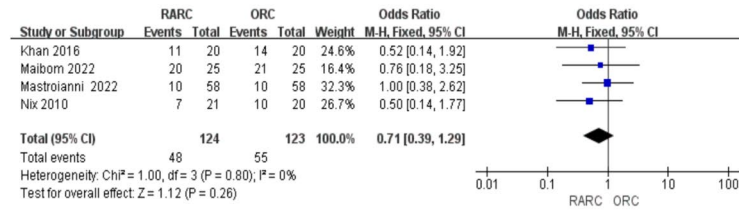


Fig. 6 Forest plots showing (a) operative time, (b) estimated blood loss, and (c) blood transfusion rate

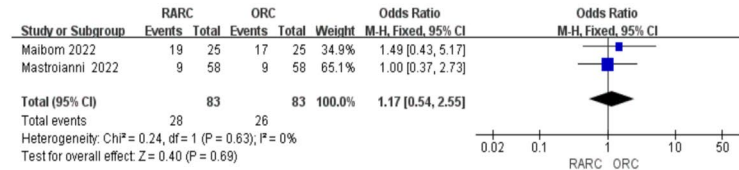
(See figure on next page.)

Fig. 7 Forest plots showing (a) complications of any Clavien-Dindo grade within 30 days, (b) complications of Clavien-Dindo grade I-II within 30 days, (c) complications of Clavien-Dindo grade III-IV within 30 days, (d) complications of any Clavien-Dindo grade within 90 days, (e) complications of Clavien-Dindo grade I-II within 90 days, and (f) complications of Clavien-Dindo grade III-IV within 90 days

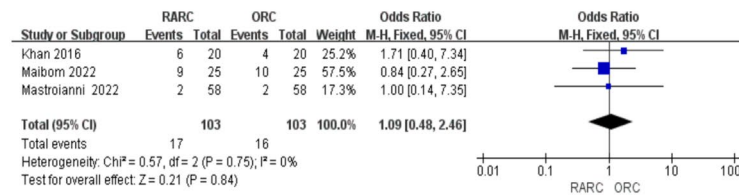
a Complications of any Clavien-Dindo grade within 30 days



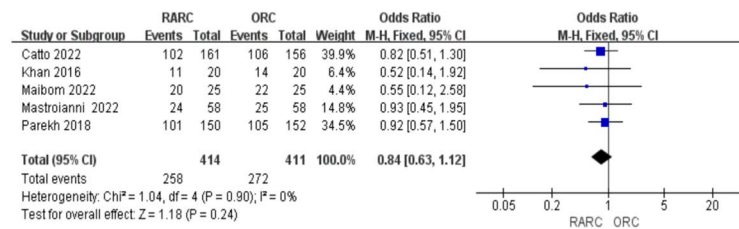
b Complications of Clavien-Dindo grade I-II within 30 days



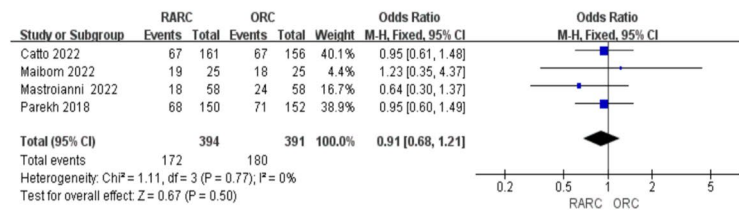
c Complications of Clavien-Dindo grade III - IV within 30 days



d Complications of any Clavien-Dindo grade within 90 days



e Complications of Clavien-Dindo grade I-II within 90 days



f Complications of Clavien-Dindo grade III - IV within 90 days

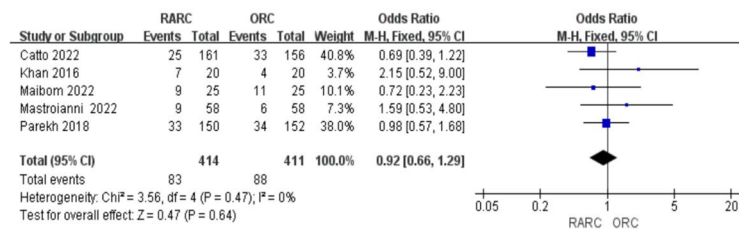


Fig. 7 (See legend on previous page.)

Length of stay

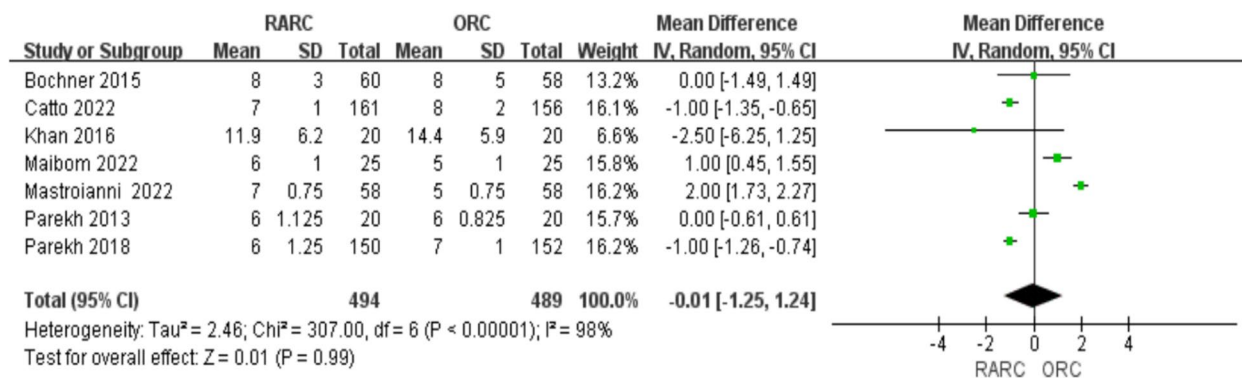


Fig. 8 Forest plots showing Length of stay

Table 2 Postoperative health-related QOL change

Author	QOL scale	Arm	QOL score baseline	QOL score at 1 month	QOL score at 3 months	QOL score at 6 months	QOL score at 9 months	QOL score at 12 months	QOL score overall
Catto 2022 [14]	EQ-5D-5L	RARC/ORC	0.89/0.90	0.83/0.77 (P=0.003)	0.88/0.86 (P=0.1)	0.87/0.87 (P=0.2)	NR	NR	NR
	QLQ-C30		87.55/87.74	76.46/68.66 (P<0.001)	86.06/81.96 (P=0.01)	87.14/84.86 (P=0.17)	NR	NR	NR
	QLQ-BLM30		NR	NR	NR	NR	NR	NR	NR
	WHODAS-2		9.3/9.2	20.9/26.4 (P=0.003)	10.2/14.9 (P=0.01)	10.8/11.1 (P=0.24)	NR	NR	NR
Vejlgaard 2022 [20]	QLQ-C30	RARC/ORC	77/78	NR	84/77 (P=0.47)	NR	NR	NR	NR
Parekh 2018 [4]	FACT-VCI	RARC/ORC	120.1/120.9	NR	122.8/125.2	126.0/127.5	NR	NR	NR
Khan 2016 [24]	FACT-BI	RARC/ORC	NR	NR	NR	NR	NR	NR	NR
Bochner 2015 [25]	QLQ-C30	RARC/ORC	78/75	NR	77/72 (P=0.40)	76/78 (P=0.5)	NR	NR	NR
Messer 2014 [26]	FACT-VCI	RARC/ORC	119/135	NR	126.5/135.5 (P=0.85)	121.5/126 (P=0.58)	141.5/127.5 (P=0.63)	116/129 (P=0.48)	NR

QOL Quality of life, RARC Robot-assisted radical cystectomy, ORC Open radical cystectomy, NA Not available

the patients’ intrinsic weakness, radical cystectomy—the recommended therapy for patients with very high-risk and muscle-invasive bladder cancer—is related to a significant prevalence of complications [1, 28]. Despite their greater cost and steeper learning curve, minimally invasive operations like RARC are being used in many areas of medicine [28, 29]. RARC has gained popularity in bladder cancer treatment because of its prospective benefits. According to reports, the percentage of cystectomies carried out with the RARC increased from 0.6% to 12.8% [30]. With a focus on the differences in results between RCTs, the purpose of the updated meta-analysis was to compare the most recent evidence

on the differential influence of these two strategies on oncologic, perioperative, and health-related (QOL) outcomes as well as complication-related outcomes.

Here we report the largest RCT outcomes analysis between RARC and ORC, including 1024 patients from eight studies. As a malignant tumor, bladder cancer patients’ long-term follow-up oncological outcomes are a major concern for surgeons. Our analysis of the existing literature showed equivalent oncologic results. Besides, we didn’t observe a difference in recurrence patterns, OS or RFS in all RCTs, indicating that RARC is a safe procedure, which has long-term survival effectiveness for bladder cancer that is comparable to that of ORC.

These conclusions are based on hypothesis and could be accessed further in a meta-analysis of individual patient data according to properly considered and standard definitions of recurrence locations. PSM and lymph node yield have a significant effect on postoperative survival. We also came to a conclusion from our study that there were no significant differences in PSM and lymph node yield.

Consistent with the benefits of the robotic approach for other malignant neoplasms, we found that RARC was related to lower blood loss and lower transfusion rates at the expense of prolonged operative time in terms of perioperative safety [31]. RARC has significant advantages in controlling bleeding, which may be due to clearer operational vision, more elaborate manipulation and the use of hemostatic devices in robotic-assisted surgery. In addition, another major factor affecting bleeding is the pneumoperitoneum used in robot-assisted surgery. The increase of pressure is conducive to the occlusion of small blood vessels, reducing the amount of bleeding [32].

In terms of the complication rate within 30 and 90 days, we observed no difference between ORC and RARC. Fewer postoperative complications are a potential benefits of RARC [33–36]. Yet, the RARC's benefit may not always be apparent. Additionally, in the Clavien–Dindo subgroup analyses, no significance was found between the two groups regarding minor and major complications at 30 days and 90 days following surgery. Urinary tract infections are typical complications following radical cystectomy [37]. Urinary diversions, however, make it hard to prevent these consequences. Despite continual improvements in surgical methods, similar complications have happened on occasion. Thus, there remains a great need to study postoperative complications [38].

Urinary construction is a key factor in postoperative complications, which is a controversial subject, with intracorporeal and extracorporeal options to choose from. In this meta-analysis, there are only three RCTs performed ICUD method [14–16]. Hussein et al. [9] analyzed 2,125 patients with radical cystectomy and concluded that the postoperative complications of ICUD decreased over time. However, ICUD has intrinsic difficulties, such as a challenging learning curve, insufficient clinical experience of the surgeons, unreasonable operating times, and the possibility of undermining the quality of the uretero-ileal anastomoses outweighing its advantages [39, 40]. Further studies about the procedure of urinary construction are needed, and it is essential to improve the understanding and management of these serious and common adverse reactions.

HRQOL relates to the influence of illness and therapy on one's physical, mental, and social spheres as related to overall well-being [41], which is considered to be one of

the important parameters after malignant tumor treatment [42, 43]. As several techniques were used to assess QOL, it was difficult to pool QOL data for our study. Five RCTs found no significant difference regarding health-related QOL. However, a new study comparing recovery after RARC with intracorporeal reconstruction vs ORC suggested that any statistically significant change at five weeks was in favour of robotic surgery in terms of postoperative health-related QOL outcomes [14]. This might be due to the change in urinary reconstruction and the large sample size in this study.

In this review, we also observed no significant difference in LOS, which reflect similar complication rates between the two procedures.

Compared with some existing meta-analyses [44–46], this study conducted the most comprehensive analysis of RCTs, both in terms of the number of RCTs included and the indicators analyzed. In addition to analyzing indicators such as PSM, EBL, blood transfer rates, ORT, LOS, etc. We also analyzed lymph node yield and health related QOL. We used more detailed methods to analyze survival indicators and postoperative complications, and conducted subgroup analysis of recurrence patterns. Nevertheless, several limitations cannot be avoided. First, a limited sample size of just 8 randomized controlled trials (1024 patients) raises concerns about the validity of our findings on effectiveness and safety. Next, the majority of the studies were not considered to use a blinding procedure for their participants, and thus there may be potential bias. The lack of information on postoperative complications is a disadvantage. Future research should follow criteria for evaluating and reporting of postoperative complications. Health-related QOL assessment tools differ significantly between eligible RCTs. In addition, most studies were performed at a single center, which is reflected in the results of the heterogeneity test of operative time and might reflect the experience of the individual surgeon. Furthermore, some included studies were carried out with enhanced recovery after surgery (ERAS) programmes. ERAS is a standardized, multimodal, and multidisciplinary scientific concept for perioperative management. ERAS aims to decrease intra-operative blood loss, decrease postoperative complications, and reduce recovery times. The main content of ERAS in urology includes admission assessment, preoperative preparation, intraoperative measures, and postoperative management. In particular, bleeding can be reduced by perioperative fluid management. Additionally, restrictive intraoperative hydration, along with norepinephrine administration, decreases intraoperative blood loss [47]. According to a study from the University of Sheffield [48], the use of the ERAS setting was

related to less blood loss and quicker recovery time following radical cystectomy, which related to study heterogeneity. It should be noted our single center has been implementing ERAS since 2015, and a retrospective cohort study including 192 patients from our center shows that ERAS may successfully speed up patient rehabilitation and is associated with less blood loss and LOS [49]. Furthermore, we performed a meta-analysis about this theme, evaluating and confirming the effectiveness of ERAS in the perioperative outcomes of radical cystectomy [50].

Conclusion

In conclusion, RARC had similar oncological outcomes compared with ORC as shown in our systematic review and meta-analysis. RARC leads to less EBL and lower blood transfusion rates at the expense of prolonged operative time. RARC and ORC resulted in similar rates of postoperative complications and health-related QOL. Further well-designed RCTs are essential to confirm this conclusion.

Abbreviations

ROB2	The version 2 of the Cochrane risk-of-bias tool for randomized trials
RARC	Robot-assisted radical cystectomy
ORC	Open radical cystectomy
QOL	Quality of life
ICUD	Intracorporeal urinary diversion
RCTs	Randomized controlled trials
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
OS	Overall survival
RFS	Recurrence-free survival
PSM	Positive margin status
EBL	Estimated blood loss
LOS	Length of stay
WMD	Weighted mean difference
CI	Confidence intervals
OR	Odds ratio
FACT-VCI	Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index
QLQ-C30	Quality of Life Questionnaire Core 30
FACT-BI	the Functional Assessment of Cancer Therapy – Bladder
EQ-5D-5L	The EuroQoL-5 dimension-5 level
WHODAS 2.0	WHO Disability Assessment Schedule 2.0
ERAS	Enhanced recovery after surgery
ASA	American Society of Anesthesiologists physical status classification
BMI	Body mass index

Acknowledgements

Not applicable.

Authors' contributions

Hongquan Liu and Zhongbao Zhou: Data curation; Investigation; Formal analysis; Writing original draft. Huihao Yao: Data curation; Investigation; Methodology; Resources; Supervision; Visualization; Writing—original draft. Qiancheng Mao: Formal analysis; Investigation; Methodology; Validation; Visualization; Writing—review & editing. Yongli Chu: Formal analysis; Investigation; Methodology; Validation; Visualization; Writing—review & editing. Yuanshan

Cui and Jitao Wu: Conceptualization; Funding acquisition; Methodology; Project administration; Writing—review & editing. All authors reviewed the manuscript.

Funding

This work was supported by Joint Fund of Shandong Natural Science Foundation (ZR2021LSW019), grants from the National Nature Science Foundation of China (Nos. 81870525) and the Taishan Scholars Program of Shandong Province (No. tsqn201909199).

Availability of data and materials

The datasets that support the findings of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The research does not involve patients, so ethical approval was not necessary.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Urology, The Affiliated Yantai Yuhuangding Hospital of Qingdao University, NO. 20 East Yuhuangding Road, Yantai 264000, Shandong, China. ²Department of Urology, Fengtai District, Beijing TianTan Hospital, Capital Medical University, No. 119 South 4Th Ring West Road, Beijing 100070, China. ³Department of Scientific Research, The Affiliated Yantai Yuhuangding Hospital of Qingdao University, NO. 20 East Yuhuangding Road, Yantai 264000, Shandong, China.

Received: 22 March 2023 Accepted: 2 August 2023

Published online: 05 August 2023

References

1. Lenis AT, Lec PM, Chamie K, Mshs M. Bladder Cancer: A Review. *JAMA*. 2020;324:1980.
2. Richters A, Aben KKH, Kiemeny LALM. The global burden of urinary bladder cancer: an update. *World J Urol*. 2020;38:1895–904.
3. Alfred Witjes J, Lebre T, Compérat EM, Cowan NC, De Santis M, Bruins HM, et al. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. *Eur Urol*. 2017;71:462–75.
4. Parekh DJ, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS, et al. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. *The Lancet*. 2018;391:2525–36.
5. Shabsigh A, Korets R, Vora KC, Brooks CM, Cronin AM, Savage C, et al. Defining Early Morbidity of Radical Cystectomy for Patients with Bladder Cancer Using a Standardized Reporting Methodology. *Eur Urol*. 2009;55:164–76.
6. Falagarío U, Veccia A, Weprin S, Albuquerque EV, Nahas WC, Carrieri G, et al. Robotic-assisted surgery for the treatment of urologic cancers: recent advances. *Expert Rev Med Devices*. 2020;17:579–90.
7. Menon M, Hemal AK, Tewari A, Shrivastava A, Shoma AM, El-Tabey NA, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion: NERVE-SPARING ROBOT-ASSISTED CYSTOPROSTATECTOMY and URINARY DIVERSION. *BJU Int*. 2003;92:232–6.
8. Fujimura T. Current status and future perspective of robot-assisted radical cystectomy for invasive bladder cancer. *Int J Urol*. 2019;26:1033–42.
9. Hussein AA, May PR, Jing Z, Ahmed YE, Wijburg CJ, Canda AE, et al. Outcomes of Intracorporeal Urinary Diversion after Robot-Assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium. *J Urol*. 2018;199:1302–11.
10. Wang GJ, Barocas DA, Raman JD, Scherr DS. Robotic vs open radical cystectomy: prospective comparison of perioperative outcomes

- and pathological measures of early oncological efficacy. *BJU Int.* 2007;101:89–93.
11. Pruthi RS, Wallen EM. Robotic Assisted Laparoscopic Radical Cystoprostatectomy: Operative and Pathological Outcomes. *J Urol.* 2007;178:814–8.
 12. Johar RS, Hayn MH, Stegemann AP, Ahmed K, Agarwal P, Balbay MD, et al. Complications After Robot-assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium. *Eur Urol.* 2013;64:52–7.
 13. Satkunasivam R, Tallman CT, Taylor JM, Miles BJ, Klaassen Z, Wallis CJD. Robot-assisted Radical Cystectomy Versus Open Radical Cystectomy: A Meta-analysis of Oncologic, Perioperative, and Complication-related outcomes. *European Urology Oncology.* 2019;2:443–7.
 14. Catto JWF, Khetrapal P, Ricciardi F, Ambler G, Williams NR, Al-Hammouri T, et al. Effect of Robot-Assisted Radical Cystectomy With Intracorporeal Urinary Diversion vs Open Radical Cystectomy on 90-Day Morbidity and Mortality Among Patients With Bladder Cancer: A Randomized Clinical Trial. *JAMA.* 2022;327:2092.
 15. Mastroianni R, Ferriero M, Tuderti G, Anceschi U, Bove AM, Brassetti A, et al. Open Radical Cystectomy versus Robot-Assisted Radical Cystectomy with Intracorporeal Urinary Diversion: Early Outcomes of a Single-Center Randomized Controlled Trial. *J Urol.* 2022;207:982–92.
 16. Maibom SL, Røder MA, Aasvang EK, Rohrsted M, Thind PO, Bagi P, et al. Open vs robot-assisted radical cystectomy (BORARC): a double-blinded, randomised feasibility study. *BJU Int.* 2022;130:102–13.
 17. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Int J Surg.* 2021;88:105906.
 18. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898.
 19. Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS. Prospective Randomized Controlled Trial of Robotic versus Open Radical Cystectomy for Bladder Cancer: Perioperative and Pathologic Results. *Eur Urol.* 2010;57:196–201.
 20. Vejlggaard M, Maibom SL, Joensen UN, Thind PO, Rohrsted M, Aasvang EK, et al. Quality of life and secondary outcomes for open versus robot-assisted radical cystectomy: a double-blinded, randomised feasibility trial. *World J Urol.* 2022;40:1669–77.
 21. Khan MS, Omar K, Ahmed K, Gan C, Van Hemelrijck M, Nair R, et al. Long-term Oncological Outcomes from an Early Phase Randomised Controlled Three-arm Trial of Open, Robotic, and Laparoscopic Radical Cystectomy (CORAL). *Eur Urol.* 2020;77:110–8.
 22. Venkatramani V, Reis IM, Castle EP, Gonzalvo ML, Woods ME, Svatek RS, et al. Predictors of Recurrence, and Progression-Free and Overall Survival following Open versus Robotic Radical Cystectomy: Analysis from the RAZOR Trial with a 3-Year Followup. *J Urol.* 2020;203:522–9.
 23. Bochner BH, Dalbagni G, Marzouk KH, Sjoberg DD, Lee J, Donat SM, et al. Randomized Trial Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: Oncologic Outcomes. *Eur Urol.* 2018;74:465–71.
 24. Khan MS, Gan C, Ahmed K, Ismail AF, Watkins J, Summers JA, et al. A Single-centre Early Phase Randomised Controlled Three-arm Trial of Open, Robotic, and Laparoscopic Radical Cystectomy (CORAL). *Eur Urol.* 2016;69:613–21.
 25. Bochner BH, Dalbagni G, Sjoberg DD, Silberstein J, Keren Paz GE, Donat SM, et al. Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial. *Eur Urol.* 2015;67:1042–50.
 26. Messer JC, Punnen S, Fitzgerald J, Svatek R, Parekh DJ. Health-related quality of life from a prospective randomised clinical trial of robot-assisted laparoscopic vs open radical cystectomy: Health-related quality of life in trial of ORC vs RARC. *BJU Int.* 2014;114:896–902.
 27. Parekh DJ, Messer J, Fitzgerald J, Ercole B, Svatek R. Perioperative Outcomes and Oncologic Efficacy from a Pilot Prospective Randomized Clinical Trial of Open Versus Robotic Assisted Radical Cystectomy. *J Urol.* 2013;189:474–9.
 28. Kimura S, Iwata T, Foerster B, Fossati N, Briganti A, Nasu Y, et al. Comparison of perioperative complications and health-related quality of life between robot-assisted and open radical cystectomy: A systematic review and meta-analysis. *Int J Urol.* 2019;26:760–74.
 29. Tang J-Q, Zhao Z, Liang Y, Liao G. Robotic-assisted versus open radical cystectomy in bladder cancer: A meta-analysis of four randomized controlled trials. *Int J Med Robotics Comput Assist Surg.* 2018;14:e1867.
 30. Leow JJ, Reese SW, Lipsitz SR, Bellmunt J, Trinh Q-D, et al. Propensity-Matched Comparison of Morbidity and Costs of Open and Robot-Assisted Radical Cystectomies: A Contemporary Population-Based Analysis in the United States. *Eur Urol.* 2014;66:569–76.
 31. Leow JJ, Chang SL, Meyer CP, Wang Y, Hanske J, Sammon JD, et al. Robot-assisted Versus Open Radical Prostatectomy: A Contemporary Analysis of an All-payer Discharge Database. *Eur Urol.* 2016;70:837–45.
 32. Farnham SB, Webster TM, Herrell SD, Smith JA. Intraoperative blood loss and transfusion requirements for robot-assisted radical prostatectomy versus radical retropubic prostatectomy. *Urology.* 2006;67:360–3.
 33. Nepple KG, Strobe SA, Grubb RL, Kibel AS. Early oncologic outcomes of robotic vs. open radical cystectomy for urothelial cancer. *Urologic Oncology.* 2013;31:894–8.
 34. Hanna N, Leow JJ, Sun M, Friedlander DF, Seisen T, Abdollah F, et al. Comparative effectiveness of robot-assisted vs. open radical cystectomy. *Urologic Oncology.* 2018;36(88):e1-88.e9.
 35. Cacciamani GE, Winter M, Medina LG, Ashrafi AN, Miranda G, Tafuri A, et al. Radical cystectomy pentaffecta: a proposal for standardisation of outcomes reporting following robot-assisted radical cystectomy. *BJU Int.* 2020;125:64–72.
 36. Brassetti A, Tuderti G, Anceschi U, Ferriero M, Guaglianone S, Gallucci M, et al. Combined reporting of surgical quality, cancer control and functional outcomes of robot-assisted radical cystectomy with intracorporeal orthotopic neobladder into a novel trifecta. *Minerva Urol Nefrol.* 2019;71:590–6.
 37. Lawrentschuk N, Colombo R, Hakenberg OW, Lerner SP, Månsson W, Sagalowsky A, et al. Prevention and Management of Complications Following Radical Cystectomy for Bladder Cancer. *Eur Urol.* 2010;57:983–1001.
 38. Djaladat H, Katebian B, Bazargani ST, Miranda G, Cai J, Schuckman AK, et al. 90-Day complication rate in patients undergoing radical cystectomy with enhanced recovery protocol: a prospective cohort study. *World J Urol.* 2017;35:907–11.
 39. Hosseini A, Ebbing J, Collins J. Clinical outcomes of robot-assisted radical cystectomy and continent urinary diversion. *Scand J Urol.* 2019;53:81–8.
 40. Kurpad R, Woods M, Pruthi R. Current Status of Robot-Assisted Radical Cystectomy and Intracorporeal Urinary Diversion. *Curr Urol Rep.* 2016;17:42.
 41. Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *Pharmacoeconomics.* 2016;34:645–9.
 42. Chhabra KR, Sacks GD, Dimick JB. Surgical Decision Making: Challenging Dogma and Incorporating Patient Preferences. *JAMA.* 2017;317:357.
 43. Mastroianni R, Tuderti G, Ferriero M, Anceschi U, Bove AM, Brassetti A, et al. Open vs robotic intracorporeal Padua ileal bladder: functional outcomes of a single-centre RCT. *World J Urol.* 2023;41:739–46.
 44. Fallara G, Di Maida F, Bravi CA, De Groot R, Piramide F, Turri F, et al. A systematic review and meta-analysis of robot-assisted vs. open radical cystectomy: where do we stand and future perspective. *Minerva Urol Nephrol.* 2023;75:134–43.
 45. Fontanet S, Basile G, Baboudjian M, Gallioli A, Huguet J, Territo A, et al. Robot-assisted vs. open radical cystectomy: systematic review and meta-analysis of randomized controlled trials. *Actas Urol Esp (Engl Ed).* 2023;S2173–5786(23):00005–7.
 46. Kowalewski K-F, Wieland VLS, Kriegmair MC, Uysal D, Sicker T, Stolzenburg J-U, et al. Robotic-assisted Versus Laparoscopic Versus Open Radical Cystectomy-A Systematic Review and Network Meta-analysis of Randomized Controlled Trials. *Eur Urol Focus.* 2022;S2405–4569(22):00285–91.
 47. Azhar RA, Bochner B, Catto J, Goh AC, Kelly J, Patel HD, et al. Enhanced Recovery after Urological Surgery: A Contemporary Systematic Review of Outcomes, Key Elements, and Research Needs. *Eur Urol.* 2016;70:176–87.
 48. Pang KH, Groves R, Venugopal S, Noon AP, Catto JWF. Prospective Implementation of Enhanced Recovery After Surgery Protocols to Radical Cystectomy. *Eur Urol.* 2018;73:363–71.

49. Wei C, Wan F, Zhao H, Ma J, Gao Z, Lin C. Application of enhanced recovery after surgery in patients undergoing radical cystectomy. *J Int Med Res.* 2018;46:5011–8.
50. Zhang D, Sun K, Wang T, Wu G, Wang J, Cui Y, et al. Systematic Review and Meta-Analysis of the Efficacy and Safety of Enhanced Recovery After Surgery vs. Conventional Recovery After Surgery on Perioperative Outcomes of Radical Cystectomy. *Front Oncol.* 2020;10:541390.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

