Original Article

Comparative analysis of partial versus radical nephrectomy for renal cell carcinoma: Is oncologic safety compromised during nephron sparing in higher stage disease?

Nizar Hakam[1,2], Nassib Abou Heidar[1], Jose El-Asmar[1], Mark Khauli[1,3], Jad Degheili[1], Mouhamad Al-Moussawy[1], Rami Nasr[1], Albert El-Hajj[1], Wassim Wazzan[1], Muhammad Bulbul[1], Raja B Khauli[1]

[1]Division of Urology and Renal Transplantation, American University of Beirut Medical Center, Beirut, Lebanon, [2]Department of Urology, University of California San Francisco, CA, [3]Department of Radiology, Massachusetts General Hospital, Boston, MA, USA

Abstract

Objectives: Over the past 20 years, the utility of partial nephrectomy (PN), compared to radical nephrectomy (RN), for the management of localized renal cell carcinoma (RCC) has progressively increased, particularly for larger and more complex masses. We sought to compare the recurrence-free survival (RFS) outcomes of PN versus RN in a single-institution cohort.

Methods: Between 2002 and 2017, 228 patients underwent RN or PN for lcT1a-T2b, N0M0 RCC at a single tertiary referral center, performed by five surgeons. The clinical end point result was (local or distant) RFS. Univariate and multivariate (cox regression) models were used to evaluate the association between type of surgery (PN vs. RN) and RFS, in the overall cohort and in a subgroup of patients with cT1b.

Results: The median age was 59 (interquartile range [IQR] 48–66), and the median tumor size was 4.5 cm (IQR 3–7). There were 128 PN and 100 RN. Over a median follow-up of 4.2 years (IQR 2.2–6.9), the Kaplan–Meier analysis showed no significant RFS difference between PN and RN (logrank $P = 0.53$). On multivariate analysis, pathologic stage ≥T2a, Fuhrman Grade ≥3, and chromophobe histology were associated with a worse RFS. PN was not significantly associated with diminished RFS (Hazard ratio [HR] 1.78, 95% confidence interval [CI] 0.74–4.3, $P = 0.199$) in the overall cohort compared to RN. However, in the cT1b subgroup, PN was associated with a significant increase in recurrence compared to RN (HR = 12.4, 95% CI 1.45–133.4, $P = 0.038$).

Conclusions: Our institutional data highlight the possibility of compromise in RFS for clinically localized RCC treated with PN compared to RN, particularly for larger and more complex masses. These data raise concern, especially in light of the nonproven association of survival benefit of PN over RN, warranting future randomized prospective studies for further evaluation.

Keywords: Nephron sparing surgery, partial nephrectomy, radical nephrectomy, renal cell carcinoma

Address for correspondence: Prof. Raja B Khauli, Department of Surgery, Division of Urology, American University of Beirut Medical Center, 11-0236/D50, Riad El-Solh 1107 2020, Beirut, Lebanon.
E-mail: rkhauli@aub.edu.lb

Received: 27.06.2022, **Accepted:** 17.01.2023, **Published:** 14.02.2023.

Access this article online	
Quick Response Code:	**Website:** www.urologyannals.com
	DOI: 10.4103/ua.ua_98_22

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Hakam N, Heidar NA, El-Asmar J, Khauli M, Degheili J, Al-Moussawy M, *et al*. Comparative analysis of partial versus radical nephrectomy for renal cell carcinoma: Is oncologic safety compromised during nephron sparing in higher stage disease? Urol Ann 2023;15:226-31.

INTRODUCTION

The decision-making process for the surgical management of localized renal cell carcinoma (RCC) has been increasingly difficult over the past several years. The choice between partial nephrectomy (PN) and radical nephrectomy (RN) for managing localized RCC has been increasingly challenging, given the opposing advantages and disadvantages of each, in the paucity of randomized prospective trials. PN is believed to diminish the risk of overall risk of cardiovascular events, by virtue of superior renal functional preservation;[1] thus, many urologic surgeons have increasingly adopted the principle of PN, "whenever technically feasible," with the goal of improving noncancer-related survival. However, the only clinical trial in the literature to randomize patients with small renal masses (≤5 cm) to receive PN or RN did not demonstrate a survival benefit in the PN group.[2] The recent guidelines by the American Urological Association shifted away from PN whenever feasible to recommend RN, whenever the tumor is suggestive of increased oncologic potential.[3]

Other important factors in the decision-making process between PN and RN include the technical ability to partially remove the tumor with minimal morbidity, without compromising the oncological outcomes. Herein, RN has potential advantages since it allows for complete tumor removal without opening Gerota's fascia, abiding by the well-established axiom in renal cancer surgery. Hence, RN may obviate the additional risk of incomplete tumor resection and positive surgical margins that could occur with PN.[4] Many observational studies have compared survival outcomes across PN versus RN, while disease recurrence has scarcely been examined.

In this study, we report the experience in a tertiary referral center focusing on the management of localized renal cancer. We aim to compare the oncological outcomes of PN versus RN in terms of RCC recurrence, with specific interest in oncologic outcome for higher stage/higher complexity tumors. This contemporary series comprises a cohort of consecutive patients who were managed by RN of PN by the same group of surgeons and represents a continuity of care and comparable follow-up.

METHODS

Study cohort

After Institutional Review Board approval, we performed a retrospective chart review of patients treated for RCC at our tertiary care referral center between 2002 and 2017. We identified a total of 286 patients with pathologically confirmed RCC. We excluded patients with non-N0M0 disease (n = 8), patients managed by active surveillance (n = 3), and those with clinical stage T3a or higher (n = 37). We also excluded 10 patients who were lost to local follow-up after the first postoperative visit due to residence in other countries. For each patient, we extracted demographic characteristics such as age, sex, comorbidities (coronary artery disease, hypertension requiring medication, and diabetes mellitus), pathologic features (tumor maximal diameter, clinical and pathological T stage, Fuhrman grade, histology, and RENAL nephrometry score), type of surgery (partial vs. radical nephrectomy), operative approach (open vs. laparoscopic vs. robotic), estimated blood loss, and preoperative creatinine. Patient follow-up visits consisted of a postoperative visit within 2 weeks of surgery, followed by two annual visits with cross-sectional imaging. Recurrence-free survival (RFS) was defined as the postoperative time period before any tumor detection, including recurrence in the renal bed, local recurrence, or distant metastasis (with or without histopathological confirmation).

Statistical analysis

Descriptive statistics were reported as counts and percentages or medians (interquartile ranges [IQR]). Univariate analysis using Mann–Whitney, Chi-square, or Fisher's exact tests was performed to explore associations between type of surgery and patient, surgical, and tumor characteristics. The proportion of patients undergoing PN versus RN was determined for every clinical T stage, and statistical significance of trend over stage was determined using the Cochran–Armitage trend test. We calculated estimates of the probability of RFS and mortality using the Kaplan–Meier estimates. The logrank test was used to compare the oncological outcomes of patients according to surgery type (PN vs. RN). We also used multivariable Cox proportional hazard models to assess the association of surgery type on RFS and mortality while controlling for pathologic T stage, tumor size, grade, and histology. The proportional hazards assumption was evaluated using the Schoenfeld test. Due to imbalances in clinical T stage distribution among the PN versus RN groups, we conducted a subgroup analysis of patients with cT1b specifically, which had an almost equal number of patients who underwent PN or RN. All statistical analyses were performed using Stata (College Station, Texas, USA) version 16.1, and all P values were two-sided with statistical significance set at <0.05. We followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational studies.[5]

RESULTS

The cohort consisted of 228 patients, of which 128 underwent PN and 100 underwent RN. The median age was 59 years (IQR: 48–66), and 164 patients (71.9%) were male. The median tumor size was 4.5 cm (IQR: 3–7). Table 1 depicts the demographic and pathologic characteristics, stratified by type of surgery. There were no statistically significant differences between the two groups in terms of comorbidities or preoperative creatinine; however, the PN group was relatively favored in terms of tumor size, pathologic T stage, Fuhrman grade, and tumor complexity compared to the RN group. There was a step-wise decrease in the proportion of patients undergoing PN with each increase in clinical T stage ($P < 0.0001$) from 85% in cT1a to 4.8% in cT2b [Figure 1].

Over a median follow-up of 4.15 years (IQR: 2.2–6.9), there were 33 disease recurrence events. The median follow-up was longer for the RN group (median: 5.9 years IQR: 3.4–7.8) compared to the PN group (median: 2.9 years IQR: 1.8–5.5). The 1-year, 3-year, and 5-year RFS for the PN group, were 97.6%, 88.9%, and 82.9%, respectively, compared to 96.9%, 94.7%, and 85.6%, respectively, for the RN group. The Kaplan–Meier survival curves [Figure 2] were not statistically significantly different for PN versus RN groups (logrank $P = 0.53$). In the adjusted Cox model [Table 2], PN patients had 78% increased likelihood of recurrence compared to RN patients (Hazard ratio [HR] = 1.78, 95% confidence interval [CI]: 0.74–4.3); yet, this difference was not statistically significant ($P = 0.19$).

Table 1: Characteristics of the overall cohort stratified by surgery type

	PN	RN	*P*
Number of cases	128	100	
Age[a]	58 (50-65.5)	60.5 (47-68)	0.55
Sex (male)[b]	95 (74.2)	69 (69)	0.38
CAD	12 (9.4)	16 (16)	0.13
HTN	76 (59.4)	47 (47)	0.06
DM	33 (25.8)	18 (18)	0.16
Preoperative creatinine	0.9 (0.7-1.1)	0.9 (0.8-1.1)	0.42
Tumor size	3.5 (2.5-4.6)	7 (5-9.9)	<0.0001
Pathologic T stage			
T1a	84 (65.6)	15 (15)	<0.001
T1b	36 (28.1)	36 (36)	
T2a	6 (4.7)	22 (22)	
T2b	0	12 (12)	
T3a	2 (1.6)	14 (14)	
T3b	0	1 (1)	
Fuhrman grade			
G 1-2	88 (68.8)	51 (51)	0.017
G 3-4	27 (21.1)	37 (37)	
Grade unknown	13 (10.2)	12 (12)	
Histology			
Clear cell	88 (68.8)	63 (63)	0.003
Papillary	22 (17.2)	6 (6)	
Chromophobe	15 (11.7)	24 (24)	
Mixed/unknown	3 (2.3)	7 (7)	
Renal category			
Low (<7)	53 (41.4)	14 (14)	<0.001
Intermediate (7-9)	47 (36.7)	32 (32)	
High (>9)	6 (4.7)	33 (33)	
Missing	22 (17.2)	21 (21)	
EBL	200 (100-400)	200 (100-300)	0.26
Approach			
Open	49 (38.3)	57 (57)	<0.001
Laparoscopic	3 (2.3)	25 (25)	
Robotic	76 (59.4)	18 (18)	
Disease recurrence	17 (13.3)	16 (16)	0.56

[a]All continuous variables are expressed as median (IQR), [b]All categorical variables are expressed as count (%). EBL: Estimated blood loss in cc, IQR: Interquartile ranges, CAD: Coronary artery disease, HTN: Hypertension, DM: Diabetes mellitus, PN: Partial nephrectomy, RN: Radical nephrectomy

Subgroup analysis

We performed a subgroup analysis by evaluating patients who underwent PN or RN for cT1b tumors exclusively. In this subgroup, 36 patients were managed by PN and 40 patients by RN. The characteristics of patients in the subgroup analysis are depicted in Table 3. Patients in the PN group were again demonstrated to have smaller tumors (median size 5 vs. 6 cm, $P = 0.008$), and lower tumor complexity scores (25% low RENAL and 2.8% high RENAL in the PN group vs. 10% low RENAL and 37.5% high RENAL group, $P = 0.002$). In addition, PN was more likely to be performed using the robotic approach (50% vs. 20%) and less likely using the laparoscopic approach (32.5% vs. 2.8%) compared to RN ($P < 0.001$). There were five recurrence events in the 36 PN group versus three recurrences in 40 patients who underwent RN. The Kaplan–Meier survival curves for the cT1b subgroup revealed no statistically significant difference among the two modalities (logrank $P = 0.118$) [Figure 3]. In the Cox model adjusted for tumor size, pathologic stage, Fuhrman grade, and histology, PN for cT1b subgroup was significantly associated with a large increase in the hazard of RCC recurrence compared to RN (HR = 12.4, 95% CI: 1.15–133.4, $P = 0.038$).

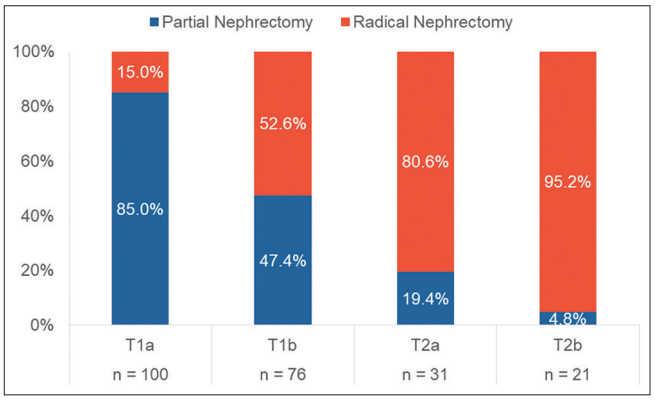

Figure 1: Surgery type versus clinical T stage (test for trend $P < 0.0001$)

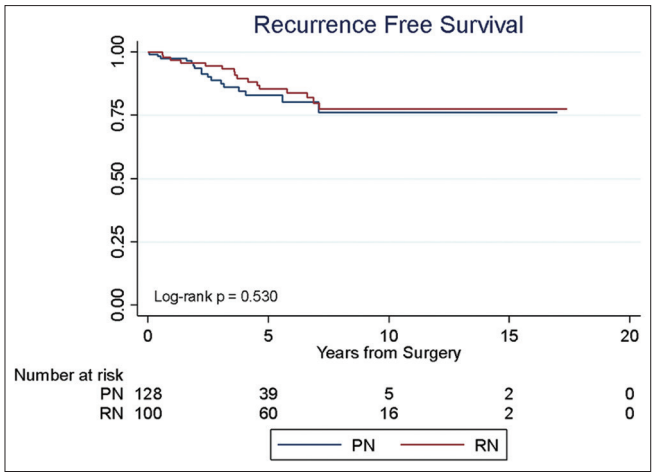

Figure 2: The Kaplan–Meier survival curves for the overall cohort comparing PN versus RN groups. PN: Partial nephrectomy, RN: Radical nephrectomy

Table 2: Cox regression evaluating the adjusted risk of recurrence after radical or partial nephrectomy

	HR	95% CI	*P*
Treatment			
RN	Reference		
PN	1.78	0.74–4.3	0.19
Size	0.79	0.61–1.03	0.07
pT stage			
T1a	Reference		
T1b	1.47	0.4–5.4	0.56
T2a	11.8	1.7–83.9	0.01
T2b	8.1	0.37–174	0.18
T3a	6.9	1.01–47.4	0.04
T3b	2001	7.2–555211	0.008
Fuhrman grade			
G 1–2	Reference		
G 3–4	3.05	1.33–6.9	0.008
Grade unknown	3.56	0.84–15.1	0.08
Histology			
Clear cell	Reference		
Papillary	0.28	0.06–1.2	0.08
Chromophobe	0.22	0.04–0.98	0.04

CI: Confidence interval, HR: Hazard ratio, PN: Partial nephrectomy, RN: Radical nephrectomy

DISCUSSION

The past two decades have witnessed a gradual and progressive shift in the surgical management of renal tumors from RN to PN.[6] This has been attributed to several factors.[1] Many urologists are inclined to favor PN due to its inherent advantage in preserving maximal renal parenchyma and maintaining a better long-term renal function.[2] The introduction of robotic-assisted PN facilitated kidney reconstruction (compared to laparoscopic approach) and minimized the morbidity of open PN.[3] Advancements in hemostatic techniques substantially improved perioperative and postoperative outcomes related to PN complications. Observational studies have suggested a role of PN in improved overall survival;[7] yet, PN or RN randomization in patients with small masses did not reproduce these findings.[2] In the absence of high-quality evidence demonstrating the causal benefit of PN in terms of long-term overall survival, urologists should be aware of the possibility of compromising long-term oncologic safety for a possible inconsequential gain in renal function.

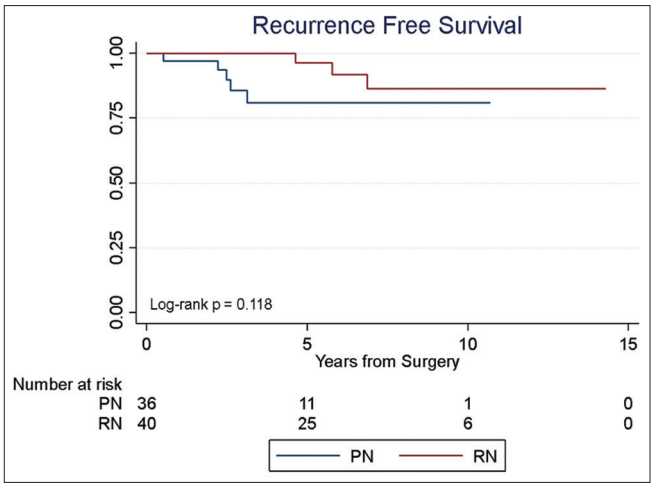

Figure 3: The Kaplan–Meier survival curves for the subgroup of patients with clinical stage T1b comparing PN versus RN. PN: Partial nephrectomy, RN: Radical nephrectomy

We report the 15-year experience of a tertiary care referral center in the surgical management of localized RCC. We found substantial differences in baseline characteristics of patients undergoing PN versus RN, demonstrating that tumors managed by PN had overall lower complexity scores. Despite this selection bias, that is likely to favor the PN group in oncological outcomes, multivariate adjusted survival analysis showed a trend toward an increased risk of recurrence in the PN versus RN group (HR = 1.78, 95% CI: 0.74–4.3), but this was not statistically significant ($P = 0.19$). Given the relatively small sample size and low number of outcome events, the question arises whether the same impact would be achieved in a larger sample of patients. However, in a subgroup of patients with cT1b tumors, PN was significantly associated with a large increase in the hazard of recurrence compared to RN (HR = 12.4, 95% CI: 1.45–133.4, $P = 0.038$). This observation is concerning, especially that the PN group had smaller tumors, lower RENAL scores, and shorter follow-up versus RN patients (median follow-up 2.9 vs. 5.9 years, respectively). These results have important implications on the surgical decision-making in the management of localized renal masses, and may divert against the preference of routine PN, especially in patients with a normal contralateral kidney and minimal risk factors for developing chronic kidney disease (CKD).

Table 3: Characteristics of patient subgroup with clinical stage T1b

Clinical stage T1b	PN	RN	*P*
Number of cases	36	40	
Age	59 (50–67)	60.5 (44–65)	0.44
Sex (male)	26 (72.2)	29 (72.5)	0.97
CAD	3 (8.3)	8 (20)	0.14
HTN	22 (61.1)	22 (55)	0.59
DM	11 (30.6)	9 (22.5)	0.42
Preoperative creatinine	0.9 (0.7–1.2)	0.95 (0.8–1.1)	0.93
Tumor size	5 (4.5–6)	6 (5–6.5)	0.008
Upstage to T3a	0	4 (10)	0.11
Fuhrman grade			
G 1–2	21 (58.3)	19 (47.5)	0.46
G 3–4	8 (22.2)	14 (35)	
Grade unknown	7 (19.4)	7 (17.5)	
Histology			
Clear cell	20 (55.6)	22 (55)	0.25
Papillary	5 (13.9)	1 (2.5)	
Chromophobe	9 (25)	12 (30)	
Mixed/undetermined	2 (5.6)	5 (12.5)	
Sarcomatoid	0	0	
LVI	0	4 (10)	0.11
Renal category			
Low (<7)	9 (25)	4 (10)	0.002
Intermediate (7–9)	19 (52.8)	13 (32.5)	
High (>9)	1 (2.8)	15 (37.5)	
Missing	7 (19.4)	8 (20)	
EBL	250 (150–400)	200 (150–300)	0.21
Approach			
Open	17 (47.2)	19 (47.5)	0.001
Laparoscopic	1 (2.8)	13 (32.5)	
Robotic	18 (50)	8 (20)	
Disease recurrence	5 (13.9)	3 (7.5)	0.46

CAD: Coronary artery disease, HTN: Hypertension, DM: Diabetes mellitus, EBL: Estimated blood loss in cc, LVI: Lymphovascular invasion, PN: Partial nephrectomy, RN: Radical nephrectomy

Several studies have commented on RCC recurrence after PN or RN. Simmons *et al.* assessed patients undergoing PN (n = 35) or RN (n = 75) between 2001 and 2005 after a median follow-up of 57 months. Recurrence rates were reported as 6% in the PN versus 3% in the RN group (P = 0.43), despite RN patients harboring larger tumors (median size 5.3 vs. 4.6 cm, = 0.026).[8] In another propensity score matched cohort of 310 patients who had PN or RN, the 5-year local recurrence-free survival rate was 94.2% versus 97.9%, respectively; however, the difference was not statistically significant (P = 0.283).[9] On the other hand, Mir *et al.* conducted a meta-analysis of studies comparing PN versus RN for T1b and T2 renal masses between 1970 and 2012. PN was associated with a lower likelihood of tumor recurrence (odds ratio: 0.6, 95% CI: 0.46–0.79; P < 0.001), with an important observation that patients in the PN group had significantly smaller tumors.[10] In another matched cohort including around 360 matched pairs of patients by Gershman *et al.*, RN was significantly associated with a reduced risk of local recurrence compared to PN (HR: 0.27, 95% CI: 0.13–0.58).[11]

In summary, our single-center cohort study demonstrated a diminished RFS with PN compared to RN in multivariate analysis. The inconsistent conclusions in the current literature emphasize the need for a well-designed randomized trial comparing PN to RN with long-term follow-up. Of particular interest, are patients with intermediate-size sporadic tumors and normal contralateral kidney who are not at risk for developing CKD due to comorbidities? This subset of patients could represent a cohort whereby treatment equipoise might exist.

Our study has some limitations including the retrospective design and small number of outcome events. The use of observational data to compare the effects of treatment modalities confers inherent selection bias. A multivariate-adjusted analysis was done, and a subgroup analysis according to T stage was reported, but available data did not allow for a propensity score-matched analysis. There could also be unmeasured confounders affecting the outcomes of PN or RN. However, we believe that residual confounding does not undermine our findings since the direction of bias caused by nonrandomization of treatment favors (in terms RFS) PN over RN, since there was predominance of higher risk tumors with adverse characteristics in the RN group (85/100 pT1b or higher in the RN group vs. 44/128 pT1b or higher in the PN group). Despite that, we observed a statistically significant association of PN with worse RFS compared to RN in the subgroup analysis of T1b stage. The worse RFS observed in the cT1b subgroup may or may not be extrapolated to other T stages, as the possible effect modification per T stage group remains unknown.

Despite these limitations, our observations were in conditions where surgical technique and follow-up are consistent. This emphasizes the importance of reconsidering the reflex choice of PN in higher-risk RCC and adopting RN in cases harboring high oncologic potential and normal baseline renal function.

CONCLUSIONS

We report a statistically significant association between PN and compromised RFS compared to RN in T1b RCC. Improved postoperative parameters and outcomes, mainly attributed to kidney function preservation with PN versus RN, should be weighed against the risk of possible compromised oncological safety. Longer follow-up intervals, larger sample sizes, and randomized controlled trials are needed to better elucidate the associated intermediate and long-term risks of PN, especially for higher risk localized RCC.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Capitanio U, Terrone C, Antonelli A, Minervini A, Volpe A, Furlan M, *et al*. Nephron-sparing techniques independently decrease the risk of cardiovascular events relative to radical nephrectomy in patients with a T1a-T1b renal mass and normal preoperative renal function. Eur Urol 2015;67:683-9.
2. Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, *et al*. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol 2011;59:543-52.
3. Campbell SC, Clark PE, Chang SS, Karam JA, Souter L, Uzzo RG. Renal mass and localized renal cancer: Evaluation, management, and follow-up: AUA guideline: Part I. J Urol 2021;206:199-208.
4. Hakam N, Abou Heidar N, Khabsa J, Hneiny L, Akl EA, Khauli R. Does a positive surgical margin after nephron sparing surgery affect oncological outcome in renal cell carcinoma? A systematic review and meta-analysis. Urology 2021;156:e30-9.
5. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Lancet 2007;370:1453-7.
6. Ljungberg B, Bensalah K, Canfield S, Dabestani S, Hofmann F, Hora M, *et al*. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913-24.
7. Maurice MJ, Zhu H, Kim S, Abouassaly R. Survival after partial and radical nephrectomy for high-risk disease: A propensity-matched comparison. Can Urol Assoc J 2016;10:E282-9.
8. Simmons MN, Weight CJ, Gill IS. Laparoscopic radical versus partial nephrectomy for tumors>4 cm: Intermediate-term oncologic and functional outcomes. Urology 2009;73:1077-82.
9. Simone G, Tuderti G, Anceschi U, Papalia R, Ferriero M, Misuraca L, *et al*. Oncological outcomes of minimally invasive partial versus minimally invasive radical nephrectomy for cT1-2/N0/M0 clear cell renal cell carcinoma: A propensity score-matched analysis. World J Urol 2017;35:789-94.
10. Mir MC, Derweesh I, Porpiglia F, Zargar H, Mottrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: A systematic review and meta-analysis of comparative studies. Eur Urol 2017;71:606-17.
11. Gershman B, Thompson RH, Boorjian SA, Lohse CM, Costello BA, Cheville JC, *et al*. Radical versus partial nephrectomy for cT1 renal cell carcinoma. Eur Urol 2018;74:825-32.