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Laparoscopic Versus Open Radical Nephrectomy for Renal Cell Carcinoma: a Systematic Review and Meta-Analysis

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Abstract

BACKGROUND: The aim of this study is to summarize and quantify the current evidence on the therapeutic efficacy of laparoscopic radical nephrectomy (LRN) compared with open radical nephrectomy (ORN) in patients with renal cell carcinoma (RCC) in a meta-analysis. *METHODS:* Data were collected by searching Pubmed, Embase, Web of Science, and ScienceDirect for reports published up to September 26, 2016. Studies that reported data on comparisons of therapeutic efficacy of LRN and ORN were included. The fixed-effects model was used in this meta-analysis if there was no evidence of heterogeneity; otherwise, the random-effects model was used. *RESULTS:* Thirty-seven articles were included in the meta-analysis. The meta-analysis showed that the overall mortality was significantly lower in the LRN group than that in the ORN group (odds ratio [OR] =0.77, 95% confidence interval [CI]: 0.62-0.95). However, there was no statistically significant difference in cancer-specific mortality (OR = 0.77, 95% CI: 0.55-1.07), local tumor recurrence (OR = 0.86, 95% CI: 0.65-1.14), and intraoperative complications (OR = 1.27, 95% CI: 0.83-1.94). The risk of postoperative complications was significantly lower in the LRN group (OR = 0.71, 95% CI: 0.65-0.78). In addition, LRN has been shown to offer superior perioperative results to ORN, including shorter hospital stay days, time to start oral intake, and convalescence time, and less estimated blood loss, blood transfusion rate, and anesthetic consumption. *CONCLUSION:* LRN was associated with better surgical outcomes as assessed by overall mortality and postoperative complications compared with ORN. LRN has also been shown to offer superior perioperative results to ORN.

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Introduction

Renal cell carcinoma (RCC) is the third most common urological malignancy after prostate and bladder cancer [1]. Open radical nephrectomy (ORN) was considered as the primary treatment method for RCC until 1990, as described by Robon et al. in1969 [2]. After that, laparoscopic radical nephrectomy (LRN) has gained wide acceptance as a standard treatment for RCC since it was first reported in 1991 [3]. Many studies indicate that LRN is associated with oncologic long-term outcomes similar to those of ORN [4,5]. Moreover, LRN has been shown to markedly decrease postoperative discomfort and shorten overall recovery duration compared with ORN. Some researchers have even regarded LRN as the new gold standard in therapy of stage T1 to T2 kidney cancer [6]. However, to our knowledge, a comprehensive comparison of LRN and ORN for RCC from a meta-analysis is not currently available. We therefore conducted a systematic review and meta-analysis to summarize and quantify the current evidence on the therapeutic outcomes of LRN compared with ORN in patients with RCC.

Material and Methods

Search Strategy and Selection Criteria

We followed the PRISMA guidelines [7] to complete the meta-analysis. Pubmed, Embase, Web of Science, and ScienceDirect were systematically

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searched for reports published between January 1, 1991, and September 26, 2016, using a combined text and MeSH heading search strategy with the following terms: "laparoscopic," "laparoscopy," "nephrectomy," "radical nephrectomy," "open radical nephrectomy," "carcinoma, renal cell," "renal cell carcinoma," "renal cancer," "renal tumor," "kidney tumor," and "kidney cancer." The search strategy was limited to human studies and those published in the English language. We included studies after 1990 because the LRN method was first reported in 1991. Reference lists of identified studies were also checked for other potentially relevant studies. We contacted the authors for additional data as needed.

An eligible study should meet the following inclusion criteria: prospective design or retrospective design; masked assessment of outcomes; reported data on results of therapy of LRN and ORN (overall mortality, cancer-specific mortality, tumor recurrence, and/or complications); and reported sufficient information to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for the association between LRN and ORN for therapy of RCC. Studies were excluded if they did not provide information to calculate the estimate, did not make comparison between LRN and ORN, used partial nephrectomy method, or were review studies.

Data Extraction and Study Quality Evaluation

The characteristics of each included study were extracted, including author, country, study design, sample size, mean age of participants, gender proportion, mean follow-up duration, mean tumor size, number of death from all cause, number of death from RCC, number of tumor recurrence, number of complications, mean operative time, estimated blood loss, hospital stay, number of blood transfusion required, time to start oral intake, convalescence time, and/or anesthetic consumption, if available. The quality of each included study was assessed using the Newcastle-Ottawa Scale recommended by Wells and colleagues [8]. The quality of each study ranges from one to nine stars.

Statistical Analysis

Associations with continuous outcome variables were pooled as weighted mean differences (WMDs) with 95% CI. Associations with dichotomous were pooled as ORs with 95% CI. The fixed-effects model was used in this meta-analysis if there was no evidence of heterogeneity; otherwise, the random-effects model was used. We used χ^2 test and the I^2 statistic to explore the heterogeneity among studies. $P < .10$ for χ^2 test or large I^2 (>50%) suggests substantial heterogeneity among studies. We did several subgroup analyses: geographic location (Europe, North America, or Asia), study design (prospective or retrospective), mean age of participants (<60 years vs ≥ 60 years), and mean tumor size (< cm in both groups vs ≥7 cm in both groups). We use 7 cm as the cutoff value of mean tumor size because most studies regard kidney tumor of over 7 cm as large tumor [9]. Publication bias were examined using funnel plots, and Egger's regression test and Begg-Mazumdar test were used to further assess publication bias. Statistical significance was defined as a two-tailed $P < .05$. All statistical analyses were conducted with RevMan, version 5, from the Cochrane Collaboration (http://www.cochrane.org/) or Stata Version 12.0 software (Stata Corp, College Station, TX).

Results

Study Characteristics

Our initial search yielded 2045 records, of which 1984 remained after removal of duplications (Figure 1). After title and abstract assessment, 71 articles were qualified for selection. Overall, 37 studies met the inclusion criteria and were included in the meta-analysis [9–45]. Table 1 shows the baseline characteristics of all 37 included studies. Data were available from 14,515 RCC patients, of whom 4844 used LRN and 9671 used ORN for treatment of RCC.

Overall Mortality

Data on overall mortality were available for analysis in 1934 patients in LRN group with 176 deaths and 2902 patients in ORN group with 295 deaths. The meta-analysis showed that the overall mortality was significantly lower in the LRN group than that in the ORN group (OR = 0.77, 95% CI: 0.62-0.95) (Figure 2). There was no evidence of heterogeneity among individual studies ($P = .50$ and $I^2 = 0\%$). The results varied in some subgroup analyses (Table 2). Particularly, the beneficial outcome on overall mortality for LRN was only seen in patients with mean tumor size smaller than 7 cm (OR = 0.72, 95% CI: 0.58-0.91) but not in those with mean tumor size larger than 7 cm (OR = 1.17, 95% CI: 0.65-2.10), and in patients with tumor grade of T_1 to T_2 only (OR = 0.73, 95% CI: 0.58-0.91) but not in those with tumor grade of T_3 or above involved (OR = 1.07, 95% CI: 0.51-2.24).

Cancer-Specific Mortality

Data on cancer-specific mortality were available for analysis in 804 patients in LRN group with 71 deaths and 1016 patients in ORN group with 170 deaths. The results of meta-analysis indicated that LRN group had lower cancer-specific mortality than ORN group, but it did not reach statistical significance (OR = 0.77, 95% CI: 0.55-1.07) (Figure 3). There was no substantial between-study heterogeneity ($P = .37$ and $I^2 = 8\%$). The nonsignificant results were not materially changed in the subgroup analyses of geographic location, study design, mean age of participants, mean tumor size, and tumor grade (Table 2).

Local Tumor Recurrence

Data on local tumor recurrence were available for analysis in 1757 patients in LRN group with 83 events and 2774 patients in ORN group with 152 events. Meta-analysis did not show significant difference in local tumor recurrence between LRN group and ORN group (OR = 0.86, 95% CI: 0.65-1.14) (Figure 4). No evidence of heterogeneity was observed ($P = .96$ and $I^2 = 0\%$). The nonsignificant results were not materially changed in the subgroup analyses of geographic location, study design, mean age of participants, mean tumor size, and tumor grade (Table 2).

Intraoperative Complications

Data on intraoperative complications were available for analysis in 695 patients in LRN group with 64 events and 559 patients in ORN group with 48 events. The pooled analysis showed that there was no significant difference in intraoperative complications between LRN group and ORN group (OR = 1.27, 95% CI: 0.83-1.94) (Figure 5). There was no substantial between-study heterogeneity ($P = .10$ and $I^2 = 40\%$). Subgroup analyses showed that LRN group had significantly higher risk of intraoperative complications than ORN group in patients with mean tumor size smaller than 7 cm (OR = 2.48, 95% CI: 1.03-5.93) (Table 2).

Postoperative Complications

Data on postoperative complications were available for analysis in 4282 patients in LRN group with 905 events and 8295 patients in ORN group with 2646 events. The meta-analysis showed that the

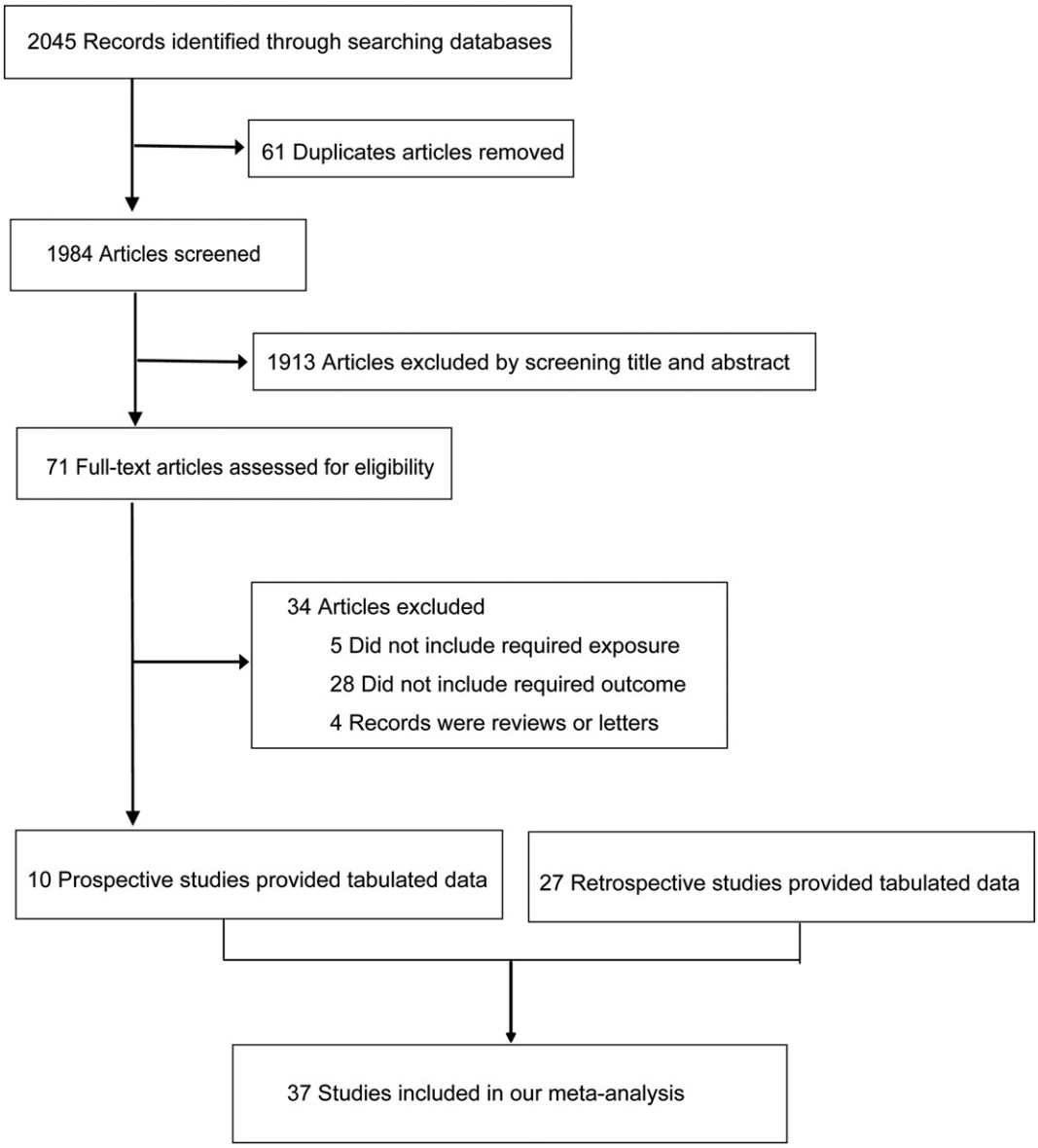

Figure 1. Flowchart for the selection of eligible studies.

risk of postoperative complications was significantly lower in the LRN group compared with the ORN group (OR = 0.71, 95% CI: 0.65-0.78) (Figure 6). There was no evidence of heterogeneity among individual studies (P = .36 and I^2 = 7%). We observed that the study of Tan et al. [44] accounted for a large weight (74.5%). Therefore, we pooled the results again by omitting this study, and the OR was not materially changed (OR = 0.65, 95% CI: 0.54-0.79). The results varied in some subgroup analyses (Table 2). Similarly, the significantly lower risk of postoperative complication for LRN was only seen in patients with mean tumor size smaller than 7 cm (OR = 0.62, 95% CI: 0.49-0.79) but not in those with mean tumor size larger than 7 cm (OR = 0.89, 95% CI: 0.62-1.27). The significant results were not materially changed in the subgroup analyze of tumor grade (Table 2).

Perioperative Results

Table 3 shows the pooled WMDs or ORs of perioperative results among the included studies, comparing LRN group with ORN group, from those studies for which relevant data were reported. Compared with ORN group, LRN group had significantly longer mean operative time (WMD = 24.12, 95% CI: 13.01-35.22) but significantly shorter hospital stay days (WMD = −2.87, 95% CI: −3.42 to −2.32), time to start oral intake (WMD = −31.16, 95% CI: −47.40 to −14.91), and convalescence time (WMD = −3.26, 95% CI: −4.38 to −2.14). Moreover, LRN group had significantly less estimated blood loss (WMD = −201.02, 95% CI: −246.29 to −155.75), blood transfusion rate (OR = 0.59, 95% CI: 0.43-0.81), and anesthetic consumption (WMD = −36.86, 95% CI: −52.82 to −20.90) compared with ORN group.

Publication Bias

There was no potential publication bias in the meta-analyses of overall mortality, cancer-specific mortality, local tumor recurrence, intraoperative complications, and postoperative complications as assessed by funnel plots, Egger's regression test (all P values > .05), and Begg-Mazumdar test (all P values > .05) (Figure 7).

Table 1. Characteristics of Included Studies

Study	Country	Study design	Sample size (n)	Mean age (Year)	Gender (M/F)	Mean Follow-Up Duration (Year)	Mean Tumor Size (cm, L/O)	Tumor Grade	NOS
Abbou et al. 1999	France	Retrospective	58	61	33/25	1.1	4.02/5.71	T_1-T_3	5
Acar et al. 2014	Turkey	Prospective	111	55.27	70/41	NR	5.71/7.16	T_1-T_4	8
Baldwin et al. 2003	United States	Retrospective	36	67.2	NR	0.55	NR	T_1-T_3	7
Bayrak et al. 2014	Turkey	Retrospective	173	58.4	NR	2.6	9.54/9.90	T_2-T_3	8
Bensalah et al. 2009	France	Retrospective	179	63.5	114/65	4	5.1/5.3	T_3	8
Burgess et al. 2007	United Kingdom	Prospective	45	50.3	16/29	NR	NR	NR	7
Chan et al. 2001	United States	Retrospective	121	60.1	78/43	3.3	5.1/5.4	T_1-T_2	6
Colombo et al. 2007	United States	Retrospective	88	59.5	62/26	5.5	5.8/6.2	T_1-T_2	8
Colombo et al. 2008	United States	Retrospective	116	60	73/43	5.9	5.4/6.4	T_1-T_2	8
Dunn et al. 2000	Egypt	Retrospective	93	62.9	49/44	2.1	5.3/7.4	NR	6
Feder et al. 2008	United States	Retrospective	88	58.7	53/35	1.9	14.6/15.0	T_1-T_4	8
Ganpule et al. 2008	India	Prospective	121	52.5	93/28	NR	7.14/8.05	T_1-T_3	9
Goel et al. 2002	India	Retrospective	29	48.7	16/13	1.9	6.5/6.8	T_1-T_3	8
Hattori et al. 2009	Japan	Retrospective	131	59.6	93/38	3.9	8.8/8.9	T_2-T_3	8
Hemal et al. 2007	India	Prospective	112	52.6	71/41	4.6	9.9/10.1	T_2	9
Hsu et al. 1999	United States	Retrospective	17	84.9	4/13	1.6	3/6.5	NR	7
Jeon et al. 2011	Korea	Retrospective	255	56	162/93	2	9.2/9.8	T_2	9
Jeong et al. 2011	Korea	Retrospective	1555	55.1	1051/504	2.3	4.2/4.7	T_1-T_2	9
Kawauchi et al. 2007	Japan	Retrospective	193	61.7	124/69	4.4	4.25/4.38	T_1-T_3	8
Kercher et al. 2003	United States	Retrospective	210	48.6	105/105	1.1	6.0/6.4	NR	7
Laird et al. 2015	United Kingdom	Prospective	50	66.2	32/18	4.7	8.7/10.0	T_3	8
Lee et al. 2003	Korea	Retrospective	104	52.2	76/28	NR	4.4/4.7	T_1-T_3	7
Luo et al. 2010	China	Retrospective	336	52.3	219/117	3.7	5.3/5.5	T_1-T_2	9
Makhoul et al. 2004	France	Retrospective	65	60.8	38/27	1.3	3.9/4.8	T_1	7
Malaeb et al. 2005	United States	Prospective	19	58	8/11	1.4	9.7/12.3	T_1-T_3	6
Miyake et al. 2007	Japan	Prospective	130	60.3	79/51	3.3	5.5/6.4	T_1-T_2	7
Ono et al. 2001	Japan	Prospective	149	57	110/39	5	3.1/3.3	T_1	8
Ono et al. 1999	Japan	Prospective	100	58.8	74/26	2.2	<5/<5	T_1-T_2	7
Park et al. 2009	Korea	Retrospective	1114	55.5	765/349	2.4	4.6/4.7	T_1-T_2	9
Permpongkosol et al. 2005	United States	Retrospective	121	NR	NR	6.3	5.1/5.4	T_1-T_2	7
Romao et al. 2014	Canada	Retrospective	45	3.6	NR	2.4	6.6/11	NR	6
Saika et al. 2003	Japan	Prospective	263	57.6	196/67	3.7	3.7/4.4	T_1	8
Shuford et al. 2004	United States	Retrospective	56	58.7	NR	1.6	4.4/7.4	NR	5
Siani et al. 2011	Italy	Retrospective	30	57	17/13	2.9	6.3/7.1	T_1-T_2	7
Steinberg et al. 2004	United States	Retrospective	99	59.7	65/34	NR	9.2/9.9	T_2	6
Tan et al. 2011	United States	Retrospective	8003	NR	4579/3424	NR	NR	NR	5
Tsujihata et al. 2008	Japan	Retrospective	100	61.5	69/31	2.6	4.3/5.5	T_1-T_2	7

L/O, laparoscopic/open; *NOS*, Newcastle-Ottawa Scale; *NR*, not reported.

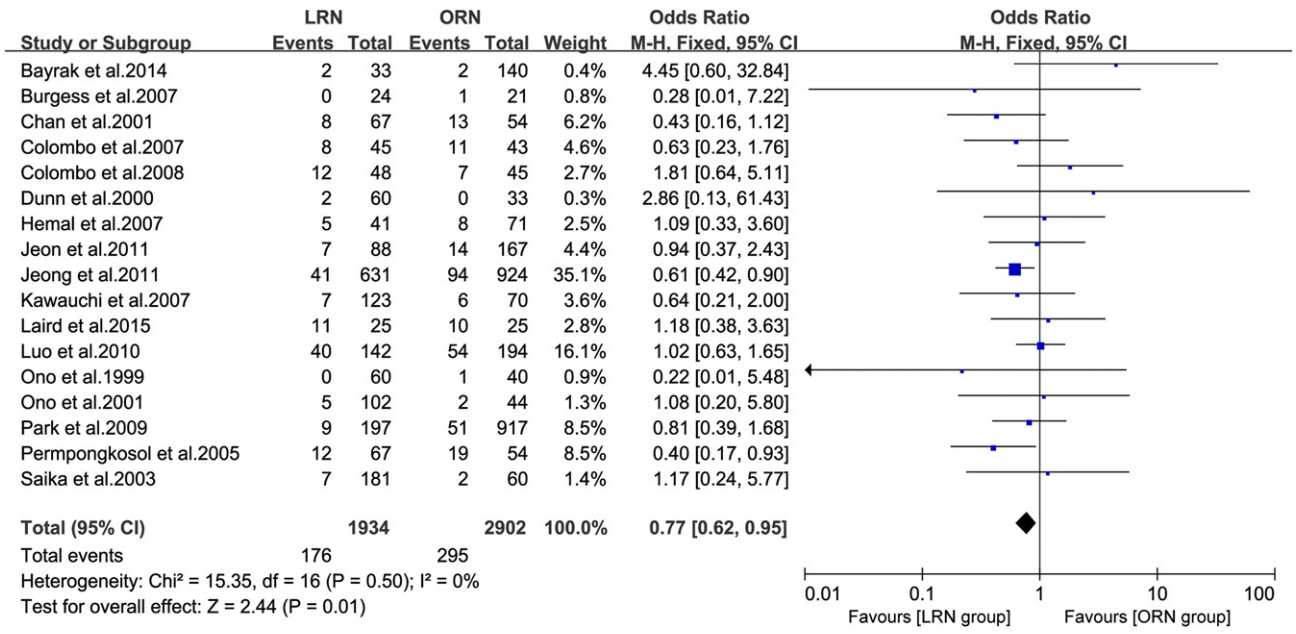

Figure 2. Relative risk of overall mortality comparing patients in the LRN group to those in the ORN group.

Table 2. Results of Subgroup Analyses

Outcome	Item Assessed in Analysis	Study Feature	Number of Studies Included	Pooled OR (95% CI), I^2 Statistics (%), and *P* Value for the Heterogeneity *Q* Test
Overall mortality	Geographic location	Europe	2	0.98 (0.35-2.78); I^2 = 0%, *P* = .41
		North America	4	0.63 (0.39-1.00); I^2 = 47%, *P* = .13
		Asia	10	0.79 (0.62-1.01); I^2 = 0%, *P* = .62
	Study design	Prospective	6	0.98 (0.52-1.84); I^2 = 0%, *P* = .90
		Retrospective	11	0.75 (0.60-0.93); I^2 = 23%, *P* = .22
	Mean age of participants	<60 years	11	0.79 (0.62-1.00); I^2 = 0%, *P* = .67
		≥60 years	5	0.90 (0.54-1.49); I^2 = 22%, *P* = .28
	Mean tumor size	<7 cm in both groups	11	0.72 (0.58-0.91); I^2 = 0%, *P* = .44
		≥7 cm in both groups	4	1.17 (0.65-2.10); I^2 = 0%, *P* = .59
	Tumor grade	T_1-T_2 only	10	0.73 (0.58-0.91); I^2 = 9%, *P* = .36
		T_3 or above involved	3	1.07 (0.51-2.24); I^2 = 27%, *P* = .25
Cancer-specific mortality	Geographic location	Europe	2	0.63 (0.28-1.42); I^2 = 48%, *P* = .16
		North America	3	0.67 (0.18-2.44); I^2 = 51%, *P* = .13
		Asia	7	0.87 (0.55-1.36); I^2 = 6%, *P* = .38
	Study design	Prospective	3	0.98 (0.39-2.49); I^2 = 0%, *P* = .79
		Retrospective	10	0.77 (0.49-1.22); I^2 = 27%, *P* = .19
	Mean age of participants	<60 years	5	0.86 (0.48-1.55); I^2 = 29%, *P* = .23
		≥60 years	7	0.89 (0.52-1.54); I^2 = 0%, *P* = .72
	Mean tumor size	<7 cm in both groups	8	0.76 (0.48-1.19); I^2 = 0%, *P* = .43
		≥7 cm in both groups	4	0.86 (0.38-1.92); I^2 = 47%, *P* = .13
	Tumor grade	T_1-T_2 only	8	0.88 (0.57-1.36); I^2 = 0%, *P* = .50
		T_3 or above involved	4	0.61 (0.36-1.05); I^2 = 46%, *P* = .13
Local tumor recurrence	Geographic location	Europe	1	0.06 (0.00-1.18)
		North America	3	1.32 (0.31-5.66); I^2 = 0%, *P* = .62
		Asia	11	0.87 (0.65-1.16); I^2 = 0%, *P* = 1.00
	Study design	Prospective	6	0.71 (0.36-1.42); I^2 = 0%, *P* = .58
		Retrospective	10	0.89 (0.66-1.22); I^2 = 0%, *P* = .96
	Mean age of participants	<60 years	12	0.81 (0.60-1.11); I^2 = 0%, *P* = .97
		≥60 years	4	1.18 (0.57-2.44); I^2 = 0%, *P* = .50
	Mean tumor size	<7 cm in both groups	8	0.89 (0.64-1.23); I^2 = 0%, *P* = .97
		≥7 cm in both groups	5	0.89 (0.47-1.70); I^2 = 0%, *P* = 1.00
	Tumor grade	T_1-T_2 only	9	0.90 (0.66-1.23); I^2 = 0%, *P* = .98
		T_3 or above involved	4	0.74 (0.33-1.65); I^2 = 46%, *P* = 1.00
Intraoperative complications	Geographic location	Europe	1	0.86 (0.11-6.73)
		North America	1	0.39 (0.11-1.38)
		Asia	7	1.52 (0.95-2.41); I^2 = 39%, *P* = .13
	Study design	Prospective	5	1.78 (0.92-3.41); I^2 = 0%, *P* = .58
		Retrospective	4	1.12 (0.32-3.88); I^2 = 66%, *P* = .03
	Mean age of participants	<60 years	8	1.27 (0.83-1.94); I^2 = 48%, *P* = .06
		≥60 years	1	1.51 (0.06-38.11)
	Mean tumor size	<7 cm in both groups	4	2.48 (1.03-5.93); I^2 = 0%, *P* = .90
		≥7 cm in both groups	4	1.00 (0.36-2.75); I^2 = 65%, *P* = .04
	Tumor grade	T_1-T_2 only	7	1.08 (0.68-1.70); I^2 = 24%, *P* = .24
		T_3 or above involved	1	7.00 (1.42-34.43)
Postoperative complications	Geographic location	Europe	5	0.64 (0.34-1.22); I^2 = 48%, *P* = .10
		North America	11	0.72 (0.65-0.80); I^2 = 28%, *P* = .18
		Asia	14	0.69 (0.55-0.87); I^2 = 0%, *P* = .70
	Study design	Prospective	10	0.82 (0.52-1.30); I^2 = 0%, *P* = .49
		Retrospective	21	0.71 (0.64-0.78); I^2 = 13%, *P* = .29
	Mean age of participants	<60 years	20	0.62 (0.50-0.77); I^2 = 0%, *P* = .55
		≥60 years	10	0.78 (0.52-1.16); I^2 = 32%, *P* = .16
	Mean tumor size	<7 cm in both groups	14	0.62 (0.49-0.79); I^2 = 0%, *P* = .47
		≥7 cm in both groups	9	0.89 (0.62-1.27); I^2 = 13%, *P* = .33
	Tumor grade	T_1-T_2 only	12	0.73 (0.57-0.92); I^2 = 13%, *P* = .32
		T_3 or above involved	12	0.61 (0.41-0.89); I^2 = 16%, *P* = .29

Discussion

Our meta-analysis indicated that LRN was associated with better surgical outcomes as assessed by overall mortality and postoperative complications compared with ORN, especially for those with small tumors (tumor size <7 cm). LRN also had better outcomes on cancer-specific mortality and local tumor recurrence compared with ORN, although these results did not reach statistical significance. In addition, LRN has been shown to offer superior perioperative results to ORN, including shorter hospital stay days, time to start oral intake, and convalescence time, and less estimated blood loss, blood transfusion rate, and anesthetic consumption.

Although many individual studies have reported the outcomes of LRN compared with ORN, they were limited by the relatively small number of enrolled patients. Randomized controlled trials (RCTs) have been accepted as the golden standard to determine the effectiveness of the intervention. However, there is still a lack of RCTs to directly compare the treatment effects and safety profile between LRN and ORN for therapy of RCC. A systematic review and meta-analysis is needed to compare LRN with ORN to compensate for the individual lack of precision in the most of previous studies. Combining estimates from all available published studies allows us to compare the outcomes of LRN and ORN with a more comprehensive

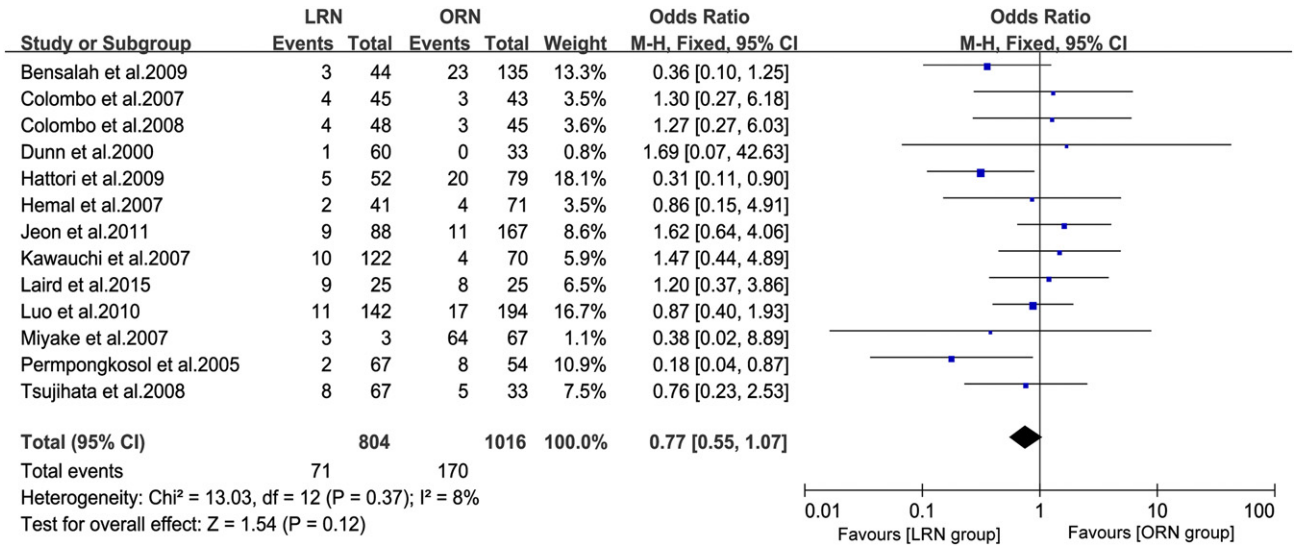

Figure 3. Relative risk of cancer-specific mortality comparing patients in the LRN group to those in the ORN group.

evidence base and greater precision than have previously been possible.

In our meta-analysis, the overall mortality and the risk of postoperative complications were significantly lower comparing patients in the LRN group to those in the ORN group, with pooled rates of 9.1% (176/1934) versus 10.2% (295/2902) and 21.1% (905/4282) versus 31.9% (2646/8295), respectively. However, in the subgroup analyses, the pooled ORs of overall mortality and postoperative complications of LRN compared with ORN shrunk following treatment for RCC with mean tumor size smaller than 7 cm and were amplified following treatment for RCC with mean tumor size larger than 7 cm. Particularly, the point estimate for overall mortality was greater than 1 (1.17, 95% CI: 0.65-2.10) in patients with tumor size larger than 7 cm. This means that LRN has superior oncological efficacy especially for small tumors. As the tumor size increases, LRN has showed several technical problems, including limited working space, decreased maintenance of operator orientation, increased potential for adjacent organ involvement, significant parasitic vessels, and difficult specimen removal [46]. Traditionally, LRN has been reserved for small renal tumors. Gill et al. [47] have successfully implemented LRN in tumors larger than 12 cm (mean 14.6 cm) in 2000. Later, Dunn et al. [19] also reported their results of LRN in patients with renal tumors lager than 10 cm. In these studies, the authors have found more advantageous results in the LRN group than the ORN group, including less blood loss, less pain, and faster recovery. However, differences on long-term oncological outcomes of the two methods have seldom been reported according to different tumor sizes.

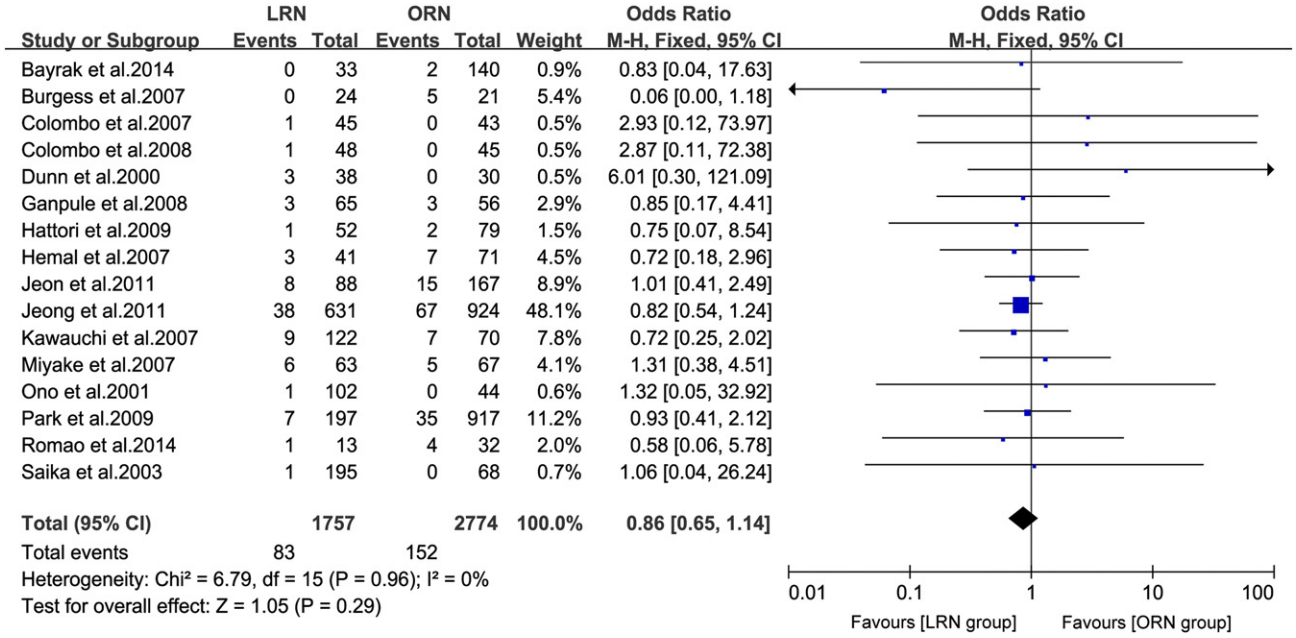

Figure 4. Relative risk of local recurrence comparing patients in the LRN group to those in the ORN group.

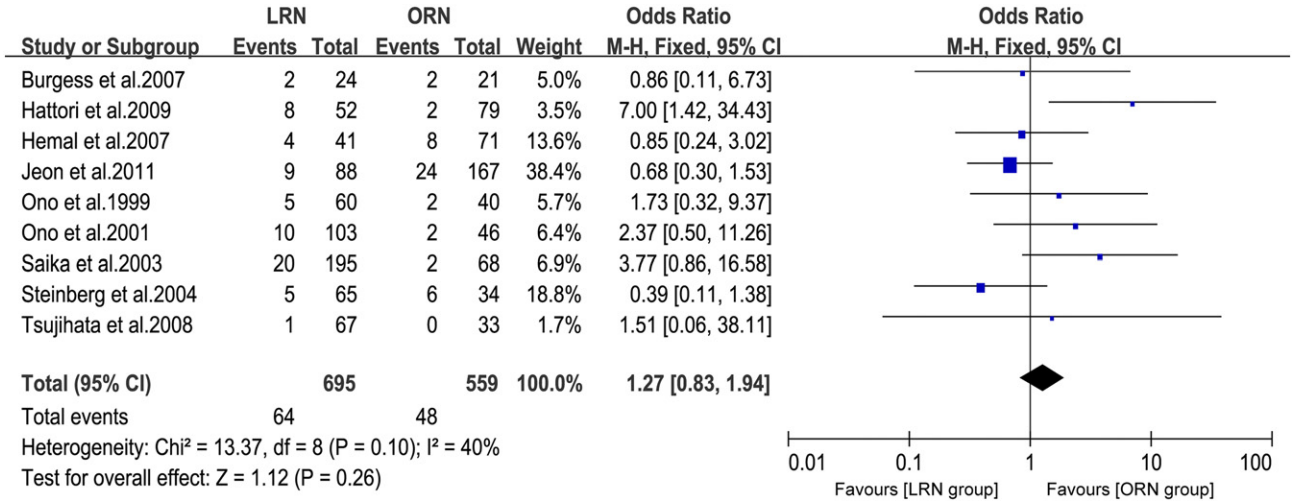

Figure 5. Relative risk of intraoperative complications comparing patients in the LRN group to those in the ORN group.

In addition, there were no significant differences in cancer-specific mortality and local recurrence between two groups, although the point estimates were below 1. Overall, the cancer-specific mortality was 8.8% (71/804) following LRN and 16.7% (170/1016) following ORN, and the local recurrence was 4.7% (83/1757) following LRN and 5.5% (152/2774) following ORN. Multiple studies have shown that the 5-year mortality after radical nephrectomy in cohorts ranges from 5% to 25% [48]. The pooled overall mortality and

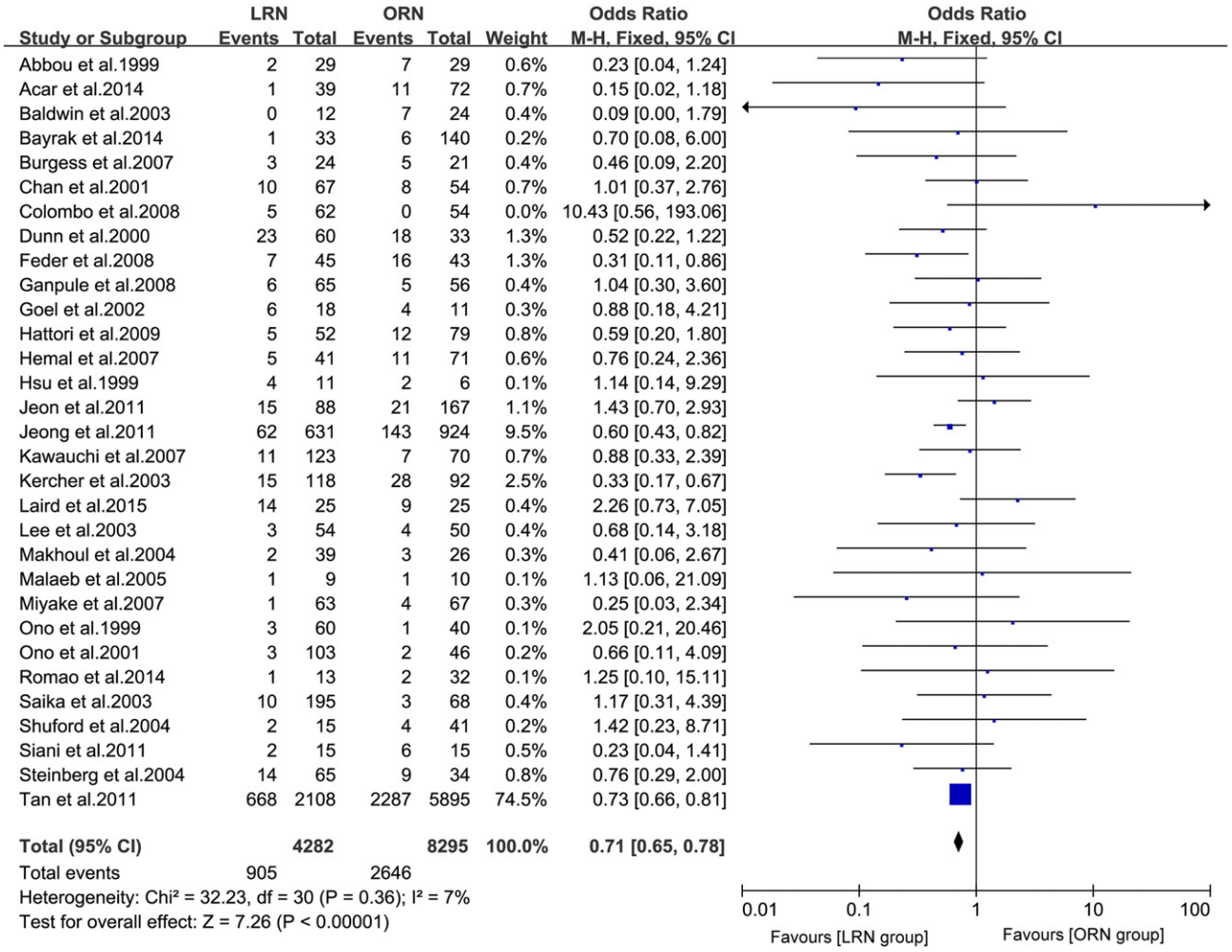

Figure 6. Relative risk of postoperative complications comparing patients in the LRN group to those in the ORN group.

Table 3. Pooled WMD/OR of Perioperative Results (LRN Versus ORN)

	Number of Studies Included	Number of Patients Involved	Pooled WMD/OR (95% CI)	*P* Value
Mean operative time (min)	29	5514	24.12 (13.01 to 35.22)	<.001
Estimated blood loss (ml)	29	5449	−201.02 (−246.29 to −155.75)	<.001
Hospital stay (day)	21	1797	−2.87 (−3.42 to −2.32)	<.001
Blood transfusion rate (%)	11	2873	0.59 (0.43 to 0.81)	.001
Time to start oral intake (hour)	8	641	−31.16 (−47.40 to −14.91)	<.001
Convalescence time (week)	7	731	−3.26 (−4.38 to −2.14)	<.001
Anesthetic consumption (mg)	7	458	−36.86 (−52.82 to −20.90)	<.001

cancer-specific mortality for LRN and ORN in our study were both in this interval.

In almost all the individual studies included in our meta-analysis, the ORs of overall mortality, cancer-specific mortality, local tumor recurrence, intraoperative complications, and postoperative complications did not reach statistical significances with 95% CI across 1, which can be seen in Figures 2 to 6 in our study. This means that the most previous studies found that the oncological outcomes of LRN were similar to those of ORN. One of the strengths of our meta-analysis is that we found significantly better oncological outcomes for LRN compared with ORN according to overall

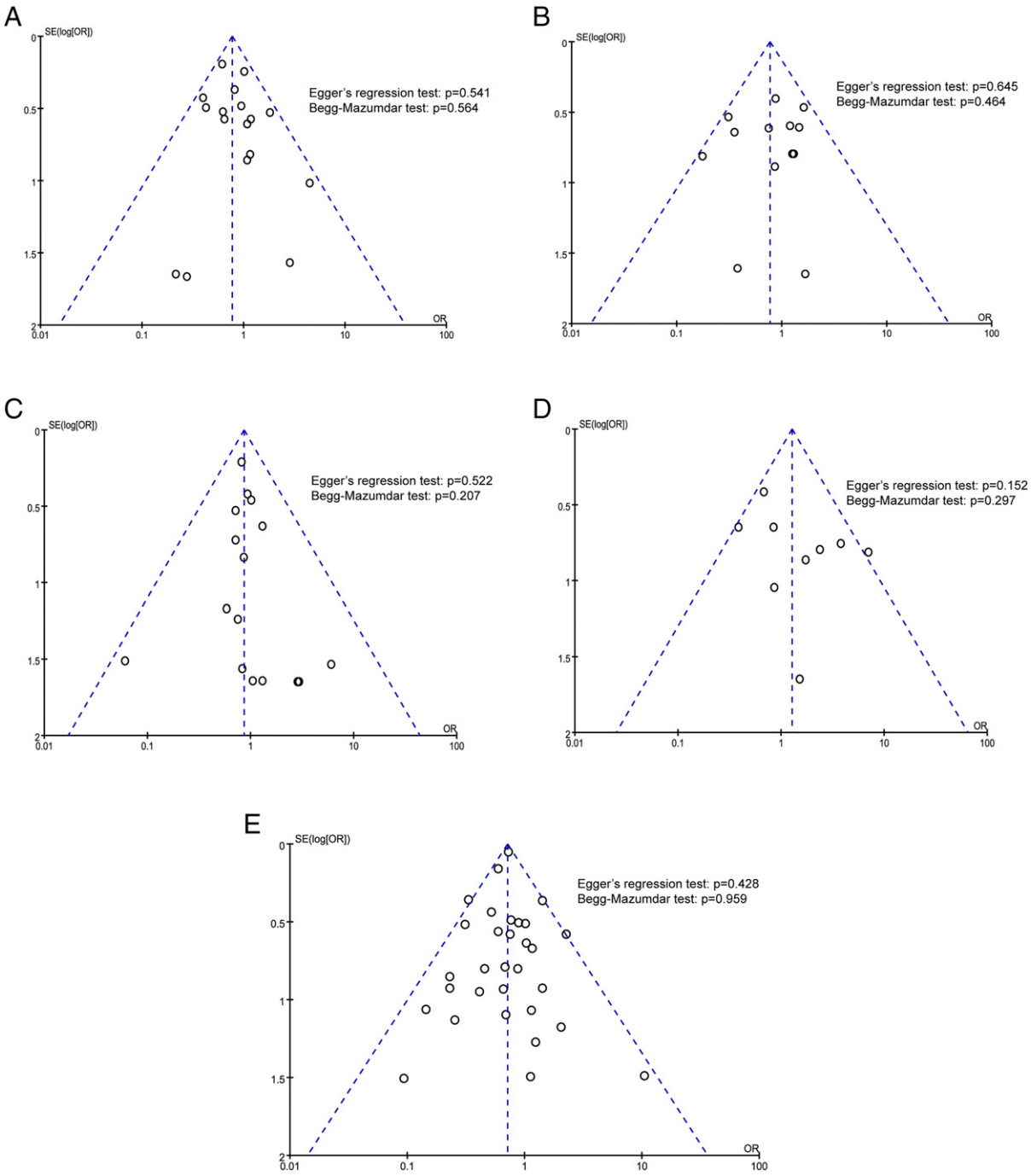

Figure 7. Funnel plots to explore publication bias in the estimates of overall mortality (A), cancer-specific mortality (B), local recurrence (C), intraoperative complications (D), and postoperative complications (E). The vertical line is at the mean effect size.

mortality and postoperative complications. This may be due to the limited sample size in the previous studies, and our pooled results of previous studies were much more precise with more narrow CIs due to the larger sample size. In addition, there was no evidence of heterogeneity among individual studies in most pooled analyses. Another strength of our study is that there was no potential publication bias in all the analyses, as assessed by funnel plots, Egger's regression test, and Begg-Mazumdar test. Taken together, the results of this meta-analysis are sound and reliable.

Our meta-analysis has some limitations that merit additional comments. Firstly, the defining criteria for the outcome measures we were interested in may be slightly different in different studies. This would particularly apply to intraoperative complications and postoperative complications. In meta-analysis, we attempted to select outcome measures that are as absolute as possible to reduce heterogeneity. Second, our inference is mainly based on observational studies; although most included studies have made adjustments for confounding factors to make the studies reliable, we cannot exclude chance, residual, or unmeasured confounding factors, such as the performance status of the patients, tumor size, tumor grade, and differences in tumor thrombus involvement, as alternative explanation for our results. Thirdly, there was variation in inclusion criteria, study design, and treatment protocols between studies. Finally, the follow-up duration was quite short in several included studies, and the long-term oncological outcomes may not necessarily be identified in these studies.

Conclusions

In conclusion, our meta-analysis indicated that, compared with ORN, LRN was associated with better surgical outcomes in treatment of RCC as assessed by overall mortality and postoperative complications. LRN has also been shown to offer superior perioperative results to ORN. Further large-scale, well-designed RCTs are needed to identify the current findings and investigate the long-term effects of LRN compared with ORN for therapy of RCC.

Competing Interests

All authors declare that they have no competing interests.

Authors' Contributions

G. L., S. W., and D. G. designed the study; Y. M. and X. H. coordinated the study; G. L. and Y. M. performed the acquisition of data and the statistical analysis; S. W., X. H., and D. G. interpreted the data; G. L. drafted the manuscript. All authors revised the final manuscript and approved this version to be published.

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