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Bayesian network analysis of open, laparoscopic, and robot-assisted radical cystectomy for bladder cancer

Lin Dong, MD[a], Yu Qin, MD[b], Lu Ya, MD[c], Cao Liang, MD[a], Hu Tinghui, MD[a], He Pinlin, MD[d], Yang Jin, MD[d], Wang Youliang, MD[e], Cui Shu, MD[a,*], Wu Tao, MD[a]

Abstract

Background: We have performed the direct and network meta-analysis to evaluate the safety and efficacy of robot-assisted (RARC) versus laparoscopic (LRC) versus open radical cystectomy (ORC) for bladder cancer (BCa).

Methods: A systematic search of PubMed, Cochrane Library, and Embase was performed up until Dec 20, 2019. Outcome indexes include oncologic outcomes (the recurrence rate, mortality), pathologic outcomes (lymph node yield (LNY), positive lymph node (PLN), positive surgical margins (PSM)), perioperative outcomes (operating time (OP), estimated blood loss (EBL), blood transfusion rate, the length of hospital stay (LOS) and the time to regular diet) and postoperative 90-day complications.

Results: We have analyzed 6 RCTs, 23 prospective studies, and 25 retrospective studies (54 articles: 6382 patients). On one hand, the direct meta-analysis shows RARC is better than LRC or ORC. On the other hand, the clinical effects of the recurrence rate, Morbidity, PSM, LNY, PLN, and postoperative 90-day complications of RARC, LRC and ORC are all no statistical significance by network meta-analysis. Moreover, the probability rank shows that the comprehensive rank of RARC is better than LRC or ORC. The clinical effects of OP, EBL, LOS, blood transfusion rate and the time to regular diet are all statistical significance by network meta-analysis. There are ORC > LRC > RARC in the EBL ranking. Patients with RARC exhibited a decrease of LOS compared to those with LRC or ORC. Patients with RARC exhibited a decrease in blood transfusion rate and the time to regular diet compared to those with ORC. Patients with ORC exhibited an increase of OP compared to those with RARC or LRC. The heterogeneity tests of most studies are < 50%. Most studies have no publication bias and the quality of the selected studies is good.

Conclusion: The direct meta-analysis and network meta-analysis suggest that RARC is better than LRC or ORC according to comprehensive analysis. However, we need a large sample size and more high-quality studies to verify and improve in the further.

Abbreviations: BCa = bladder cancer, EBL = estimated blood loss, LNY = lymph node yield, LOS = the length of hospital stay, MIRC = minimally invasive radical cystectomy, OP = operating time, ORs = odds ratios, PLN = positive lymph node, PSM = positive surgical margins.

Keywords: Bayesian network analysis, laparoscopic radical cystectomy, open radical cystectomy, robot-assisted radical cystectomy

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LD and YQ contributed equally to this work.

There is not involving ethics because it is the system review and network meta-analysis.

Research involving Human Participants and/or Animals: The authors declare that there is no involving Human Participants and/or Animals.

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The authors declare that there is no conflict of interest.

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The datasets generated during and/or analyzed during the current study are publicly available.

[a] Department of Urology, Affiliated Hospital of North Sichuan Medical College, Nanchong, Sichuan, [b] Department of Orthopaedics, West China Hospital, Sichuan University, Chengdu, [c] Department of Respiratory, Affiliated Hospital of Chengdu Medical College, [d] Department of Urology, Affiliated Hospital of Chengdu University, [e] Department of Laboratory, Pengzhou People's Hospital, Chengdu, Sichuan, China.

[*] Correspondence: Cui Shu, Department of Urology, Affiliated Hospital of North Sichuan Medical College, No. 1 Maoyuan South Road, Shunqing, Nanchong, Sichuan, China (e-mail: ld913487290@163.com).

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1. Introduction

In recent years, the incidence and mortality of bladder cancer have increased significantly,[1] ORC is the gold standard for muscle or non-muscle invasive bladder cancer.[2] However, its blood loss, operating time (OP), the length of hospital stay (LOS), and complications are significantly higher than minimally invasive radical cystectomy (MIRC).[3,4] With the innovation of surgical techniques, the overall survival of RARC or LRC is comparable to ORC.[5] Their safety and feasibility have been widely recognized. LRC has a history of more than 20 years. With Da Vinci Robot applying to surgery, RARC has obvious advantages compared with LRC in terms of blood loss, OP, LOS, and complications.[6] So far, no literature has been used to direct and indirect comparisons to expound outcome indexes between the three approaches. Therefore, our article aims to apply network meta-analysis to compare oncology-related indexes between the three surgical approaches.

2. Methods

2.1. Literature search and selection

The methodology involved in this meta-analysis was based on the preferred reporting items for systematic reviews and meta-analysis protocols (PRISMA-P) statement and the protocol for this systematic review and NMA was registered a priori in PROSPERO. There is not involving ethics because it is the system review and network meta-analysis. The systematic literature was searched by databases such as PubMed, Cochrane Library, and Embase. Besides, we manually search for relevant journals. We base on the Population, Intervention, Comparator, Outcomes (PICO) methodology. PICO was defined as follows: population consisted of patients who had biopsy-proven clinical stage T1-T4, N0-N1, M0 bladder cancer, or refractory carcinoma in situ (P). RARC or LRC or ORC: (I) or (C). the recurrence rate, mortality, OP, EBL, LNY, PLN, PSM, blood transfusion rate, LOS, the time to the regular diet, postoperative 90-day complications (O). The retrieval strategy was in the Supplementary material 1, http://links.lww.com/MD/F364. Search the database until Dec 20, 2019. The network meta-analysis method is more comprehensive than direct meta-analysis. The advantage is that not only can it produce a direct comparison of "A" and "C", but also produce "A" and "B", "B" and "C". Moreover, the comparison between "A" is compared with "C" by "B" as an indirect bridge. The indirect results of "A" and "C" can be judged more comprehensive reasonably.[7] The assistance strategy by the manual way was found as much detailed article information as possible. After reading the full text, the data were extracted. Data extraction includes author, publication, age, study interval, male proportion, and so on.

2.2. Data extraction and quality evaluation

The two researchers (HTH, CL) independently have reviewed the retrieved literature by the inclusion and exclusion criteria. When disagreements were encountered, the third researcher (MXX) was required to participate in the discussion to determine whether to include. In case of missing or incomplete data, we contact the original author of the article to obtain relevant information by phone or email. If the following inclusion criteria were met, the studies were included in the network analysis:

(1) *patients were diagnosed with bladder cancer based on their pathological data;*
(2) *patients in the group had a history of* ORC, LRC, and RARC.
(3) Outcome indexes should include at least one of the following, OP, EBL, PSM, PLN, LNY, LOS, blood transfusion rate, the time to the regular diet, complications.
(4) It was limited to a randomized controlled trial or a retrospective case-control or a prospective cohort design.
(5) The studies were limited to English.

Any study that did not conform to the above criteria was excluded. We have used the Newcastle-Ottawa Scale (NOS) scoring criteria in the cohort study and Cochrane Collaborative Network bias risk assessment criteria in RCTs.

2.3. Statistical analysis

Statistical analysis was performed by Review 5.3, Stata 12.0, and GeMTC 0.14.3 software.[8–10] For the meta-analysis, the heterogeneity test was $P < .1$, $I^2 > 50\%$, the random effect model was used; the heterogeneity test was $P > .1$, $I^2 < 50\%$, the meta-analysis was performed using a fixed utility model. The combined r values and 95% CI of each study were calculated, and the characteristics of each study result were displayed by the forest map. Egger's test was used to test the publication bias. The $P < .05$ was considered statistically significant. For network analysis, fill in the extracted data information in the Excel table, the multiple three-arm trials were Sorted out a two-arm trial format, and a net-like relationship diagram comparing multiple interventions was drawn by Stata 12.0 software. Calculate the relative odds ratio and implement an inconsistency test to evaluate the closed-loop consistency in the network relationship. According to the Z test, if the lower limit of 95% Confidence Interval (CI) is 1, $P > .05$, it is considered that is no inconsistency, the consistency model is used for network meta-analysis, otherwise, it is inconsistency, the inconsistency model is used for network meta-analysis. Use GeMTC 0.14.3 software and 4 Markov chain simulations, set the number of tuning iterations to 20,000, the number of simulation iterations to 50,000, and the thinning interval to 10. A close to 1 indicates that the model is satisfied with convergence;[7] draw a rank probability map and predict the possible rank probability.

3. Results

3.1. Literature search results

A total of 2324 articles were retrieved according to the customized search strategy and 16 additional articles. 735 articles that were repeatedly published and cross-published were deleted. After reading the text and abstract, 1399 articles were excluded. After the remaining 206 articles were searched for full text, reading, and quality assessment, 54 articles (6382 participants)[2,6,11–62] were eventually included (Fig. 3 Guidelines Flow Diagram). The methodological quality evaluation of 54 articles included in this study can be found in Table 1 and risk bias included in RCTs in Supplementary material 2, http://links.lww.com/MD/F365.

3.2. Direct meta-analysis

The summary odds ratios (ORs) of the outcomes (oncologic outcomes: the recurrence rate and mortality; pathologic out-

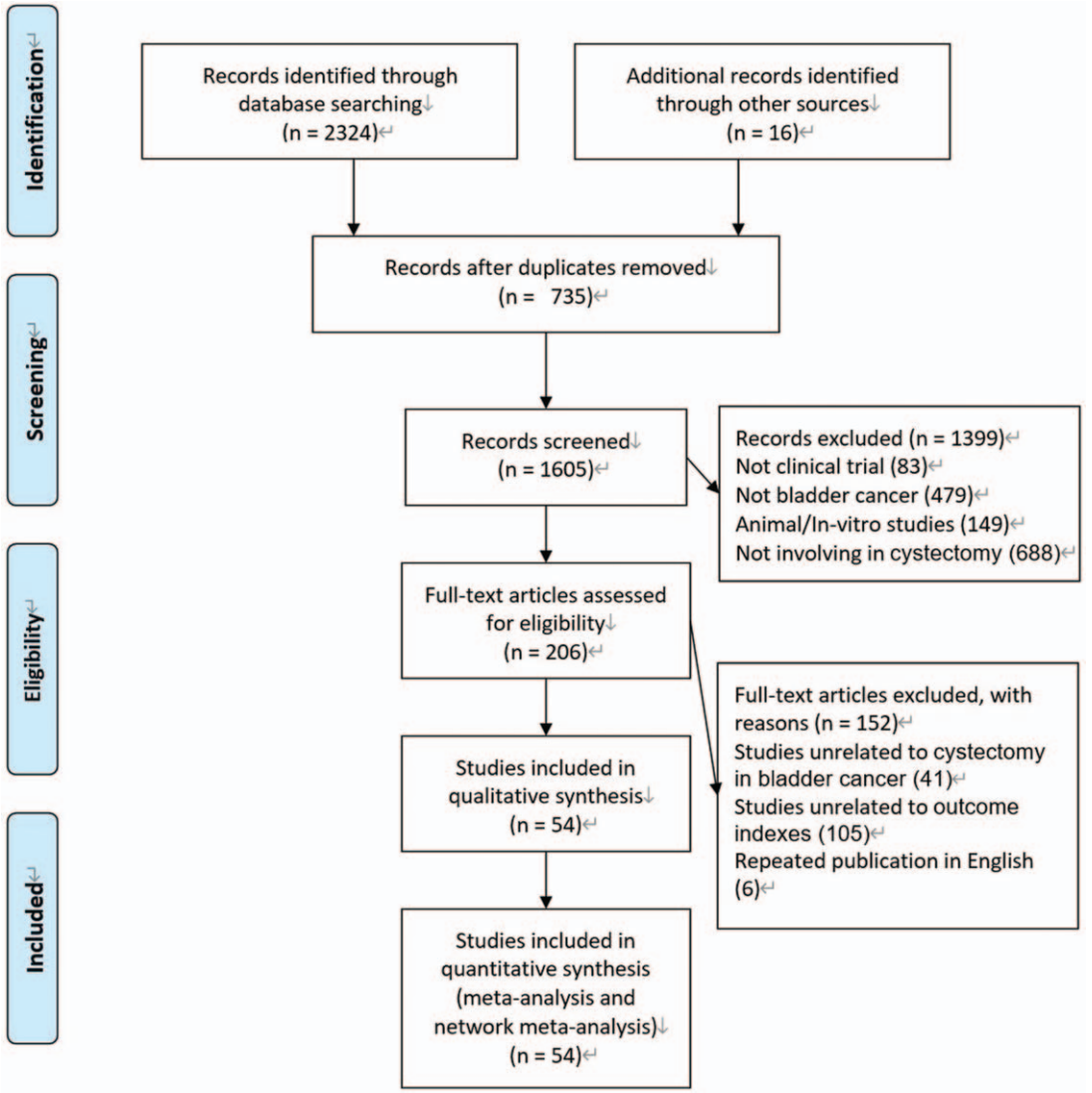

Figure 1. The rank probability of the three surgical approaches for kidney cancer included in this meta-analysis: (A) The recurrence rate. (B) morbidity. (C) Positive surgical margins. (D) Lymph node yield. (E) Positive lymph node. (F) Postoperative 90-day complications.

comes: LNY, PLN, and PSM; perioperative outcomes: OP, EBL, blood transfusion rate, LOS and the time to regular diet and postoperative 90-day complications) for every two direct comparisons were calculated in Table 2.

We consider that neoadjuvant chemotherapy has an impact on postoperative recurrence rate and mortality.[63] Therefore, we analyzed the postoperative recurrence rate and mortality by subgroups with indifference in neoadjuvant chemotherapy ($P > .05$). Patients with LRC exhibited increase of the recurrence rate compared to those with RARC (OR = 0.45, 95% CI = 0.29, 0.68, $P < .001$). Patients with RARC exhibited decrease of the morbidity rate compared to those with ORC (OR = 0.60, 95% CI = 0.38, 0.93, $P = .023$) or LRC (OR = 0.60, 95% CI = 0.39, 0.93, $P = .021$).

There are basically T0-T4 in clinical and pathological stages included articles in our direct meta-analysis. Patients with RARC exhibited decrease of PSM compared to those with ORC (OR = 0.41, 95% CI = 0.30, 0.45, $P < .001$) or LRC (OR = 0.40, 95% CI = 0.21, 0.77, $P = .006$). Patients with RARC exhibited increase of LNY compared to those with LRC (OR = 0.98, 95% CI = 0.60, 1.35, $P < .001$). Patients with ORC exhibited increase of OP compared to those with RARC (OR = 0.63, 95% CI = 0.53, 0.72, $P < .001$) or LRC (OR = 0.66, 95% CI = 0.54, 0.78, $P < .001$). Patients with RARC exhibited decrease of EBL compared to those with ORC (OR = -1.18, 95% CI = -1.29, -1.08, $P < 0.001$) or LRC (OR = -0.45, 95% CI = −0.74, −0.17, $P = .002$) and patients with LRC exhibited decrease of EBL compared to those with ORC (OR = −1.18, 95% CI = −1.25, −0.97, $P < .001$). Patients with RARC exhibited decrease of LOS compared to those with ORC (OR = -0.66, 95% CI = −0.77, −0.55, $P < .001$) or LRC (OR = −0.55, 95% CI = −0.87, −0.23, $P = .001$) and patients with LRC exhibited decrease of LOS compared to those with ORC (OR = −0.38, 95% CI = −0.50, −0.27, $P < .001$). Patients with RARC exhibited decrease of blood transfusion rate compared to those with ORC (OR = 0.70, 95% CI = 0.54, 0.89, $P = 0.004$). Patients with RARC exhibited decrease of the time to regular diet compared to those with ORC (OR = 0.63, 95% CI = 0.33, 1.21, $P = .019$).

Table 1

The main characteristics of included studies.

Author	Year	Country	Publication	Study design	Study interval	Matching	Group	Cases	Age	BMI (kg/m^2)	ASA	Male proportion (%)	Neoadjuvant chemotherapy(%), (*P*)		Clinical stage	Pathological stage	NOS score(max:9)
Borghesi	2019	Italy	Current Urology	P	2015-2016	1,2,3,4,5,6,7	RARC	17	70 ± 11.2	26.5 ± 4.1	2						6
							ORC	33	70 ± 11.2	26.5 ± 4.1	2						
Flamiatos	2019	USA	Journal of Robotic Surgery	R	2009-2015	1,2,4,5,6,7	RARC	100		27.8 ± 5.2		84	23	.65	T0-T4	T0-T4	7
							ORC	149		28.2 ± 5.7		72	26				
Lenfant	2019	France	World Journal of Urology	P	2010-2016	1,2,3,5,6,7	RARC	124	66 (61–74)	25.6 (23.6–27.8)	1-4	85	52	<.001		Ta-T2	8
							ORC	118	68 (61–73)	25.5 (22.7–28.1)	1-4	80	30				
Matsumoto	2019	Japan	Asian Journal of Surgery	P	2008-2017	1,2,3,5,6,7	RARC	10	67.3 (51–78)	22.5 (19.1–26.7)	2	80					5
							LRC	19	67.0 (41–77)	23.3 (18.4–27.9)	1–2	80					
							ORC	16	69.2 (44–82)	23.1 (18.6–28.7)	1–3	69					
Su	2019	China	Clinical Genitourinary Cancer	R	2011-2016	1,2,3,5,6,7	RARC	189	63 (54–70)	24.2 (22.6–26.7)	1–3	84.7	3.2	.298		T0-T4	7
							LRC	126	64 (54–70)	23.7 (22.0–26.2)	1–3	78.6	5.6				
Dosis	2018	UK	Journal of Clinical Urology	R	2010-2016	1,5,7	LRC	127	69.58 ± 8.9			76.4					7
							ORC	92	69.52 ± 8.3			58.7					
Panwar	2018	India	Indian Journal of Urology	P	2014-2016	1,2,5,6,7	RARC	24	57	23.22 ± 4.17			4,16	.878		T0-T3	6
							LRC	54	54	21.86 ± 4.02			20				
							ORC	5	58	23.08 ± 3.79			14.8			T0-T4	
Ram	2018	India	J Minim Access Surg	P	2014-2015	1,2,3,5,6,7	RARC	125	61.76	24.18		87					6
							ORC	45	60.07	23.87		89					
Sharma	2017	USA	World J Urol	P	2010-2014	1,2,3,5,6,7	RARC	65	70.9 (65.0–77.0)	28.0 (25.8–31.0)	2–3	96.9	21.5	.006		T0-T4	6
							ORC	407	70.2 (62.7–76.8)	27.8 (24.8–31.0)	2–4	73.2	39.3				
Cusano	2016	USA	Int Braz J Urol	R	2003-2013	1,2,3,5,6,7	RARC	121	65.9 ± 10.4	28.2 ± 5.0	3 (2–3)	78.5	19	.045	T0-T4	T0-T4	5
							ORC	92	67.8 ± 10.4	28.4 ± 5.2	3 (2–3)	79.3	28.9				
Gandaglia	2016	Belgium	Eur J Surg Oncol	R	2004-2013	1,2,3,4,5,6,7	RARC	138	70.0 (60.7–77.0)	26.1 (22.9–28.6)	1–4	83.3	19.9	.001	T0-T4	T0-T4	7
							ORC	230	70.9 (63.1–77.5)	26.0 (23.5–29.0)	1–4	83.5	0				
Kim	2016	Korea	Journal of Endourology	R	2011-2014	1,2,3,5,6,7	RARC	58	61.5 (54.8 – 72.0)	22.8 (20.8 – 25.5)	1–3	93.1	1.7	.72	T0-T4	T0-T4	8
							LRC	22	65.0 (62.8 – 74.0)	23.3 (20.9 – 26.1)	1–4	90.9	4.5				
							ORC	150	68.0 (60.0 - 73.0)	23.9 (21.9 – 26.3)	2–3	82	2				
Tan	2016	UK	Urology oncology	R	2005-2014	1,5,6,7	RARC	90	64.3 ± 12.3			76.7			CIS-T4	T0-T4	7
							ORC	94	66.4 ± 10.6			72.3					
Winters	2016	USA	Journal of Endourology	R	2004-2015	1,2,5,6,7	RARC	29	79.2 ± 3.5	26.9 ± 3.3		62	38	.42		T0-T4	8
							ORC	58	79.6 ± 3.2	26.5 ± 4.1		64	29				
Atmaca	2015	Turkey	JSLS	R	2009-2013	1,2,3,4,5,6	RARC	32	62.2 ± 10.6	25.7 ± 3.3	1–3	90.6					6
							ORC	42	61.4 ± 10	24.8 ± 2.1	1–3	97.6					
Nguyen	2015	USA	Eur Urol	R	2001-2014	1,2,3,5,6,7	RARC	263	72 (65–79)	25 (23–28)	1–4	79	24	>.9	T0-T4	T0-T4	8
							ORC	120	69 (63–75)	24 (24–28)	1–4	71	23				
Yasui	2015	*Japan*	*Asian Pac J Cancer Prev*	R	2010-2014	1,2,3,5,6,7	LRC	8	78 (76, 81)	23.9 ± 4.4	2–3	62.5				Tis-T4	7
							ORC	8	79 (77, 83)	22.0 ± 4.0	2–3	75				Tis-T3	
Zhao	2015	China	Clin Genitourin Cancer	R	2009-2014	1,2,3,5,6	LRC	41	65.5 ± 10.1	24.7 ± 3.9		90.2			Ta-T4	Ta-T4	8
							ORC	53	66.2 ± 9.7	25.5 ± 4.1		88.7					
Agarwal	2014	India	HPB (Oxford)	R	2011-2013	1,5,6	LRC	24	44 (21–61)			27.8				T1-T3	8
							ORC	46	49 (23–70)			25					
Musch	2014	Germany	BJU international	P	RARC:2009–2012; ORC:2007-2009	1,2,3,4,5,6,7	RARC	100	71.4 ± 9.4	27.0 ± 4.6		76				T0-T4	7
							ORC	42	69.0 ± 11.5	27.0 ± 4.5		64				Tis-T4	
Zeng	2014	China	Plos one	R	2009-2013	1,2,3,5,6,7	LRC	21	77 (75,79)	23.5 ± 2.3	2–3	90.5				T0-T4	6
							ORC	25	78 (75,80)	23.4 ± 2.5	2–3	84					
Pai	2014	UK	Journal of Clinical Urology	P	ORC: 2009–2013; RARC:2012-2013	1,4,5,6,7	RARC	50	67 (62–72)			76				NMIBC, T2-T4	6

(*continued*)

Table 1
(continued).

Author	Year	Country	Publication	Study design	Study interval	Matching	Group	Cases	Age	BMI (kg/m^2)	ASA	Male proportion (%)	Neoadjuvant chemotherapy(%), (*P*)		Clinical stage	Pathological stage	NOS score(max:9)
							ORC	50	69 (63–75)			76					
Niegisch	2014	Germany	Urol Oncol	P	2010–2013, 2008-2013	1,2,3,5,6,7	RARC	64	68 (62–75)	24 (25–29)	2 (2–3)	78	9	>.05			7
							ORC	79	71 (66–78)	26 (24–29)	3 (2–3)	77	11				
Messer	2014	USA	BJU international	P	2009-2011	1,2,3,5,6,7	RARC	20	69.5 (62.3–74)	27.6 (24.2–29.9)	2–3	90				T0-T4	7
							ORC	20	64.5 (59.8–72.3)	28.3 (26.1–32.3)	2–4	80					
Akin	2013	Turkey	Urol Int	P	2008-2011	1,2,5,6,7	LRC	15	62.2±8.1	25.0±1.1							8
							ORC	15	64.0±11.9	25.1±1.4							
Kader	2013	USA	BJU international	R	2006-2010	1,2,3,5,6,7	RARC	103	67 (47–90)	26.5 (17–42)	2–4	72				T0-T4	7
							ORC	100	66 (34–86)	27.1 (16–45)	2–4	72					
Knox	2013	USA	JOURNAL OF ENDOUROLOGY	R	2008-2010	1,2,3,5,6,7	RARC	58	65.9 ± 1.2	28.6 ± 0.79	2–4	79	9	.3	T1-T4		6
							ORC	84	67.07 ± 1.2	28.9 ± 0.65	2–4	70	19				
Nepple	2013	USA	NIH Public Access	R	2007-2010	1,2,5,6,7	RARC	36	72 (67–77)	27.7 (24.1–31.4)		86	6	.39	CIS-T4a		7
							ORC	29	67 (57–79)	26.2 (22.6–29.0)		55	14		CIS-T2a		
Khan	2012	UK	Int J Clin Pract	P	2003-2008	1,2,3,5,6,7	RARC	48	66.5 (63.77–69.23)		1–3	85.4				T0-T4	6
							LRC	58	69.8 (67.50–72.05)		1–4	93					
							ORC	52	65 (61.62–68.42)		1–3	77					
Styn	2012	USA	Urology	P	2007-2010	1,2,3,5,6,7	RARC	50	66.6 ± 9.8	29.8 ± 6.1	1–4		92	.63			7
							ORC	100	65.6 ± 10	29.6 ± 4.9	1–4		42				
Sung	2012	Korea	J Endourol	R	2008-2011	1,2,3,5,6	RARC	35	62.2 ± 10.5	23.1 – 2.9	1–3	88.5			T1-T4,CIS		6
							ORC	104	65.9 ± 9.4	22.4 – 2.9	1–3	81.7			Ta, T1-T4		
Abaza	2012	USA	The Journal of urology	R	2006-2008	1,2,6	RARC	35	67.3 (45–87)	30 (20–45)		89	31	.691	T2-T4	T3-T4	5
							ORC	120	69.8 (43–87)			79	36				
Gondo	2012	Japan	Jpn J Clin Oncol	P	2008-2011	1,2,4,5,6,7	RARC	11	68.9 ± 2.86			81.8					6
							ORC	15	69.7 ± 2.36			86.7					
Ha	2010	Korea	Int J Urol	R	2003-2008	1,2,5,6	LRC	36	67.5 ± 8.9	23.2 ± 2.4		88.9				Ta-T4	7
							ORC	34	55.9 ± 9.8	22.7 ± 3.6		79.4					
Ng	2010	USA	Eur Urol	R	2002-2008	1,2,3,5,6,7	RARC	83	70.9 ± 10.8	26.3 ± 3.9		78			T0-T4		7
							ORC	104	67.2 ± 10.6	27.2 ± 6.0		70					
Richards	2010	USA	Urology	R	2007-2009	1,2,3,5,6,7	RARC	35	65 (59, 73)	27 (23, 31)	2–4	86				T0-T4	6
							ORC	35	66 (59, 73)	26 (24, 29)	2–4	71					
Wang1	2010	China	Urol Int	P	2006-2008	1,2,3,5,6,7	LRC	14	63.7 ± 10.1	22.1 ± 3.2	1.7 ± 0.6	92.9			T1-T4		7
							ORC	24	58.0 ± 11.2	21.7 ± 2.7	1.8 ± 0.5	95.8					
Wang2	2010	China	World J Urol	P	2004-2007	1,2,5,6,7	LRC	31	61.3 ± 11.9	21.9 ± 2.6		93.5				T1-T4	8
							ORC	39	55.7 ± 12.9	21.4 ± 3.6		79.5					
Guillotreau	2009	France	J Urol	P	2003-2007	1,2,3,5,6,7	LRC	38	67.9 ± 9.0	25.9 ± 3.6		94.7				T0-T4a	8
							ORC	30	64.9 ± 12.3	26.1 ± 4.3		83.3					
Haber	2008	USA	Urology oncology	R	1992-2007	1,2	LRC	50	66	27						T0-T4	5
							ORC	50	67	26							
Abraham	2007	USA	Journal of endourology	p	RARC:2005–2006; LRC:2002-2005	1,2,3,5,7	RARC	14	76.5 (66–87)	26.1 (19–35)	2.6 (2–3)						6
							LRC	20	77.6 (69–86)	27.2 (18–52)	3.3 (2–3)						
Hemal	2007	India	J Urol	P	1999-2005	1,2,3,5,6,7	LRC	30	58.2 (35–78)	24.5 ± 1.9	2.3 ± 0.6	94.3					7
							ORC	35	58.9 (30–82)	24.5 ± 1.9	2.4 ± 0.5	93.3					
Porpiglia	2007	Italy	J Endourol	P	2002-2005	1,2,3,5,6,7	LRC	20	63.5 (42–78)		2.4 (2–4)				T2		7
							ORC	22	71 (60–82)		2.2 (1–4)						
Pruthi	2007	USA	The Journal of urology	R	2006-2007	1,2,3,5,6,7	RARC	20	62.3 (54–76)						Tx-T4		5
							ORC	24	68.2 (51–82)								
Rhee	2006	USA	BJU international	P	2003-2005	1,6,7	RARC	7	60 ± 9	28 ± 4		86			Ta-T4		8
							ORC	23	67 ± 13	25 ± 5		61					
Galich	2006	USA	Jsls	P	2000-2001	1,2,3,6	RARC	13	70 (38–88)	25.05 (18.2–43.5)		77					6

(*continued*)

Table 1
(continued).

Author	Year	Country	Publication	Study design	Study interval	Matching	Group	Cases	Age	BMI (kg/m^2)	ASA	Male proportion (%)	Neoadjuvant chemotherapy(%), (*P*)	Clinical stage	Pathological stage	NOS score(max:9)
							ORC	24	70.5 (27–86)	26.5 (16.1–53.6)		75				
Basillote	2004	USA	J Urol	R	2001-2003	1,2,3,5,7	LRC	13	66.8 ± 9	27.2 ± 2.2	2.8 ± 0.7			Ta-T2b	T0-T3b	7
							ORC	11	58.9 ± 9.2	26.2 ± 2.0	2.5 ± 0.5			Tis-T4a	T0-T3a	
Taylor	2004	USA	The Journal of urology	p	2002-2003	1,2,3,5,6,7	LRC	8	66.4 (47–78)	26.6 (23–31)	2.8 (2–3)	87.5				8
							ORC	8	66.3 (51–79)	26.8 (21–41)	2.6 (2–4)	50				
Khan	2019	UK	European Urology	RCT	2009-2012	1,2,3,5,6,7	RARC	20	68.6 ± 6.8	27.5 ± 4.2	1–3	85	10 .588		T0-T3	
							LRC	19	68.6 ± 9.9	26.2 ± 3.6	1–3	79	5.26		T0-T4	
							ORC	20	66.6 ± 8.8	27.4 ± 3.9	1–3	90	15		T0-Tis, T3-T4	
Bochner	2018	USA	European Urology	RCT	2010-2013	1,2,3,6,7	RARC	60	66 (60–71)		2–4	85	32 .185		T0-T4	
							ORC	58	65 (58–69)		2–4	72	45			
Yong	2017	China	Oncotarget	RCT	2012-2015	1,2,3,5,6,7	LRC	29	78 (75–80)	22.1 ± 2.8	2–3			T0-T4		
							ORC	28	77 (75–79)	21.8 ± 3.0	2–3					
Lin	2014	China	BRITISH JOURNAL OF CANCER	RCT	2008-2011	1,2,3,5,6	LRC	35	63.2±9.1	22.0±2.7	2–3	91		T1-T3		
							ORC	35	63.6±8.9	22.9±3.1	2–3	91				
Parekh DJ	2013	USA	THE JOURNAL OF UROLOGY	RCT	2009-2011	1,2,3,5,6	RARC	20	69.5 (62.3–74)	27.6 (24.2–29.9)	3	90			T0-T4	
							ORC	19	64.5 (59.8–72.3)	28.3 (26.1–32.3)	3	80				
Nix	2010	USA	Eur Urol	RCT	2008-2009	1,2,3,5,6,7	RARC	21	67.4 (33–81)	27.5	2.71	67		lower. T1-T3		
							ORC	20	69.2 (51–80)	28.4	2.7	85				

Matching: 1 - Age; 2 - BMI; 3 - ASA; 4 - Charlson; 5 - Gender; 6 - Pathological stage; 7 - Urinary diversion type. LRC = laparoscopic radical cystectomy, NA = data not available, NOS score = Newcastle-Ottawa Scale score, ORC = open radical cystectomy, P = Prospective, R = Retrospective, RARC = robot-assisted radical cystectomy, RCT = randomized controlled trial.

3.3. Network meta-analysis

The network plot of the outcome indexes included in this network meta-analysis in Fig. 2. The median of inconsistency and consistency model in Random Effects Standard Deviation is close to each other by Supplementary material 3, http://links.lww.com/MD/F366. Therefore, we all have used the consistency model.

Table 3 summarizes all the studies within the multiple networks and shows the results of the mixed network comparisons. The results of the confidence interval in Table 3 has included "1" has been shown that there was no statistical significance. Therefore, the clinical effects of the recurrence rate, Morbidity, PSM, LNY, PLN, and postoperative 90-day complications of RARC, LRC, and ORC are similar. But in Fig. 1 and Supplementary material 4, http://links.lww.com/MD/F367, RARC may be last in the recurrence rate, morbidity, and PSM. RARC may be the first rank in LNY. RARC may be the second rank in PLN and postoperative 90-day complications. The results of the confidence interval in Table 3 included "1" have been showed that there was statistical significance. Therefore, there are ORC>LRC>RARC in the EBL rank. Patients with RARC exhibited a decrease in LOS compared to those with LRC or ORC. Patients with RARC exhibited a decrease of blood transfusion rate and the time to regular diet compared to those with ORC. Patients with ORC exhibited increase of OP compared to those with RARC or LRC.

3.4. Publication bias

Publication bias was calculated by the Egger test. The Egger test results showed that RARC vs ORC in LNY ($P=.937$, t=0.08: Supplementary Fig. 1, http://links.lww.com/MD/F353), OP ($P=.001$, t=5.12: Supplementary Figs. 3-1, http://links.lww.com/MD/F355 EBL ($P=.006$, t=-3.15: Supplementary fig 4-1, http://links.lww.com/MD/F357), LOS (P=0.619, t=-0.51: Supplementary Fig. 5-1, http://links.lww.com/MD/F359), blood transfusion rate ($P=.243$, t=1.20: Supplementary Fig. 6-1, http://links.lww.com/MD/F361) and the time to regular diet ($P=.66$, t=−0.45: Supplementary Fig. 7, http://links.lww.com/MD/F363). The Egger test results showed that LRC vs ORC in PLN ($P=.334$, t=1.00: Supplementary Fig. 2, http://links.lww.com/MD/F354), OP (P=0.025, t=2.46: Supplementary fig 3-2, http://links.lww.com/MD/F356), EBL ($P=.219$, t=−1.28: Supplementary fig 4-2, http://links.lww.com/MD/F358), LOS ($P=.020$, t=−2.60: Supplementary Fig. 5-2, http://links.lww.com/MD/F360) and blood transfusion rate ($P=.939$, t=0.08: Supplementary Fig. 6-2, http://links.lww.com/MD/F362). The possible reason for the publication bias in some studies is that our studies were limit to English.

4. Discussion

BCa is the second most common malignant tumor in the urinary system, behind prostate cancer.[1] With the development of science and technology, the application of minimally invasive surgery in radical cystectomy has become more and more mature. Comparing with ORC, RARC and LRC have many advantages.[64,65] Notably, Reports on RARC, LRC, and ORC all are direct evidence from traditional meta-analysis, but the network meta-analysis is more convincing. There is not only direct evidence from traditional meta-analysis but also indirect evidence from network meta-analysis about comparing with RARC, LRC, and ORC.

Table 2

Pair-wise meta-analyses of direct comparisons between the three surgical approaches for Bca.

End points	Direct comparisons	Neoadjuvant chemotherapy (p)	*I2*	PH values	OR (95% CI)	*POR* values
the recurrence rate	RARC VS ORC	$P > .05$	0%	0.852	0.95 (0.63, 1.45)	.819
	RARC VS LRC		64%	0.094	0.45 (0.29, 0.68)	<.001
	LRC VS ORC		-	-	-	-
morbidity	RARC VS ORC	$P > .05$	23%	0.274	0.60 (0.38, 0.93)	.023
	RARC VS LRC		80%	0.024	0.60 (0.39, 0.93)	.021
	LRC VS ORC		-	-	-	-
positive surgical margins	RARC VS ORC		32%	0.174	0.41 (0.30, 0.45)	<.001
	RARC VS LRC		0%	0.782	0.93 (0.52, 1.65)	.797
	LRC VS ORC		0%	0.678	0.40 (0.21, 0.77)	.006
lymph node yield	RARC VS ORC		79%	0	0.09 (−0.02, 0.19)	.105
	RARC VS LRC		49.00%	0.162	0.98 (0.60, 1.35)	<.001
	LRC VS ORC		49.90%	0.062	0.07 (−0.11, 0.26)	.443
positive lymph node	RARC VS ORC		0%	0.934	0.90 (0.63, 1.30)	.578
	RARC VS LRC		0%	0.714	0.96 (0.55, 1.65)	.87
	LRC VS ORC		0%	0.93	0.84 (0.61, 1.16)	.294
operating time	RARC VS ORC		97%	0	0.63 (0.53, 0.72)	<.001
	RARC VS LRC		96.30%	0	0.01 (−0.29, 0.30)	.975
	LRC VS ORC		88.60%	0	0.66 (0.54, 0.78)	<.001
estimated blood loss	RARC VS ORC		95%	0	‘−1.18 (−1.29, −1.08)	<.001
	RARC VS LRC		94.70%	0	‘−0.45 (−0.74, −0.17)	.002
	LRC VS ORC		83.60%	0	‘−1.11 (−1.25, −0.97)	<.001
length of hospital stay	RARC VS ORC		96%	0	‘−0.66 (−0.77, −0.55)	<.001
	RARC VS LRC		0%	0.464	‘−0.55 (−0.87, −0.23)	.001
	LRC VS ORC		52.10%	0.007	‘−0.38 (−0.50, −0.27)	<.001
blood transfusion rate	RARC VS ORC		0%	0.668	0.70 (0.54, 0.89)	.004
	RARC VS LRC		0%	0.707	1.15 (0.38, 3.44)	.802
	LRC VS ORC		0%	0.845	0.70 (0.54, 0.89)	.166
the time to regular diet	RARC VS ORC		0%	0.859	0.63 (0.33, 1.21)	.019
	RARC VS LRC		-	-	-	-
	LRC VS ORC		0%	0.952	0.86 (0.64, 1.15)	.306
postoperative 90-day complications	RARC VS ORC		0%	0.87	0.79 (0.56, 1.11)	.17
	RARC VS LRC		-	-	-	-
	LRC VS ORC		0%	0.908	0.78 (0.34, 1.78)	.551

*H = heterogeneity, OR = odds ratio, CI = confidence interval, RARC = Robot-assisted Radical cystectomy, LRC = laparoscopic radical cystectomy, ORC = open radical cystectomy, BCa = bladder cancer.

One study showed that RARC, LRC, and ORC have no difference for two oncologic outcomes: the recurrence rate and mortality.[66] However, For the probability of network meta-analysis, patients with RARC may be lowest in the recurrence rate, morbidity compared with the other two surgical approaches.

Menon et al[67] firstly reported RARC in 2003. Since then, the research results of many scholars[68–70] have shown that compared with ORC and LRC, RARC can complete more detailed anatomy, which can cure tumors, preserve function, and control urine to achieve better results. Reducing to OP is considered to be beneficial for surgeons to improve the efficiency of surgery, moreover, reduce to EBL, accelerate postoperative recovery, and reduce complications for patients. Direct meta-analysis indicates that RARC is shorter than LRC or ORC in OP. On the other hand, our network meta-analysis indicates that ORC has significantly longer OP than LRC or RARC. Direct meta-analysis and network meta-analysis both indicate that RARC is less than ORC in blood transfusion rate and the time to regular diet and less than LRC or ORC in LOS. there are ORC>LRC>RARC in the EBL rank. The possible reasons are RARC has a wide three-dimensional field of vision, flexible wrist with 7 degrees of freedom, and an ergonomic operating console. And the operator is less prone to fatigue.[71] On the other hand, we have to consider the outcome indexes of the three surgical approaches. At the beginning of the MIRC, ORC's surgical effect is better than MIRC. However, as surgeons become more proficient with MIRC, MIRC is even better than ORC at this stage.[6]

RARC maybe the last rank in the recurrence rate, morbidity, and PSM. RARC may be the first rank in LNY. RARC maybe second rank in PLN and postoperative 90-day complications. The possible reasons are that the advantages of RARC's 3D field of view and 7 degrees of freedom make the operation under the microscope more refined, which has improved on the original traditional surgical technology and broadened the scope of traditional surgery.[71] Comparing with LRC or ORC, RARC can better perform some difficult operations such as adhesion decomposition, hemostasis and suture, and so on. The deep lymph nodes of the pelvic cavity during the operation have the characteristics of clear vision, flexible operation, fine and stable. At the same time, RARC saves operation time, reduces patient pain, accelerates patient recovery, and reduces complications. Therefore, RARC is more worthy of clinical promotion in countries and regions with conditions.

There were three limitations to the included studies. Firstly, very few RCTs for LRC, ORC, and RARC have been compared in the study until now. Regarding the recruitment of participants, funding problems and patients choosing operation methods are obstacles to accept surgical procedures. The non-random nature

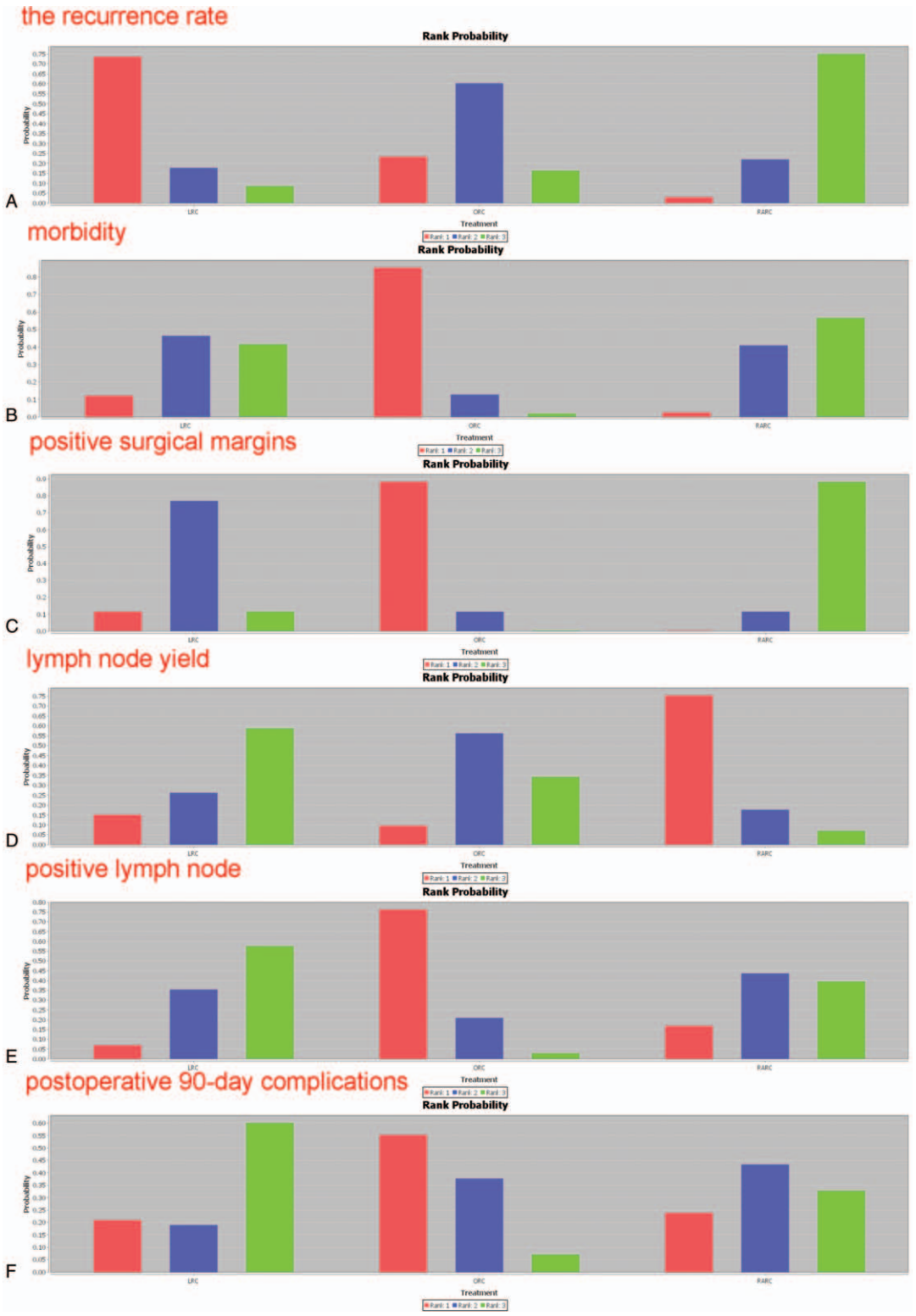

Figure 2. The network plot of the outcome indexes included in this network meta-analysis.

of observational research makes it vulnerable to selection bias, known or unknown confounding bias. The second limitation of this network meta-analysis is the small number of patients studied. Only 6944 patients, statistical testing may be inefficient, and conclusions must be treated with caution. A third limitation is that most of the retrospective observational studies included in this review were from hospitals in developed countries in Europe and America. These results may not apply to areas where conditions for robot-assisted radical cystectomy were not carried out.

Table 3

The efficacy of three surgical methods according to the network meta-analysis using odds ratios (ORs) and corresponding 95% credible intervals (CrIs).

Consistent model		
the recurrence rate		
LRC	0.62 (0.17, 3.24)	0.42 (0.14, 1.86)
	ORC	0.68 (0.26, 1.69)
		RARC
Morbidity		
LRC	2.51 (0.45, 15.43)	0.87 (0.18, 4.47)
	ORC	0.35 (0.10, 1.17)
		RARC
positive surgical margins		
LRC	1.96 (0.59, 5.77)	0.52 (0.13, 1.61)
	ORC	0.26 (0.11, 0.62)
		RARC
lymph node yield		
LRC	0.34 (−2.17, 3.03)	1.43 (−1.60, 4.64)
	ORC	1.06 (−1.03, 3.25)
		RARC
positive lymph node		
LRC	1.26 (0.90, 1.74)	1.05 (0.67, 1.65)
	ORC	0.84 (0.58, 1.24)
		RARC
operating time		
LRC	−52.21 (−73.99, −31.95)	6.55 (−21.07, 32.67)
	ORC	58.58 (38.18, 79.14)
		RARC
estimated blood loss		
LRC	409.64 (272.43, 542.53)	−206.99 (−385.55, −24.26)
	ORC	−616.41 (−760.73, −469.33)
		RARC
length of hospital stay		
LRC	1.48 (0.34, 2.62)	−0.59 (−2.13, 0.96)
	ORC	−2.07 (−3.23, −0.92)
		RARC
blood transfusion rate		
LRC	1.93 (0.98, 3.98)	1.33 (0.67, 2.89)
	ORC	0.70 (0.50, 0.98)
		RARC
the time to regular diet		
LRC	1.30 (0.82, 2.12)	0.74 (0.42, 1.31)
	ORC	0.56 (0.39, 0.81)
		RARC
postoperative 90-day complications		
LRC	1.38 (0.51, 3.90)	1.20 (0.39, 4.17)
	ORC	0.86 (0.47, 1.64)
		RARC

(*continued*)

Table 3

(continued).

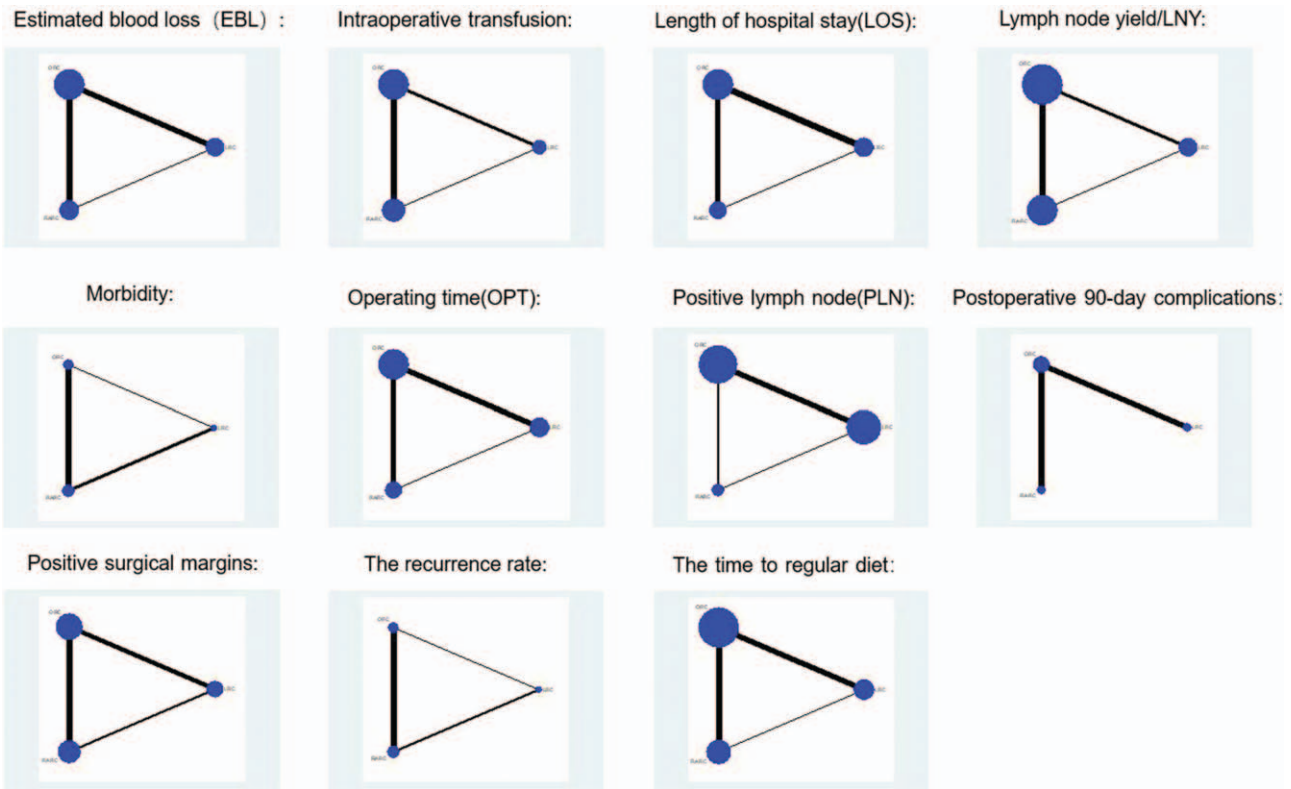

Figure 3. Guidelines Flow Diagram: Flowchart for records selection process of the meta-analysis. (According to PRISMA template: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal. Pmed 1000097).

Because the design and implementation of RCTs are more difficult, future research efforts should focus on implementing the more reasonable and simpler RCT. Additionally, a large sample size and more high-quality studies are still needed to further improve and verify.

5. Conclusion

The direct meta-analysis and network meta-analysis suggest that RARC is better than LRC or ORC according to comprehensive analysis. However, we need a large sample size and more high-quality studies to verify and improve in the further.

Author contributions

Conceptualization: Shu Cui
Funding acquisition: Yang Jin
Investigation: Lin Dong
Methodology: Yang Jin
Software: Yang Jin
Supervision: Tinghui Hu
Validation: Tinghui Hu
Visualization: Tinghui Hu
Writing – original draft: Lin Dong, Tinghui Hu
Writing – review & editing: Shu Cui

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