Partial Versus Radical Nephrectomy in Patients with Renal Cell Carcinoma: A Systematic Review and Meta-analysis

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Purpose: Radical nephrectomy (RN) and partial nephrectomy (PN) are widely used for early-stage renal cell carcinoma (RCC). However, the results were inconsistent while comparing the efficiency of RN and PN. This study aimed to assess the perioperative effectiveness of RN and PN for treating RCC.

Material and Methods: PubMed, Embase, and the Cochrane Library electronic database were searched for studies on adults with RCC comparing RN and PN published until September 2019. The perioperative efficacy and safety outcomes were calculated using odds ratio (OR) and standard mean difference (SMD) with 95% confidence intervals (CIs) for dichotomous and continuous data, respectively. Subgroup analysis were conducted based on tumor stage and surgery methods for evaluation of the treatment effect on specific subsets.

Results: A total of 23 studies involving 30,018 patients with RCC were included in this meta-analysis. Notably, RCC treated with PN was associated with low incidences of hospital mortality (OR: 0.58; 95% CI: 0.38–0.89; $P = 0.013$) and reoperation rate (OR: 0.74; 95% CI: 0.58–0.95; $P = 0.016$) as compared to RN. However, PN was associated with an increased risk of overall postoperative complications (OR: 1.40; 95% CI: 1.17–1.68, $P < 0.001$), postoperative hemorrhagic complications (OR: 1.92; 95% CI: 1.28–2.87, $P = 0.002$), and urinary fistula (OR: 17.65; 95% CI: 5.35–58.30, $P < 0.001$) as compared to RN.

Conclusion: These findings suggested that PN was associated with lower incidences of hospital mortality and reoperation rate, whereas RN was associated with fewer complications.

Keywords: radical nephrectomy; partial nephrectomy; renal cell carcinoma; perioperative; meta-analysis

INTRODUCTION

Renal cell carcinoma (RCC) is the third most common urological cancer, accounting for 2–3% of cancer-related deaths in adults[1,2]. The incidence of RCC increases with age, maximal at 70 years of age, and 2-fold more prevalent in men than women[3,4]. The predisposing factors of RCC include age, gender, smoke, excessive weight, long-term dialysis, hereditary factor, and exposure to hazardous materials (cadmium, benzene, trichloroethylene, and asbestos)[5-7].

Surgical removal is regarded as the standard treatment for patients with RCC, as the tumor is resistant to chemotherapy and radiotherapy[8,9]. Radical nephrectomy (RN) removes the affected kidney within Gerota's fascia, including the ipsilateral adrenal gland and regional lymph nodes, which is still the gold standard for treating RCC [10,11]. However, whether nephron-sparing surgery, termed as partial nephrectomy (PN), is an ideal alternative to RN is yet a controversy. PN is a feasible organ-preserving approach that avoids unnecessary loss of a viable kidney, especially in the case of small renal tumors with diameter ≤ 4 cm (stage T1a) and normal contralateral kidney[12,13]. RN and PN were both recommended according to the NCCN Guidelines for patients with RCC in the T1b stage[14]. Therefore, selection of the surgical technique is yet controversial, especially in patients with RCC in the T1b stage[15,16].

Although various treatment guidelines were available on RCC, a majority were based on personal experience[17,18]. Previous meta-analyses analyzed the differences in clinical outcomes between RN and PN, including overall mortality, cancer-related mortality, and incidence of renal failure[19-24]. Nevertheless, potential limitations are also presented. First, previous meta-analyses discussed several surgical methods or provided a qualitative comparison between RN and PN; however, the direct quantitative comparison of RN with PN was not included. Second, the impact of tumor stage on clinical outcomes was neglected. Third, previous studies primarily focused on mortality, while the perioperative side-effects were not summarized. Thus, the present study aimed to provide comprehensive results for the treatment strategies of RN and PN in patients with RCC.

MATERIALS AND METHODS

Search strategy and selection criteria

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009[25] (Checklist S1). PubMed, Embase, and Cochrane Library electronic database were systematically searched for studies published until September 2019. "Nephrectomy," "kidney neoplasms," "renal cell carcinoma*," "renal mass*," "renal tumor*," and "renal cancer*" were used as core search terms. The reference lists of all relevant original and review articles were searched manually to identify additional eligible studies.

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Received May 2019 & Accepted December 2019

Table 1. Characteristics of included studies.

Author (year)	Design	Region	Study period	No. of patients	Mean age (years)	Male (%)	Criteria for kidney lesions	TNM	Compared surgical arms	Operation	Perioperative outcomes	JADAD or NOS
Butler (1995) [36]	Retrospective	USA	1975–1992	88	62	61	Solitary (<4 cm) unilateral RCCs	T1a	Open PN (n = 46) vs. open RN (n = 42)	Open	LOS, IT, OC, PO severe hemorrhage, incidence of urinary fistula, spleen damage, reoperation, ARF, sCr levels	5
Indudhara (1997) [37]	Retrospective	UK	1989–1995	106	45	65	Solitary (<5 cm) RCCs	T1	Open PN (n = 35) vs. open RN (n = 71)	Open	Blood loss, LOS, mean PO sCr levels, incidence of urinary fistula, PO severe hemorrhage, CC, ARF	6
Uzzo (1999) [38]	Retrospective	USA	1991–1995	80	Median: 67.1 (RN) vs. 61.5 (NSS)	65	Solitary (<4 cm) unilateral RCCs	T1a	Open PN (n = 52) vs. open RN (n = 28)	Open	OC, LOS	6
Corman (2000) [39]	Prospective	USA	1991–1998	1885	62	98	Heterogeneous RCCs	NA	Open PN (n = 512) vs. open RN (n = 1373)	Open	30-day mortality, OC, ARF, PO severe hemorrhage, LOS, mean PO sCr levels	8
Shekarrizet al. (2002) [40]	Retrospective	USA	1991–1997	120	64	NA	Solitary (<7 cm) unilateral RCCs	T1	Open PN (n = 60) vs. open RN (n = 60)	Open	LOS, OC, incidence of urinary fistula, IT, blood loss	7
Kim (2003) [41]	Retrospective	USA	1998–2002	114	58	65	Solitary (<4.5 cm) unilateral RCCs	T1	LPN (n = 79)) vs. LRN (n = 35	MIPN	IT, ARF, spleen damage, OC, LOS, mean PO sCr levels	6
Stephenson (2004) [42]	Retrospective	USA	1995–2002	1049	62	NA	Renal cortical neoplasm	NA	Open PN (n = 361) vs. open RN (n = 688)	Open	OC, 30-day mortality, incidence of urinary fistula, ARF, PO severe hemorrhage, LOS, reoperation, mean PO sCr levels, CC	7
Van Poppel (2007) [43]	RCT	Multicenter	1992–2003	541	NA	67	Solitary (<5 cm) T1–T2N0M0 RCCs	T1	Open PN (n = 268) vs. open RN (n = 273)	Open	PO severe hemorrhage, incidence of urinary fistula, pleural damage, spleen damage, reoperation	3^
Miller (2008) [44]	Retrospective	USA	1991–2002	10123	75	62	RCCs	NA	Open PN (n = 763) vs. open RN (n = 10123)	Open	CC	7
Gratzke (2009) [45]	Prospective	Switzerland	January–December 2005	81	61	64	T1–T2 RCCs	NA	Open PN (n = 44) vs. open RN (n = 37)	Open	LOS, 30-day mortality, ARF, IT, PO severe hemorrhage, reoperation	7
Simmons (2009) [46]	Retrospective	USA	2001–2005	110	63	59	T1b–T3N0M0 RCCs	NA	LRN (n = 75) vs LPN (n = 35)	MIPN	OC, PO mean sCr levels	5
Roos (2010) [47]	Retrospective	Germany	1981–2007	166	Range: 23-84	57	> 4 cm RCCs	T1a	Open PN (n = 69) vs. open RN (n = 97)	Open	OC, CC, incidence of urinary fistula, IT, spleen damage	6
Lowrance (2010) [48]	Retrospective	USA	2000–2008	1712	NA	62	<7 cm RCCs	T1	Mixed PN (n = 1061) vs. mixed RN (n = 651)	Mix	OC, in-hospital mortality	6
Sun (2012) [49]	Retrospective matched	Canada	1988–2005	1680	72	59	T1aN0M0 RCCs	T1a	Open PN (n = 840) vs. open RN (n = 840)	Open	ARF	8
Becker (2014)*[50]	Retrospective	Canada	1992–2005	1223	>66	53	T1N0M0 RCCs	T1	LRN (n = 1066) vs. LPN (n = 157)	MIPN	PO severe hemorrhage, ARF, CC, 30-day mortality	7
Liu (2014) [51]	Retrospective	USA	2005–2011	8361	61	NA	RCCs	NA	MIRN (n = 3014) vs. MIPN (n = 1439); Open RN (n = 2445) vs. open PN (n = 1463)	Mix	IT, ARF, CC, 30-day mortality, reoperation	7
Hadjipavlou (2015) [52]	Prospective	UK	January–December 2012	1768	62	61	T1 RCCs	T1	Mixed RN (n = 1082) vs. mixed PN (n = 686)	Mix	OC, IT	8
Cai (2018) [53]	Retrospective	China	2005-2012	199	54	64	solitary tumor with a maximum diameter of 4.0 to 7.0 cm	T1b	LRN (n = 160) vs. LPN (n = 39)	MIPN	Overall survival	6
Rinott Mizrahi (2018) [54]	Retrospective	Israel	2012-2017	29	65	83	T2 RCC	T2	LRN (n = 16) vs. LPN (n = 13)	MIPN	OC	5
Reix (2018) [55]	Retrospective	France	2000-2014	267	60	67	localized RCC stage cT2a (7.1—10 cm)	T2a	Mixed RN (n = 176) vs. mixed PN (n = 91)	Mix	Overall survival	6
Janssen (2018) [56]	Retrospective	Germany	1980-2010	123	61	65	Large (>7cm) clear cell RCC	T1b-T3	Open RN (n = 105) vs. open PN (n = 18)	Open	Overall survival	6
de Saint Aubert (2018) [57]	Retrospective	France	2000-2013	130	58	63	Large (>7cm) RCC	T2	Mixed RN (n = 81) vs. mixed PN (n = 49)	Mix	OC, hemorrhage, hospital stay, ARF	7
Yang (2018) [58]	Retrospective	China	2014-2017	63	58	54	Clinical T1 Renal Hilar Tumor	T1	LRN (n = 38) vs. LPN (n = 25)	MIPN	OC	5

Abbreviations: ARF, acute renal failure; CC, cardiovascular complications; IT, intraoperative transfusion; LOS, length of stay; MIPN, minimally invasive PN; NSS, nephron-sparing surgery; OC, overall complications; PN, partial nephrectomy; PO, postoperative; RCC, renal cell carcinoma; RN, radical nephrectomy; sCr, serum creatinine
*Data on open PN vs laparoscopic RN were discarded
^using JADAD scale

Table 2. Subgroup analyses according to tumor stage and surgery methods

Outcome	Subgroup	No. of studies	OR or SMD and 95% CI	*P* value	Heterogeneity (%)	*P* for heterogeneity
Hospital mortality	T1	6	1.11 (0.52-2.33)	0.792	0.0	0.558
	Other	5	0.46 (0.29-0.73)	0.001	28.3	0.223
	Open	6	0.45 (0.26-0.78)	0.005	24.7	0.249
	MIPN	3	0.91 (0.37-2.24)	0.844	37.3	0.203
	Mixed	3	0.69 (0.30-1.59)	0.378	3.8	0.354
Overall postoperative complications	T1	9	1.46 (1.19-1.79)	< 0.001	25.6	0.200
	Other	5	1.38 (0.95-2.00)	0.094	50.7	0.088
	Open	6	1.20 (0.99-1.47)	0.066	0.0	0.706
	MIPN	5	1.17 (0.72-1.89)	0.536	53.2	0.058
	Mixed	3	1.73 (1.29-2.33)	< 0.001	48.6	0.143
Postoperative hemorrhagic complications	T1	4	2.25 (1.44-3.50)	< 0.001	0.0	0.555
	Other	4	1.73 (0.65-4.60)	0.275	27.0	0.250
	Open	6	1.71 (1.00-2.90)	0.048	14.1	0.324
	MIPN	1	2.20 (1.15-4.20)	0.017	-	-
	Mixed	1	12.27 (0.62-242.79)	0.100	-	-
Cardiovascular complications	T1	3	0.48 (0.07-3.20)	0.450	76.2	0.015
	Other	3	1.02 (0.92-1.12)	0.766	0.0	0.773
	Open	5	1.00 (0.82-1.22)	0.968	46.2	0.098
	MIPN	2	0.89 (0.43-1.84)	0.746	8.7	0.295
	Mixed	0	- -	-	-	
Acute renal failure	T1	5	1.25 (0.55-2.86)	0.596	49.8	0.093
	Other	5	0.78 (0.36-1.66)	0.518	58.2	0.035
	Open	7	0.87 (0.58-1.32)	0.510	34.4	0.165
	MIPN	3	0.72 (0.10-4.96)	0.737	80.9	0.005
	Mixed	1	0.51 (0.05-5.16)	0.568	-	-
Spleen damage	T1	4	0.41 (0.10-1.72)	0.224	0.0	0.769
	Other	0	- -	-	-	
	Open	3	0.31 (0.06-1.52)	0.148	0.0	0.783
	MIPN	1	1.36 (0.05-35.53)	0.853	-	-
	Mixed	0	- -	-	-	
Reoperation	T1	2	1.50 (0.59-3.85)	0.396	0.0	0.320
	Other	3	0.71 (0.55-0.91)	0.006	0.0	0.657
	Open	5	0.85 (0.49-1.47)	0.568	18.6	0.296
	MIPN	1	0.74 (0.49-1.13)	0.162	-	-
	Mixed	0	-	-	-	-
Urinary fistula	T1	5	12.55 (3.35-47.00)	< 0.001	0.0	0.981
	Other	1	82.66 (4.98-1371.41)	0.002	-	-
	Open	6	17.65 (5.35-58.30)	<0.001	0.0	0.871
	MIPN	0	-	-	-	-
	Mixed	0	-	-	-	-
Hospital stay	T1	2	0.06 (-0.21 to 0.33)	0.671	0.0	0.620
	Other	3	0.04 (-0.05 to 0.13)	0.411	0.0	0.805
	Open	4	0.05 (-0.04 to 0.14)	0.316	0.0	0.923
	MIPN	0	- -	-	-	
	Mixed	1	-0.04 (-0.39 to 0.31)	0.825	-	-
Intraoperative blood transfusion	T1	4	1.05 (0.60-1.82)	0.866	31.1	0.214
	Other	3	0.75 (0.46-1.25)	0.272	86.8	< 0.001
	Open	5	1.04 (0.55-1.99)	0.895	84.0	< 0.001
	MIPN	2	0.70 (0.53-0.94)	0.017	0.0	0.801
	Mixed	1	0.81 (0.45-1.44)	0.475	-	-
Mean postoperative sCr	T1	2	-0.41 (-2.00 to 1.18)	0.613	96.4	< 0.001
	Other	2	-0.01 (-0.11 to 0.09)	0.849	0.0	0.962
	Open	2	0.14 (-0.25 to 0.53)	0.476	70.5	0.066
	MIPN	2	-0.61 (-1.80 to 0.59)	0.319	94.0	< 0.001
	Mixed	0	-	-	-	-

The literature search was undertaken by two reviewers independently, and any inconsistencies were settled by the primary author (Yong Yang) until a consensus was reached. The study was eligible for inclusion if the following criteria were fulfilled: (1) study with retrospective/prospective cohort or randomized/non-randomized controlled design; (2) study investigating RN versus PN in patients with RCC; (3) outcomes including one of the following: hospital mortality, overall postoperative complications, postoperative hemorrhagic complications, cardiovascular complications, acute renal failure (ARF), spleen damage, reoperation, urinary fistula, intraoperative blood transfusion, hospital stay, and mean postoperative sCr. All studies describing patients with other diseases or lacking the direct comparison of RN and PN were excluded.

Data collection and quality assessment

Two reviewers independently extracted all data; the discrepancies were resolved after consulting with the primary author (Yong Yang). The following items were extracted from the included studies: first author's name, design, region, study period, number of patients, mean age, the percentage of males, criteria for kidney lesions, TNM stages, compared surgical arms, operation types, and perioperative outcomes. The following outcomes were evaluated: hospital mortality, overall

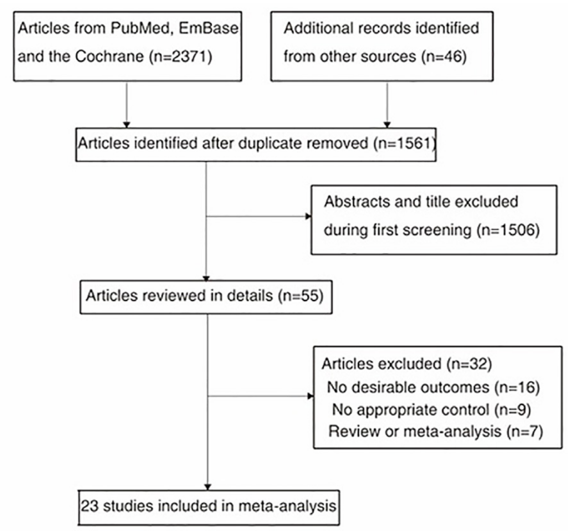

Figure 1. Schematic representation. Preferred Reporting Items for Systematic Reviews and meta-Analysis flow diagram.

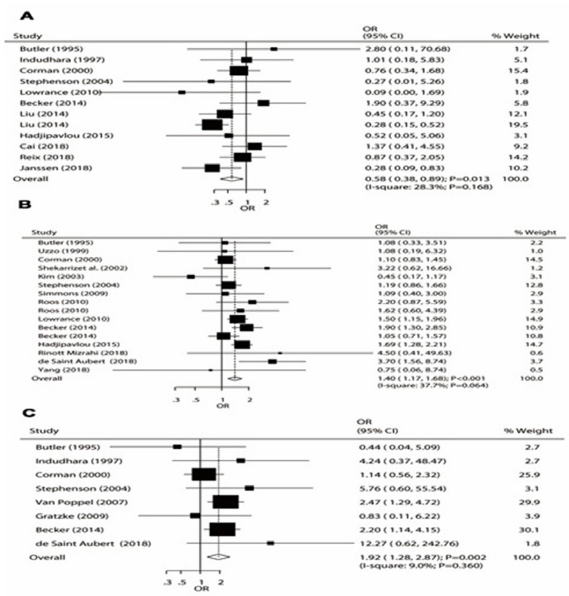

Figure 2. A:PN vs. RN on the risk of in-hospital mortality; B: PN vs. RN on the risk of overall postoperative complications; C: PN vs. RN on the risk of postoperative hemorrhagic complications

postoperative complications, postoperative hemorrhagic complications, cardiovascular complications, ARF, spleen damage, reoperation, urinary fistula, intraoperative blood transfusion, hospital stay, and mean postoperative sCr. The quality of randomized controlled trial was assessed using JADAD scale, which was based on randomization, blinding, allocation concealment, withdrawals and dropouts, and use of intention-to-treat analysis[26]. Then, the quality of prospective or retrospective observational studies was evaluated using the Newcastle–Ottawa Scale (NOS), which was based on the following three subscales: selection (4 items), comparability (1 item), and outcome (3 items)[27].

Statistical analysis

An inverse variance method was used to pool the continuous data, and the results were presented as standard mean difference (SMD) with 95% confidence intervals (CIs). The results were presented as the odds ratio (OR) with 95% CIs for dichotomous data as most of the included studies consisted of retrospective cohorts. Given the lower prevalence of investigated outcomes, the relative risk could be considered as equivalent to OR. The pooled results were further evaluated using the random-effects model[28,29]. The statistical heterogeneity was assessed with the I2 test, and I2 > 50% was considered as significant heterogeneity[30]. A sensitivity analysis assessed the influence of a single study on overall ORs and SMDs[31]. The subgroup analysis for the investigated outcomes was performed according to the tumor TNM stage (T1 stage or other) and surgical procedures (open, minimally invasive PN procedure, or mixed). Funnel plots were used for assessing the publication bias; the Begg–Mazumdar[32] and Egger tests [33,34] evaluated the publication bias quantitatively. The trim-and-fill method was used to correct the publication bias if necessary[35]. All tests were two-tailed, and a *P*-value < 0.05 was considered as statistically significant. STATA software (Version 12.0; StataCorp, TX, USA) was used to analyze the data.

RESULTS

This meta-analysis yielded 1,561 studies after removing duplications, of which, 23 assessing 30,018 patients were included in the systematic review (**Figure 1**)[36-58]. 1/23 was a randomized controlled trial (RCT) design [43], 3/23 had a prospective study design[39,45,52], and the remaining had a retrospective design. The RCT was a multicenter clinical study; however, blinding was not employed to conceal the intervener and/or the assessor[43] (**Table 1**). Moreover, the quality of remaining observational studies were assessed using the NOS; 3 studies had 8 stars, 7 had 7 stars, 8 had 6 stars, and the remaining 4 had 5 stars.

The summary results of the treatment effects between RN and PN are presented in Figures 2–5. The meta-analysis revealed that PN had a significantly lower hospital mortality (OR: 0.58; 95% CI: 0.38–0.89; *P* = 0.013; unimportant heterogeneity) and reoperation rate (OR: 0.74; 95% CI: 0.58–0.95; *P* = 0.016; no evidence of heterogeneity) as compared to RN after pooling the results. However, patients treated with PN were associated with a greater risk of overall postoperative complications (OR: 1.40; 95% CI: 1.17–1.68, *P* < 0.001; moderate heterogeneity), postoperative hemorrhagic complications (OR: 1.92; 95% CI: 1.28–2.87, *P* = 0.002; unimportant heterogeneity), and urinary fistula (OR: 17.65; 95% CI: 5.35–58.30, *P* < 0.001; no evidence of heterogeneity) as compared to RN. Finally, no significant differences were detected between PN and RN with respect to the outcomes of cardiovascular complications (OR: 0.99; 95% CI: 0.83–1.19, *P* = 0.932; moderate heterogeneity), ARF (OR: 0.91; 95% CI: 0.57–1.43, *P* = 0.675; significant heterogeneity), spleen damage (OR: 0.41; 95% CI: 0.10–1.72, *P* = 0.224; no evidence of heterogeneity), intraoperative blood transfusion (OR: 0.87; 95% CI: 0.59–1.28, *P* = 0.475; significant heterogeneity), hospital stay (SMD: 0.04; 95% CI: -0.05 to 0.13; *P* = 0.360; no evidence of heterogeneity), and mean postoperative sCr (SMD:

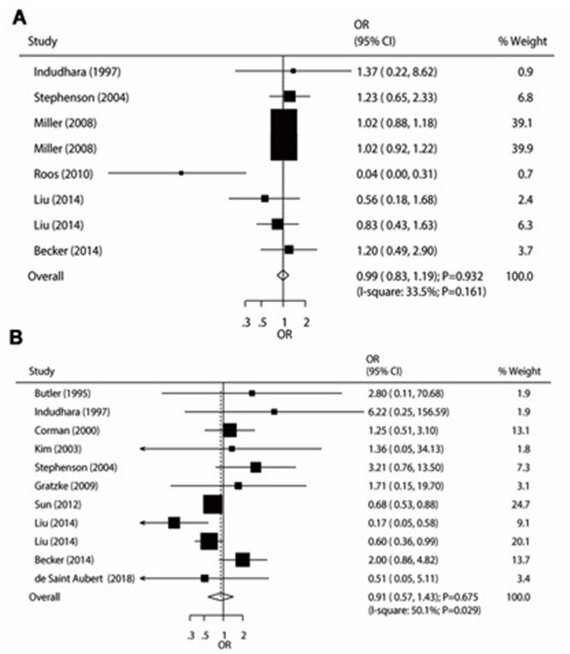

Figure 3. A: PN vs. RN on the risk of cardiovascular complications; B: PN vs. RN on the risk of acute renal failure

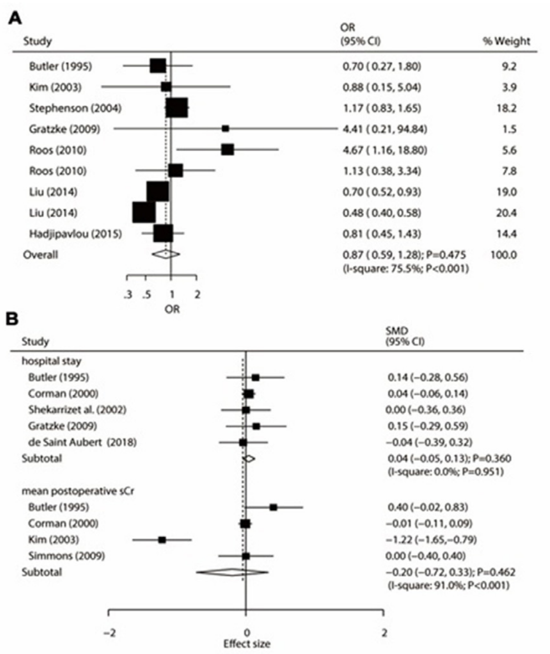

Figure 5. A: PN vs. RN on the incidence of intraoperative blood transfusion; B:. PN vs. RN on hospital stay and mean postoperative sCr

-0.20; 95% CI: -0.72 to 0.33, $P = 0.462$; significant heterogeneity). The results of sensitivity analysis indicated that the overall pooled ORs and SMDs were not affected by sequential exclusion of individual study except hospital mortality and reoperation rate (**Supplemental Figure 1**).

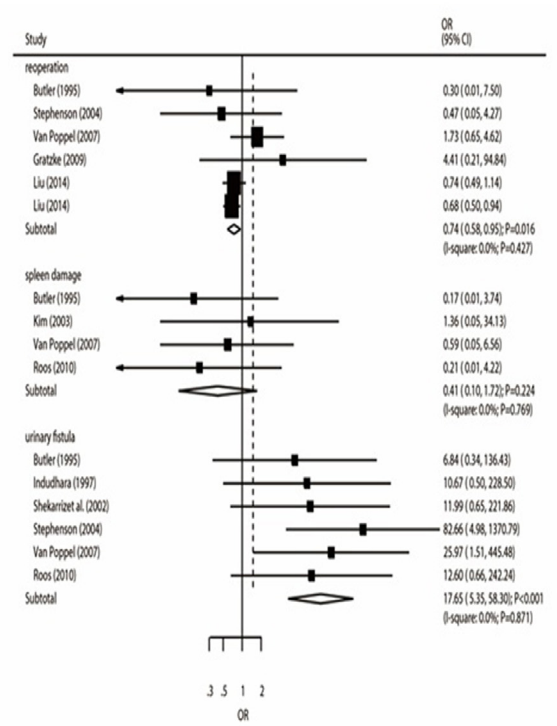

Figure 4. PN vs. RN on the risk of spleen damage, reoperation, and urinary fistula

The summary results for subgroup analyses are shown in Table 2. First, we noted that PN was associated with a reduced risk of hospital mortality if the included patients exhibited other stage of tumor and underwent an open procedure. Second, the risk of overall postoperative complications was significantly increased in T1 stage tumor patients or received mixed PN. Third, PN was associated with an increased risk of postoperative hemorrhagic complications than RN when patients with T1 stage tumor used open or minimally invasive PN procedure. Fourth, stratified results for cardiovascular complications, ARF, spleen damage, urinary fistula, hospital stay, and mean postoperative sCr were consistent with the overall analyses. Fifth, the rate of reoperation in PN was significantly lower than RN in patients with the other tumor stage. Finally, the incidence of intraoperative blood transfusion in the PN group was lower than that in the RN group when minimally invasive PN procedure was carried out.

The putative publication bias was examined in various results and was found only in the results of urinary fistula (Begg test, $P = 0.060$; Egger test, $P = 0.034$; **Supplemental Figure 2**). These results remained unaltered after trim-and-fill correction (OR: 2.87; 95% CI: 1.68–4.07; $P < 0.001$).

DISCUSSION

RN and PN used for treating RCC were analyzed in this study; 23 articles that fulfilled the inclusion criteria, comprising of 30,018 patients, were included. The present findings of this study demonstrated relatively fewer overall and hemorrhagic complications in RN, while PN had a lower hospital mortality, and reoperation.

In a previous meta-analysis, Manikandan et al. first compared the PN and RN in patients with RCC with clinical outcomes including survival rate, recurrence, and metastasis. The disease-specific survival rate ($P = 0.001$) and incidence of metastasis ($P < 0.050$) were found to be significantly enhanced in the PN group; however, no significant difference was found regarding recurrence ($P = 0.220$). They also demonstrated that the efficacy of PN was similar to that of RN in patients with renal cell tumors up to 4 cm in diameter. However, this study did not discuss the perioperative complications and analyze the differences among variances of patients in the TNM stage[24]. A meta-analysis conducted by Deng et al. contained 13 retrospective studies encompassing 2,906 patients with large (> 7 cm) renal tumors. The study speculated that PN was associated with improved OS and preserved renal function, and was also accompanied by high risk of surgical complications than RN[59]. MacLennan et al. comprehensively analyzed the laparoscopic approach, open surgery, robot-assisted surgery, and radiofrequency surgery for RCC treatment. The study considered that PN either showed an equivalent or better survival of RCC patients with tumors < 4 cm in diameter, while open surgery and laparoscopic approach achieved an equivalent survival for either RN or PN. Therefore, localized PN would be ideally managed in patients with RCC in the T1a stage, which was better in the preservation of renal function and quality of life (QOL) as compared to RN. However, these studies primarily focused on the qualitative comparison of RN and PN, while the quantitative results were not illustrated. Furthermore, the summary results of perioperative complications were less described in this study [20,21] Kim et al. compared RN and PN with respect to the overall and cancer-related mortality as primary outcomes, and severe renal failure as a secondary outcome. Their study indicated that PN was associated with a 19% reduced risk in all-cause mortality (HR: 0.81; $P < 0.001$), a 29% reduced risk in cancer-specific mortality (HR: 0.71, $P < 0.001$), and a 61% reduced risk in severe chronic kidney disease (HR: 0.39, $P < 0.001$). However, the estimation of cancer-specific mortality was limited by the lack of robust significant heterogeneity across studies [19]. Tobert et al. analyzed the overall mortality as the primary outcome measure between RN and PN in 2014 [22]; the study confirmed that PN had a 19% reduction in the all-cause mortality ($P < 0.001$) and 29% reduction in cancer-specific mortality ($P < 0.001$). Although the study did not discuss the postoperative renal function, perioperative complications, and QOL, the current study arrived at a similar conclusion on overall mortality. Intriguingly, PN had an advantage regarding reoperation, while RN had an advantage in terms of overall and hemorrhagic complications.

A multicenter prospective RCT included patients in the T1-2N0M0 stage and found that the rate of perioperative blood loss was slightly high after RN and the rate of severe hemorrhage was slightly high after PN [43]. This RCT further demonstrated that 4.4% patients developed urinary fistulas after PN; the incidences of pleural damage and spleen damage were similar in both groups. Therefore, not only mortality but improved QOL and reduced perioperative complications were evaluated in surgery modalities. [43] The present study also demonstrated a relatively low mortality in PN and fewer complications in RN. The detection rate of a tumor ≤ 4 cm in diameter would promote advanced iconography, and PN would be the ideal method for this kind of disease. The protection of normal renal function would be further strengthened with developed anatomical structure and function of kidneys as well as improved PN technology. Thus, implementation of PN would be more advantageous, avoiding inconsequential trauma in patients with RCC in the T1a stage. However, the conclusions might be variable because as a small number of studies were included in such subsets. Hence, a relative result and a synthetic and comprehensive review have been conferred.

The subgroup analysis suggested that RN had a low incidence of overall complications, hemorrhagic complications, and incidence of urinary fistula in patients in the T1 stage (maximum tumor diameter ≤ 7 cm). Nevertheless, in the patients in T1a stage (tumor ≤ 4 cm), the number of included studies was not sufficient to yield robust results. In the surgical subgroup analysis, the mortality reduced by PN was primarily based on open surgery, and minimally invasive surgery did not show any difference between RN and PN. Presently, the minimally invasive surgery is less utilized as compared to open surgery for patients with RCC. However, minimally invasive surgery, such as laparoscopy, exhibited advantages of fewer traumas, less bleeding, reduced infection probability, and reduced perioperative complications post-surgery (60). The perioperative complications may be reduced with an increase in the application of minimally invasive surgery in the future, suggesting the applicability of PN in patients with RCC [61-63].

Nonetheless, the present study had some limitations as follows: (1) specific individual data were unavailable for all trials, thereby restricting the analysis; (2) although the subgroup analysis was conducted, the heterogeneity continued to exist; (3) selection bias including tumor stages, complexity, and other potential confounders affected the resulting assessment due to the retrospective design of the study.

In conclusions, RN had relatively fewer overall complications, hemorrhagic complications, and incidence of urinary fistula, while PN had lower hospital mortality and incidence of reoperation. Thus, PN was associated with lower mortality and RN was associated with fewer complications. Finally, a minimally invasive surgery is essential for patients with early-stage RCC in the future.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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