

Review article

# Partial nephrectomy versus radical nephrectomy for large ( $\geq 7$ cm) renal tumors: A systematic review and meta-analysis

Wen Deng, M.D.<sup>a,1</sup>, Luyao Chen, M.D., Ph.D.<sup>a,1</sup>, Yibing Wang, M.D.<sup>b</sup>, Xiaoqiang Liu, M.D.<sup>a</sup>, Gongxian Wang, M.D., Ph.D.<sup>a</sup>, Bin Fu, M.D., Ph.D.<sup>a,\*</sup>

<sup>a</sup> Department of Urology, The First Affiliated Hospital of Nanchang University, Nanchang City, Jiangxi Province, China

<sup>b</sup> Department of Emergency, The Second Affiliated Hospital of Nanchang University, Nanchang City, Jiangxi Province, China

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## Abstract

We conducted a meta-analysis to evaluate the efficiency and safety of partial nephrectomy (PN) compared with radical nephrectomy (RN) for large ( $\geq 7$  cm) renal tumors. A comprehensive literature search with no restrictions on language or region was conducted from August up to October in 2018 in the electronic databases of PubMed, EMBASE, the Cochrane Library, and Scopus. Studies meeting the inclusion criteria were subjected to a systematic review and cumulative meta-analysis to assess the oncological, functional, and perioperative outcomes of PN compared with RN for large renal tumors. Sensitivity analyses were performed by repeating the original meta-analyses with exclusion of the lowest-weighted or lowest-scored study. Thirteen retrospective studies including 2906 patients (PN: 1172; RN: 1734) were included in our analyses. The pooled hazard ratio (HR) of overall survival (OS) indicated significant differences between the PN and RN groups (HR: 0.76;  $p = 0.001$ ), although no significant difference was observed between the two groups in terms of cancer-specific survival (CSS; HR: 0.91;  $p = 0.51$ ). The pooled eGFR decrease was significantly lower in the PN group than that in the RN group (mean difference (MD): 11.59;  $p < 0.001$ ). PN was associated with longer operative time and more estimated blood loss (MD: 65.33 min,  $p < 0.001$  and MD: 97.83 ml,  $p < 0.001$ , respectively). Pooled odds ratios (ORs) revealed that, compared with RN, PN is associated with a significantly higher risk of low-grade and high-grade (OR: 1.59,  $p = 0.01$  and OR: 7.35,  $p < 0.001$ , respectively) surgical complications. No statistical significances were changed in sensitivity analyses on all outcome variables, except for that on the low-grade complication when excluding the lowest-scored study. All results were pooled using the fixed-effects model due to the nil or low heterogeneity. No obvious publication bias was screened about reporting OS. In conclusion, while PN for large ( $\geq 7$  cm) renal tumors is associated with better OS compared with RN, these methods show a similar CSS. However, the advantages of PN, a more involved procedure than RN, in preserving renal function are accompanied by a higher risk of surgical complications. Large-sample and well-designed randomized controlled trials with extensive follow up are needed to confirm and update our conclusions. © 2018 Elsevier Inc. All rights reserved.

**Keywords:** Partial nephrectomy; Radical nephrectomy; Renal tumor; Renal function; Meta-analysis

## 1. Introduction

Whenever technically feasible, partial nephrectomy (PN), rather than radical nephrectomy (RN), is recommended as the preferred surgical option for T1 renal tumors as it allows better nephron preservation without

compromising oncological outcomes [1]. PN for T2 tumors may be considered a valid alternative to RN in selected cases while RN is generally considered the reference option [2,3]. Whether the existing advantages of PN in T1 renal tumors are maintained in T2 renal tumors remains controversial and will go on. Better postoperative renal function is deemed to be related to fewer renal and cardiovascular complications and better overall survival (OS) [4,5]. Considering the technical, oncological, and functional outcomes of PN for large renal tumors [3,6,7], use of PN for this type of tumors has increased annually considering

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\*Corresponding author. Tel: +86-88698102; fax: +86-88698102.

E-mail address: urofbn@163.com (B. Fu).

<sup>1</sup>Wen Deng and Luyao Chen contributed equally to this article.

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improvements in surgical techniques and increase in doctor experience [8]. Many studies agree that superior OS is possible after PN on account of the technique's ability to better preserve nephrons when compared with RN [9–12]. However, concern that cancer control may be undermined in patients with renal tumors  $\geq 7$  cm undergoing PN compared with those who undergoing RN has been raised [13].

Comparative studies assessing the efficiency and safety of PN and RN for large ( $\geq 7$  cm) renal tumors are limited, and most of the available works involve a few cases undergoing PN with conflicting results [8,10,13–16]. Given the increasing proportion of PN candidates with large renal tumors owing to less stringent PN indications [13], utilizing the existing evidence to examine the outcomes of PN and RN for large renal tumors is of great importance.

Herein, we systemically searched and analyzed the available literature to evaluate the efficiency and safety of PN compared with RN for large ( $\geq 7$  cm) renal tumors.

## 2. Materials and methods

The literature search methods, inclusion and exclusion criteria, outcomes measured, and statistical analytical methods were defined prospectively according to the proposal for reporting meta-analysis of the MOOSE group [17].

### 2.1. Search strategy

No restriction on region or language was applied during the literature search, which was conducted from August up to October in 2018. The primary sources of articles included the electronic databases of PubMed, EMBASE, the Cochrane Library, and Scopus. Diagnosis keywords (“renal carcinoma,” “renal tumor,” “renal tumour,” “renal cancer,” “renal mass,” and “kidney cancer”) and intervention items (“partial nephrectomy,” “nephron sparing surgery,” and “radical nephrectomy”) were combined to identify records. References from the relevant literatures, including the identified studies and reviews, were screened manually to supplement the computer search, which was further broadened using the related articles function. The corresponding author was contacted for unpublished studies on the association.

### 2.2. Inclusion and exclusion criteria

The included studies met all of the following criteria: (1) Studies that compared PN and RN for large ( $\geq 7$  cm) renal tumors and (2) data on at least one of the required outcomes were extractable. Whenever reduplicative or updated reports describing the same population were published, the most recent or complete one was included.

The excluded studies met at least one of the following criteria: (1) Noncomparative study, (2) no available data could be extracted from relevant studies, (3) editorials or

letters, (4) conference abstracts, (5) case reports, and (6) animal experimental studies.

### 2.3. Data extraction and outcomes of interest

Two reviewers (Wen Deng and Luyao Chen) participated in the study selection procedure. The data and characteristics of the included studies were extracted and evaluated independently by the same 2 reviewers. Any disagreement was resolved by discussion until a consensus was reached. Local scientists fluent in the original language of the article were contacted for translation.

The following outcomes were used to compare PN and RN for large ( $\geq 7$  cm) renal tumors: (1) Oncological variables: OS and cancer-specific survival (CSS); (2) renal functional variables: decrease in estimated glomerular filtration rate (eGFR); and (3) preoperative outcomes: operative time, estimated blood loss, overall complications, low-grade (Clavien–Dindo grades I–II) complications, and high-grade (Clavien–Dindo grade  $\geq$  III) complications.

### 2.4. Quality assessment and statistical analysis

The methodological quality of retrospective studies was assessed by using the modified Newcastle-Ottawa scale ([http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.htm](http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm)) [18,19], which comprises 3 factors: patient selection, comparability of study groups, and assessment of outcomes. Each study was scored from 0 to 9.

The criteria implemented by the Center for Evidence-Based Medicine in Oxford was used to rate the included studies for level of evidence [20].

Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) was used to conduct the meta-analyses. Hazard ratios (HR) with 95% confidence intervals (CIs) were extracted to measure oncological outcomes. *P* value computed using the log-rank test, events and numbers in each arm, and Kaplan-Meier curves were used to calculate HRs with 95% CIs if they were not given directly according to the method described by Tierney et al. [21]. Mean difference (MD) with 95% CI was used to assess the eGFR decrease. The technique described by Hozo et al. [22] was used to convert continuous data presented as medians and ranges into means and standard deviations. Odds ratios (ORs) with 95%CI were used to compare surgical complications between the PN and RN groups. A *P* value of  $<0.05$  was considered to indicate statistically significant differences.

The chi-square test with significance set to  $P < 0.10$  was used to assess statistical between-study heterogeneity, which was also quantified utilizing  $I^2$  statistic. The fixed-effects model was used to pool the data extracted from relevant studies in the absence of significant heterogeneity. Otherwise, the data were pooled with the random-effects model [23].

Sensitivity analyses were performed by repeating each original meta-analysis without inclusion of the lowest-

weighted or the lowest-scored publication. Funnel plot reporting OS was used to visually inspect the potential for publication bias.

### 3. Results

Thirteen studies meeting the inclusion criteria were included in the final analysis [8–10,13–16,24–29]. Of these studies, 2 separate analyses for 2 endpoints of the same population of patients were reported by the same group [26,29]. Details of the study selection process are shown in Fig. 1. No other studies for evaluation were obtained after screening the references from relevant literature, and no unpublished studies were identified after the rigorous database-searching and hand-searching.

#### 3.1. Characteristics of the eligible studies

The characteristics of the included studies are presented in Table 1. All studies were designed retrospectively and compared contemporary series of patients (level of evidence: III). Data reported in 8 studies were collected from multiple institutions [8–10,13,14,26,27,29], while other studies reported data collected from a single center [15,16,24,25,28]. Data were collected prospectively in 2 retrospective studies [10,16]. Renal function and oncological outcomes of the same population of patients with large renal masses were described separately in 2 studies by Kopp et al. [26,29], and the relevant parameters were counted only once in our final analysis. Some characteristics were matched statistically between the PN and RN groups in several studies [8,9,13,24,25]. Eight studies obtained a score  $\geq 6$  [8,10,15,16,24,26–28] and could be considered high-quality

studies. It is also worth noting that in only one study [28] all surgeries were performed with laparoscopy assistance; in the majority of the studies, some or all nephrectomies were conducted via open surgery. Data about the rate of malignancy, tumor stage, and tumor grade were incomparable in 3, 2, and 1 studies, respectively.

#### 3.2. Methodological quality of the included studies

Limited to the nature of those retrospective studies, none of the included studies drafted an appropriate protocol in advance for treatment assignment. Patient allocation was usually up to the discretion of the physician. No information on allocation concealment or the blinding method was provided in all of the included studies. Tumor size in most studies was comparable between the PN and RN groups [8–10,13,16,24,25,27,28]. Information about the matching criteria between the 2 groups was not provided in some studies. The length of follow-up in both the PN and RN groups was mentioned in all included studies, except for that reported by Chebbi et al. [14], which only provided follow-up information on the RN group. Most of the included studies did not adequately describe the methods for handling missing data and intention-to-treat analysis.

#### 3.3. Evidence synthesis

OS data were available in 7 of 13 studies [8–10,14,24,26,27]. Significant difference in OS was found between the PN and RN groups (HR: 0.76; 95%CI: 0.64–0.90;  $P=0.001$ ; Fig. 2). The result was pooled with nil heterogeneity. In terms of CSS, the pooled HR for the RN group was 0.91 when compared with that of the PN group, with a low heterogeneity (95%CI: 0.68–1.21;  $P=0.51$ ;  $I^2=17\%$ ; Fig. 3).

Five studies [14–16,28,29] including 535 patients provided data on postoperative eGFR changes. The data showed significantly better preservation of renal function in the PN group compared with that in the RN group (MD: 11.59; 95%CI: 9.99–13.20;  $P<0.001$ ). Between-study heterogeneity stayed at a low level ( $I^2=25\%$ ; Fig. 4).

The significant differences detected in Figs. 5 and 6 indicate that PN is associated with longer operative time and lower estimated blood loss ([MD: 65.33 minutes; 51.93–78.73;  $P\leq 0.001$ ] and [MD: 97.75 ml; 84.65–110.84;  $P\leq 0.001$ ], respectively). Data assessing surgical complications were extractable in 6 studies [10,14,15,24,26,28], although the study described by Rinott et al. [28] only provided information about low-grade complications. Significant differences were observed between the PN and RN groups in terms of overall complications (PN: 99; RN: 130), low-grade complications (PN: 61; RN: 114), and high-grade complications (PN: 45; RN: 18) ([OR: 2.82; 95%CI: 2.03–3.93;  $P<0.001$ ], [OR: 1.59; 95%CI: 1.10–2.29;  $P=0.01$ ], and [OR: 7.35; 95%CI: 4.09–13.22;  $P<0.001$ ], respectively) (Figs. 7–9). These results were pooled using the fixed-effects model owing to the low

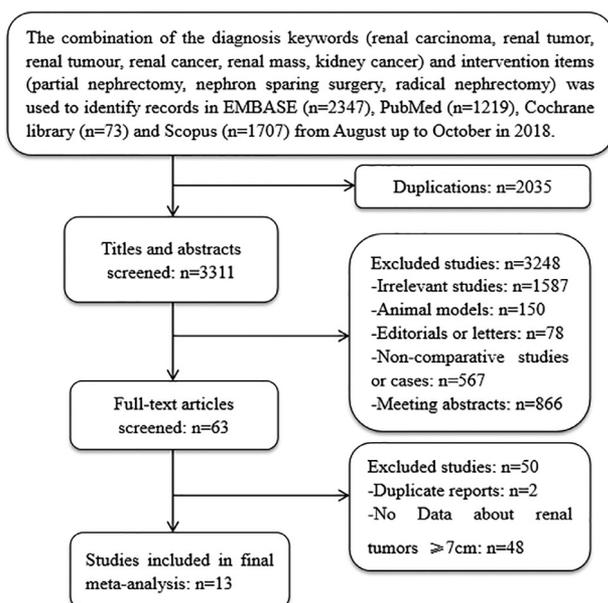


Fig. 1. Flowchart of study selection.

Table 1  
Characteristics of included studies.

Study	Study origin	Design	Study period	Patients, no		Surgical technique	Matching	Follow-up	Tumor stage	Tumor grade	level of evidence	Quality Score
				PN	RN							
Breau [24]	USA	RM, SC	1970–2008	69	207	NS	1,2,4,5,7,9	38.4/38.4	C	C	III	7
Chebbi [14]	France	R, MI	2004–2014	32	138	open/lap/robot	1,2,5	NS/47	C	C	III	5
de Aubert [15]	France	R, SC	2000–2013	49	81	open/lap	1,2,3,5,9	31/45	IC	C	III	6
Hansen [25]	USA	RM, SC	1988–2008	245	245	NS	1,2,4,7	60/60	C	C	III	5
Janssen [10]	GER	RP, MI	1980–2010	18	105	open	1,2,4,6,7	163/93	NS	NS	III	6
Jeldres [13]	CA, France	RM, MI	1984–2001	17	45	NS	1,2,4,7	49.2/54	C	C	III	5
Kopp [26, 29]	USA	R, MI	2002–2012	80	122	open/lap	1,2,3,5,7,8,9	35.1/47.4	C	C	III	7
Lee [18]	Korea	RM, MI	1994–2014	15	44	NS	1,2,3,4,6,7,9	46/46	C	C	III	8
Reix [27]	France	R, MI	2000–2014	91	176	open/lap/robot	1,2,4,6,7,8	24/24	IC	IC	III	7
Kinott [28]	Israel	R, SC	2012–2017	13	16	lap	1,2,4,5,9	44.5/44.5	NS	NS	III	6
Roos [16]	GER	RP, SC	1988–2007	16	28	open	1,2,4,6,7,9	56.4/45.6	C	C	III	7
Shum [9]	USA	RM, MI	2004–2009	527	527	NS	1,2,4,7,9	49.2/49.2	C	C	III	6

C = comparable; IC = incomparable; lap = laparoscopic; m = months; MI = multi-institutional; NS = not specified; PN = partial nephrectomy; R = retrospective; RM = retrosective design, patient-matched; RN = radical nephrectomy; RP = retrosective design, prospective data collection; SC = single center.  
 Comparability variables: 1 = age, 2 = gender, 3 = body mass index, 4 = tumor size, 5 = preoperative renal function, 6 = American Society of Anesthesiologists (ASA) score, 7 = clinical T stage, 8 = RENAL score, 9 = Charlson comorbidity index.

heterogeneity observed. In terms of pathology, the RN group revealed a significantly higher rate of malignancy than the PN group (OR: 0.39; 95%: 0.17–0.87;  $P = 0.02$ ) while no statistical difference in tumor size was found between groups (MD:  $-0.47$  cm; 95%:  $-0.99$  to  $0.04$ ;  $P = 0.07$ ).

### 3.4. Sensitivity analysis and publication bias

Sensitivity analyses were performed by repeating the original meta-analyses with exclusion of the lowest-weighted or lowest-scored study. All results, except for that on low-grade complication without including the lowest-scored study, were consistent with the original pooled results (Table 2). While the degree of between-study heterogeneity increased slightly remained low level for 3 outcomes (i.e., CSS excluding the lowest-weighted study, low-grade complications excluding the lowest-weighted study, and high-grade complications excluding the lowest-weighted or -scored study), the degree of between-study heterogeneity decreased for other outcomes. The fixed-effects model was utilized to pool all results with low heterogeneity.

A funnel plot of the studies included in the meta-analysis reporting OS is shown in Fig. 10. All studies lay within the 95% CIs, indicating no obvious publication bias.

## 4. Discussion

PN for T1 renal tumors has been widely acknowledged to be as efficacious as RN for cancer control; indeed, PN is recommended as a preferable treatment over RN owing to better preservation of renal function [1,30]. The odds of malignancy, higher tumor grade, poorer histological subtype, and coagulative necrosis increase with tumor volume enlarging [31–34]. Given improvements in surgical technique and doctor experience, large renal masses can increasingly and successfully be removed by PN [7,35,36]. The debate on whether the advantage of PN in protecting renal function without compromising oncologic outcomes, however, continues to exist for large ( $\geq 7$  cm) renal tumors, and less is known.

We report the first meta-analysis of eligible studies comparing PN with RN for large ( $\geq 7$  cm) renal masses. Thirteen retrospective studies fulfilled the predefined inclusion criteria. Along with these existing evidences, some key information on the better option for treating large renal tumors was obtained. According to the pooled results, PN for treating large ( $\geq 7$  cm) renal tumors was associated with a significantly higher risk of surgical complications compared with RN. However, this shortcoming is counterbalanced by a better OS, comparable CSS, and better protection of renal function.

After matching patient comorbidities, which could be an equally or even more important determinant of renal function than surgery [37], the pooled results on OS remained significant in the PN group. Tumor complexity, which is usually

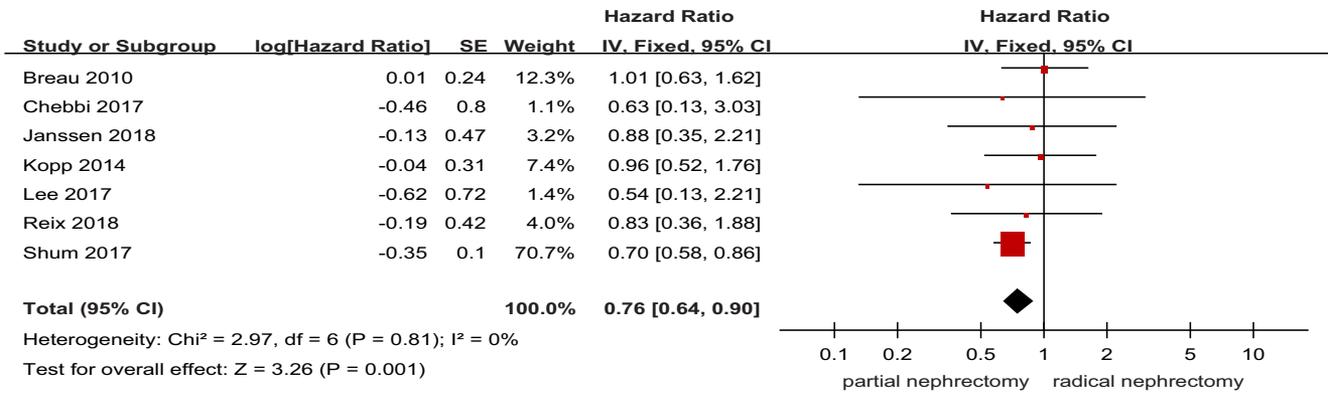


Fig. 2. Forest plot and meta-analysis of overall survival.

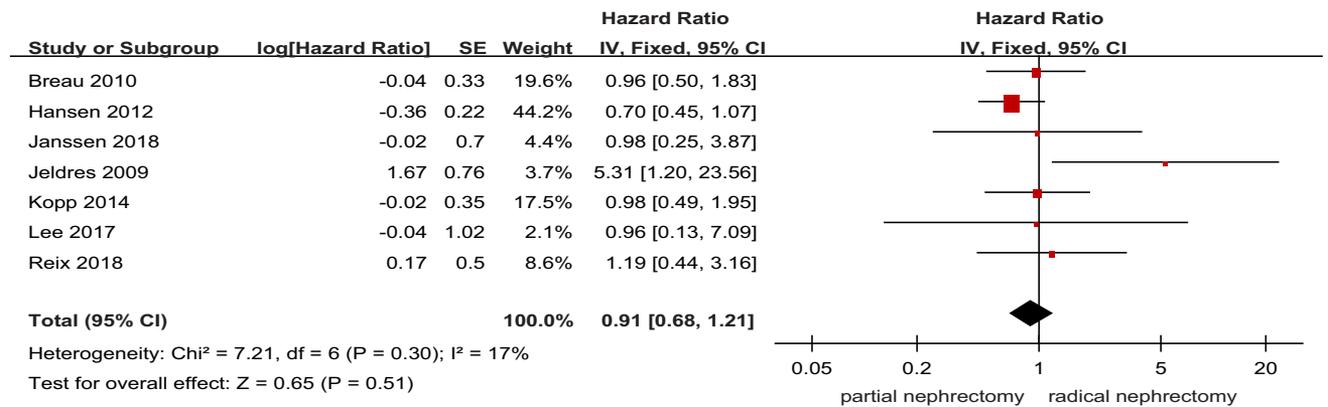


Fig. 3. Forest plot and meta-analysis of cancer-specific survival.

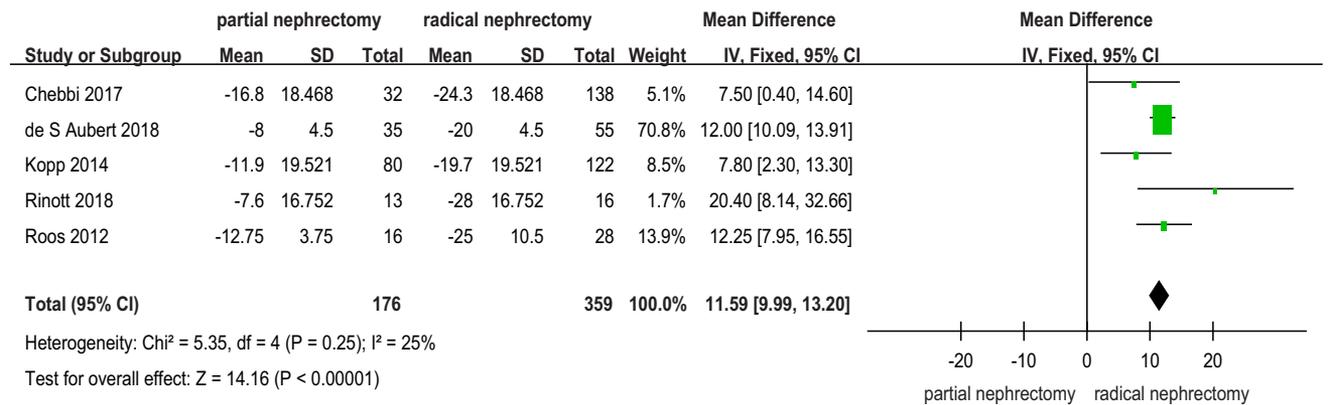


Fig. 4. Forest plot and meta-analysis of eGFR decrease.

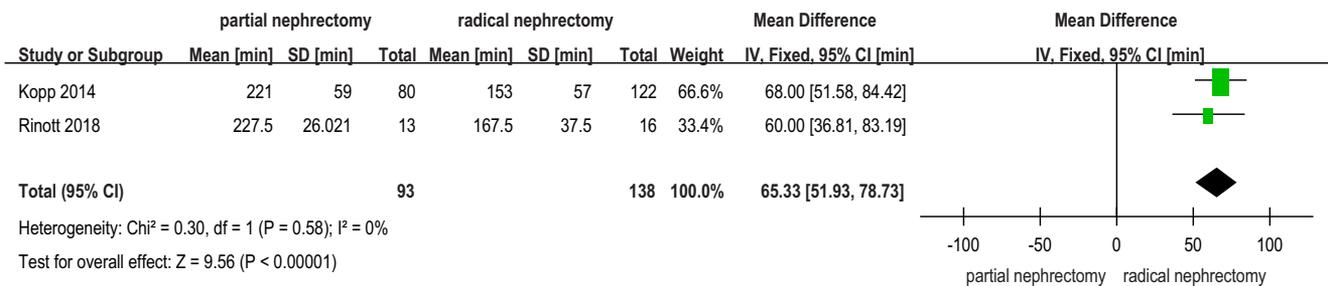


Fig. 5. Forest plot and meta-analysis of operative time.

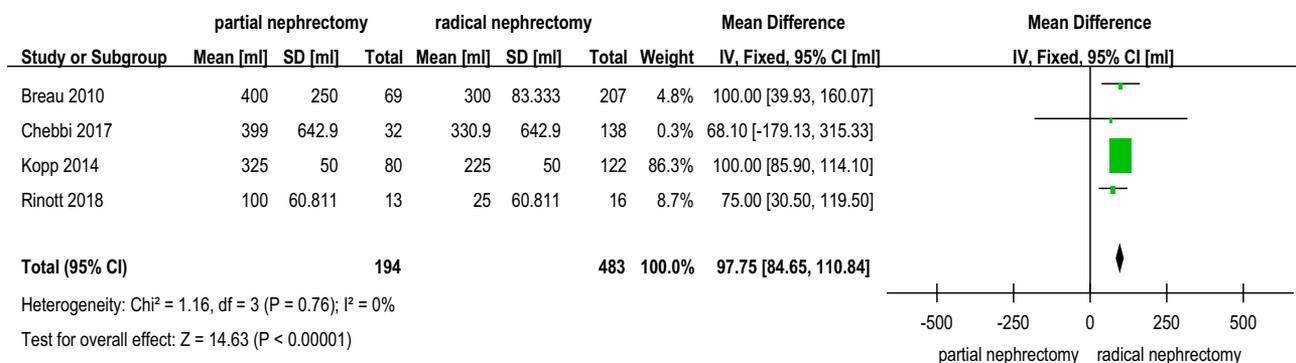


Fig. 6. Forest plot and meta-analysis of estimated blood loss.

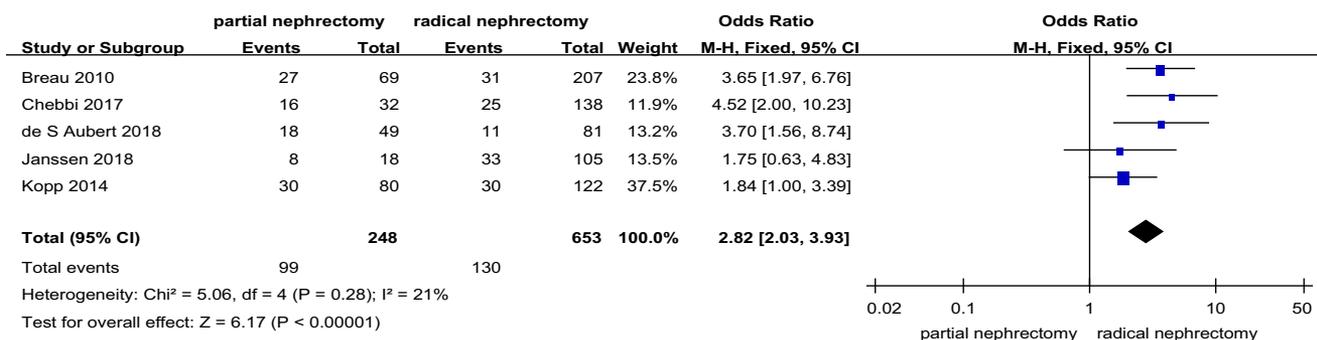


Fig. 7. Forest plot and meta-analysis of overall complications.

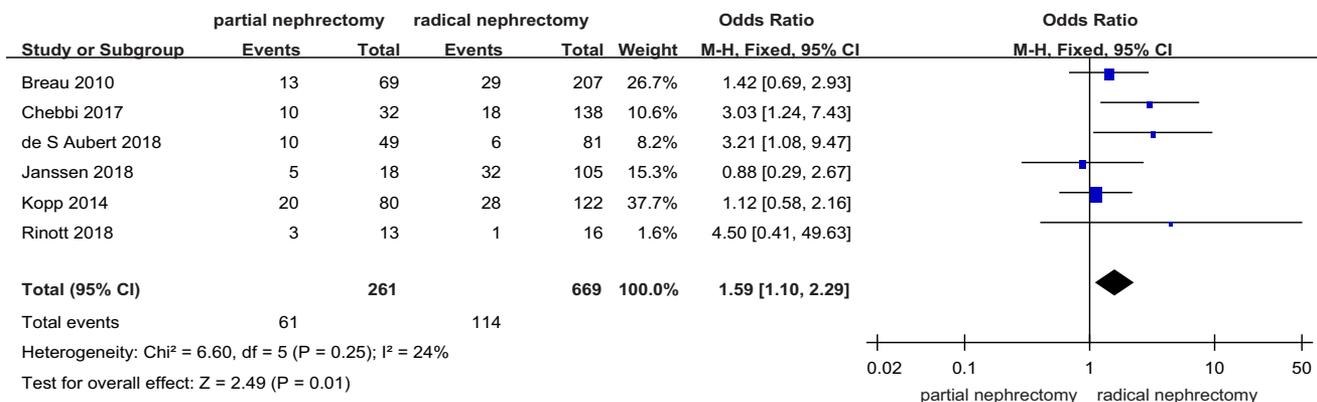


Fig. 8. Forest plot and meta-analysis of low-grade complications.

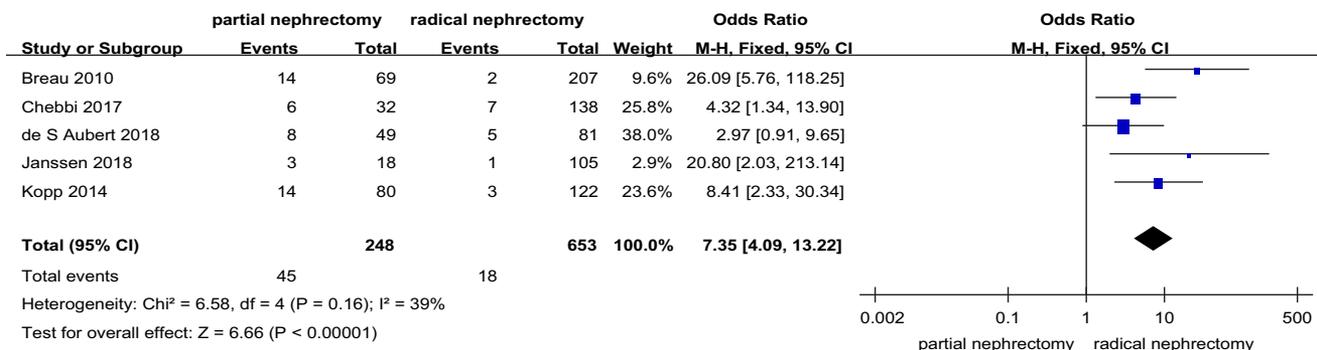


Fig. 9. Forest plot and meta-analysis of high-grade complications.

Table 2  
Results of meta-analysis and sensitivity analysis about comparison of PN and RN.

Outcomes of interest	Studies, no	PN patient, no	RN patients, no	HR/MD/OR (95%CI)	P value	Study heterogeneity			
						Chi <sup>2</sup>	df	P	I <sup>2</sup> , %
<i>Oncologic outcomes</i>									
<b>Overall survival</b>	7	832	1319	0.76 (0.64, 0.90) <sup>c</sup>	0.001	2.97	6	0.81	0
Exclusion of [14], <sup>a</sup>	6	800	1181	0.76 (0.65,0.90) <sup>c</sup>	0.001	2.91	5	0.71	0
Exclusion of [14], <sup>b</sup>	6	800	1181	0.76 (0.65,0.90) <sup>c</sup>	0.001	2.91	5	0.71	0
<b>Cancer-specific survival</b>	7	535	944	0.91 (0.68,1.21) <sup>c</sup>	0.51	7.21	6	0.30	17
Exclusion of [8], <sup>a</sup>	6	520	900	0.91 (0.68,1.21) <sup>c</sup>	0.51	7.21	5	0.21	31
Exclusion of [25], <sup>b</sup>	6	290	699	1.12 (0.76, 1.64) <sup>c</sup>	0.56	4.63	5	0.46	0
<b>Renal function outcomes</b>									
<b>eGFR decrease</b>	5	176	356	11.59 (9.99,13.20) <sup>d</sup>	<0.001	5.35	4	0.25	25
Exclusion of [28], <sup>a</sup>	4	163	343	11.44 (9.82,13.06) <sup>d</sup>	<0.001	3.33	3	0.34	10
Exclusion of [14], <sup>b</sup>	4	144	221	11.81 (10.17,13.46) <sup>d</sup>	<0.001	4.00	3	0.26	25
<i>Postoperative outcomes</i>									
<b>Operative time</b>	2	93	138	65.33 (51.93,78.73) <sup>d</sup>	<0.001	0.30	1	0.58	0
Exclusion of [28], <sup>a</sup>	1	80	122	68.00 (51.58,84.42) <sup>d</sup>	<0.001	Not Applicable			
Exclusion of [28], <sup>b</sup>	1	80	122	68.00 (51.58,84.42) <sup>d</sup>	<0.001	Not Applicable			
<b>Estimated blood loss</b>	4	194	483	97.75 (84.65,110.84) <sup>d</sup>	<0.001	1.16	3	0.76	0
Exclusion of [14], <sup>a</sup>	3	162	345	97.83 (84.71,110.94) <sup>d</sup>	<0.001	1.11	2	0.57	0
Exclusion of [14], <sup>b</sup>	3	162	345	97.83 (84.71,110.94) <sup>d</sup>	<0.001	1.11	2	0.57	0
<b>Overall complications</b>	5	248	653	2.82 (2.03,3.93) <sup>e</sup>	<0.001	5.06	4	0.28	21
Exclusion of [14], <sup>a</sup>	4	216	515	2.59 (1.81,3.72) <sup>e</sup>	<0.001	3.62	3	0.31	17
Exclusion of [14], <sup>b</sup>	4	216	515	2.59 (1.81,3.72) <sup>e</sup>	<0.001	3.62	3	0.31	17
<b>Low-grade complications</b>	6	261	669	1.59(1.10,2.29) <sup>e</sup>	0.01	6.60	5	0.25	24
Exclusion of [28], <sup>a</sup>	5	248	653	1.54 (1.07,2.23) <sup>e</sup>	0.02	5.88	4	0.21	32
Exclusion of [14], <sup>b</sup>	5	229	531	1.42 (0.95,2.11) <sup>e</sup>	0.09	4.28	4	0.37	6
<b>High-grade complications</b>	5	248	653	7.35(4.09,13.22) <sup>e</sup>	<0.001	6.58	4	0.16	39
Exclusion of [10], <sup>a</sup>	4	230	548	6.94 (3.79,12.72) <sup>e</sup>	<0.001	5.66	3	0.13	47
Exclusion of [14], <sup>b</sup>	4	216	515	8.40 (4.22,16.72) <sup>e</sup>	<0.001	5.73	3	0.13	48

CI = confidence interval; df = degrees of freedom; eGFR = estimated glomerular filtration rate; HR/WMD/OR = hazard ratio/weighted mean difference/ odds ratio; PN = partial nephrectomy; RN = radical nephrectomy.

<sup>a</sup> the lowest-weighted study.

<sup>b</sup> the lowest-scored study.

<sup>c</sup> hazard ratio.

<sup>d</sup> weighted mean difference.

<sup>e</sup> Odds ratio.

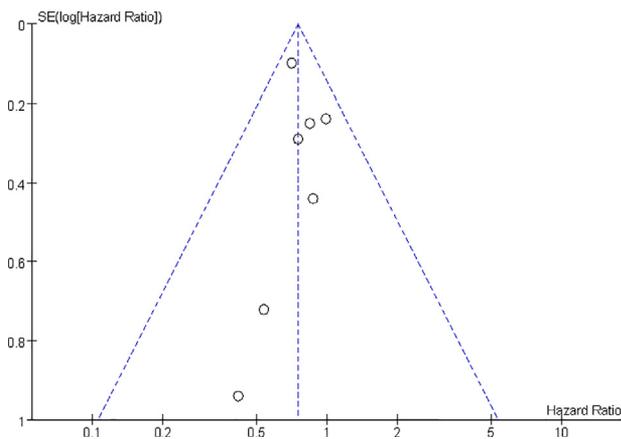


Fig. 10. Funnel plot of the studies that reported overall survival.

quantified using RENAL or PADUA scores, could influence the discretion of a physician and provide the inherent survival benefit to the PN cohort compared with the RN cohort in those retrospective studies. Unfortunately, in only 2 series

the RENAL score was comparable between groups [26,27,29]. But the oncologic equivalence was established in both series irrespective of RENAL score, while the RENAL score was proven to be associated with renal functional benefit for PN compared with RN [29].

PN was associated with significantly better OS compared with RN on the basis of the results pooled with no heterogeneity. After utilizing statistical matching to ensure high similarity in patient demographics and tumor characteristics between the PN and RN groups, the same conclusion was drawn with large sample size by Shum et al. [9]. The result of sensitivity meta-analysis of OS was as stable as that in the original outcome. Better preservation of renal function was associated with fewer renal and cardiovascular complications and subsequently better OS [4,5,9,38]. RN has been reported to be a significant risk factor for developing chronic kidney disease and cardiovascular events [39,40]. In the study reported by Andrade et al. [41], the median amount of nephron preservation impacting OS seemed to be 57% according to the more divergent OS rates for the PN and RN groups

with a median follow-up duration of 21 months, though no statistical difference was achieved likely due to the small sample size. In our study, the significantly improved OS of patients undergoing PN could be attributed to either the technique's protection of renal function and consequently fewer noncancerous (metabolic and cardiovascular) adverse events or to the selection bias. A higher rate of malignancy in the RN group was observed due to the non-negligible selection bias, which impacted oncological outcomes. After matching for tumor size, histology, and grade, however, significantly better OS from T2 renal tumors after PN compared with that after RN was still observed [9].

No statistically significant difference in CSS was detected between the PN and RN groups. In fact, similar CSS between the PN and RN groups was observed in all eligible studies, except for that described by Jeldres et al. [13], in which PN was associated with a 5.3-fold higher rate of cancer-specific mortality compared with RN for large renal tumors. Considering the small sample size in the matched analysis, the conclusion that PN may undermine cancer control for large renal tumors is weakened. Even when this study was included in our analyses, the results of data pooled with low heterogeneity were not significantly different. The results were also confirmed to be stable using sensitivity meta-analysis.

Resection of larger renal tumors means the remaining functional nephron is usually smaller than that obtained after surgical treatment for T1 renal tumors, which may reduce the significance of PN [24]. Technical challenges due to larger tumor sizes could lead to longer warm ischemia, which impacts renal function negatively [42]. Despite these adverse factors, in our meta-analysis the pooled data on postoperative changes in renal function indicated a significant difference between the PN and RN groups for tumors  $\geq 7$  cm. The average decline of renal function after RN was associated with an estimated 25% higher risk of cardiac death and 17% higher risk of any-cause mortality [43]. Interestingly, many studies have demonstrated a linear inverse correlation between eGFR and cancer-specific mortality once renal function decreased below a "breakpoint" [37,44–46]. Though varying from different studies, the highest breakpoint was the postoperative baseline eGFR of 60 ml/min. In other words, the risk of cancer-specific mortality influenced by the descending eGFR increased only when the patients suffered CKD, which could be the preexisting or postoperative de novo CKD [46]. The annual renal function decline for patients with preexisting CKD and de novo CKD after surgery would be close to 5% and 0.7%, respectively, and survival curves between patients with de novo CKD after surgery and the overall population were approximated [47]. It was also observed that patients with postoperative de novo CKD survived approximating that for those without CKD in a retrospective study with a large sample size [48]. Preexisting CKD could be equally or an even more important determinant

to influence the survival outcomes than surgically induced CKD [37,49], which was associated with more stable renal function [37,48,49].

PN for large renal masses, which is a more involved procedure than RN in terms of tumor resection and renal reconstruction, was associated with longer operative time and more estimated blood loss. Compared with RN, PN for large renal tumors is more technically challenging and may result in an increased risk of complications [24]. Our results pooled with low heterogeneity showed a significantly higher risk of surgical complications in the PN group compared with that in the RN group, regardless of grade. In terms of overall complications, statistically significant differences were observed between the PN and RN groups in all eligible studies except for that published by Janssen et al. [10], which attributed findings to the patients' selection bias. Data revealed significantly increased risk of high-grade complications from PN compared with that from RN for large renal tumors in all data-available studies except for that ( $P=0.06$ ) reported by de Saint Aubert et al. [15], which was explained by a small sample size. Unfortunately, no stratified data were available to obtain refined results according to surgical methods (e.g., open, laparoscopy, robot-assisted), which may lead to significant differences in surgical outcomes [50–52].

## 5. Limitations and strengths

Several limitations are noted in this work. First, none of the included studies were randomized controlled studied; instead, all of them were retrospectively designed, which means they may be structurally weak in terms of capturing and gathering information. Second, patient allocation and treatment assignment were usually based on the physician's judgement on patients' and tumors' characteristics, which could lead to significant selection biases. Third, the operations were conducted by surgeons with different levels of surgical expertise and different surgical approaches. Fourth, conducting an analysis of the different surgical methods to estimate their impacts on surgical outcomes was not possible. We could not evaluate the difference between PN and RN in terms of incidence of moderate renal dysfunction (eGFR  $< 60$  ml/min). Fifth, the measurements of eGFR differed over time, which may bring bias to our outcomes. Finally, some patient demographics and tumor characteristics, such as age and tumor size, may significantly differ between the PN and RN groups and could be sources of biases.

Although the limitations above exist in this study, several strengths should be recognized. This work is the first meta-analysis to assess the efficacy and safety of PN and RN for large ( $\geq 7$  cm) renal tumors, which is exceedingly important and necessary for contemporary evidence-based patient counseling. This meta-analysis was conducted at an appropriate time with a sufficient number of eligible studies accumulated for inspection. All of the results were pooled utilizing the fixed-effects model due to the absence of or

low heterogeneity, and sensitivity analyses were conducted to evaluate the stability of all results. Our systematic review and meta-analyses were reported according to the MOOSE guidelines. No obvious publication bias was determined from the funnel plot.

## 6. Conclusions

While PN for large ( $\geq 7$  cm) renal tumors is associated with better OS compared with RN, the two methods reveal similar CSS. The advantages of PN, a more involved procedure than RN, in preserving renal function better are accompanied by a higher risk of surgical complications. Large-sample and well-designed randomized controlled trials with extensive follow-up are needed to confirm and update our conclusions.

## Author's contribution

Protocol/project development: Wen Deng, Luyao Chen, Bin Fu, Gongxian Wang.

Data collection or management: Wen Deng, Luyao Chen.

Manuscript writing/editing: Wen Deng, Yibing Wang, Xiaoqiang Liu.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.urolonc.2018.12.015>.

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