

Peer Review File

Article information: <http://dx.doi.org/10.21037/tau-20-1262>

Reviewer A

Comment 1: Authors suggest universal application of partial nephrectomy for pT3a RCC due to preservation of renal function and improvement of the health-related quality after surgery. Although survival outcomes are thoroughly analyzed, manuscripts completely lacks of data in terms of complications rate, which is pivotal when assessing differential safety of PN and RN in more complex renal tumors.

Reply 1: Dear reviewers, we have re added the content of complications to the original text. Three studies performed complications. Complications include secondary bleeding and wound infection. Meta analysis found that the complications rate difference between PN and RN was not statistically significant.(RR =0.78, 95%CI =0.50~1.23)(Fig.6).

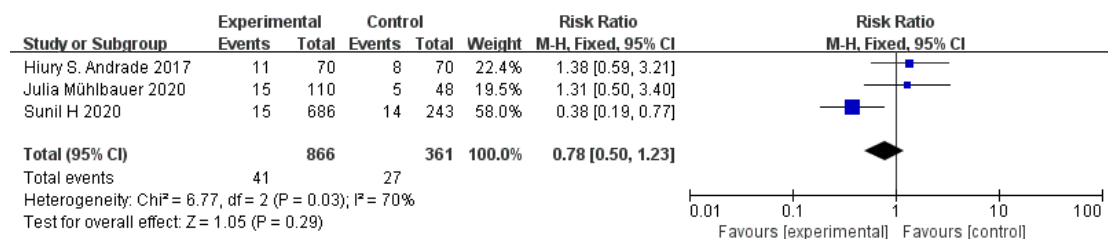


Fig. 6 Forest plot of complication between PN and RN

Changes in the text: Three studies performed complications. Complications include secondary bleeding and wound infection. Meta analysis found that the complications rate difference between PN and RN was not statistically significant.(RR =0.78, 95%CI =0.50~1.23)(Fig.6).



Fig. 6 Forest plot of complication between PN and RN

Comment 2: Similarly, it would have been appropriate to assess also impact of PN and RN on renal function preservation. Unfortunately, no functional data is provided, ultimately undermining the strength of clinical message.

Reply 2: Dear reviewers, we have carefully read the included articles. There is no data on renal function in the original text, which makes it impossible for us to analyze the protection of renal function

Comment 3: Authors suggests that oncological safety of PN is the same as that of RN focusing their attention on OS, CSS and CSM. However, some would argue that this could be related also to the volume load of the centre. Data regarding the volume load and surgeon’s experience would have been of great clinical interest.

Reply 3: Dear reviewers, we have carefully read the included articles. There is no data on the volume load and surgeon’s experience in the original text, which makes it impossible for us to analyze the protection of the volume load and surgeon’s experience

Comment 4: As regards oncological outcomes, it would have been useful to assess also the positive surgical margins rate and the recurrence free survival.

Reply 4: Dear reviewers, we have analyzed the positive surgical margins rate and the recurrence free survival. Three studies invovled RFS. Meta analysis found that the RFS rate difference between PN and RN was not statistically significant.(RR =0.93, 95%CI =0.75~1.16)(Fig.5).Five studies performed positive surgical margin. Meta analysis found that the positive surgical magrin rate difference between PN and RN was not statistically significant.(RR =1.05, 95%CI =0.78~1.41)(Fig.7).

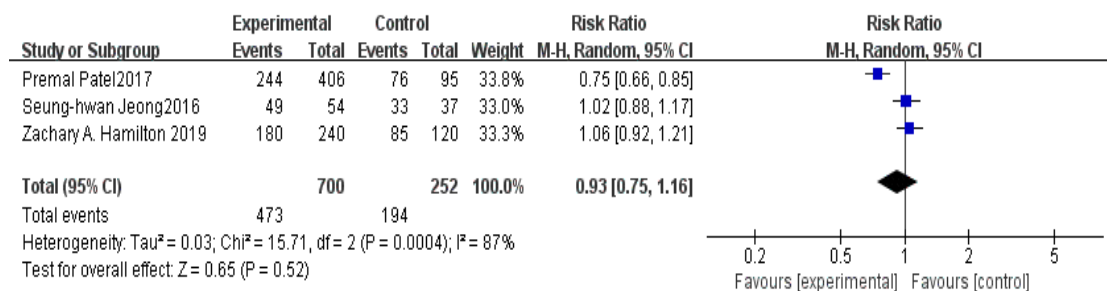


Fig. 5 Forest plot of RFS rates between PN and RN

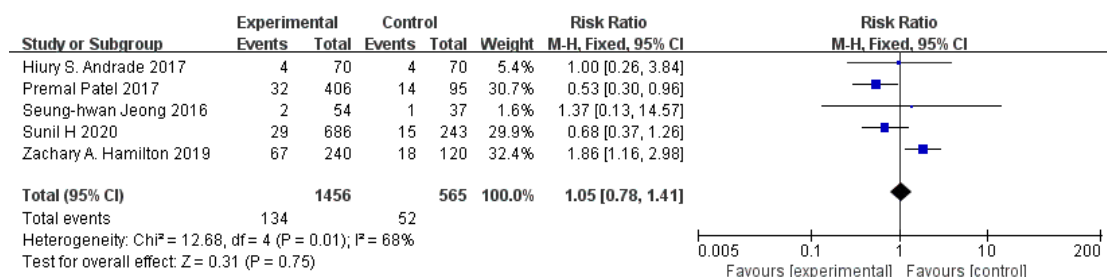


Fig. 7 Forest plot of Positive surgical margin between PN and RN

Changes in the text: Three studies invovled RFS. Meta analysis found that the RFS rate difference between PN and RN was not statistically significant.(RR =0.93, 95%CI =0.75~1.16)(Fig.5).Five studies performed positive surgical margin. Meta analysis found that the positive surgical magrin rate difference between PN and RN was not

statistically significant. (RR =1.05, 95%CI =0.78~1.41)(Fig.7).

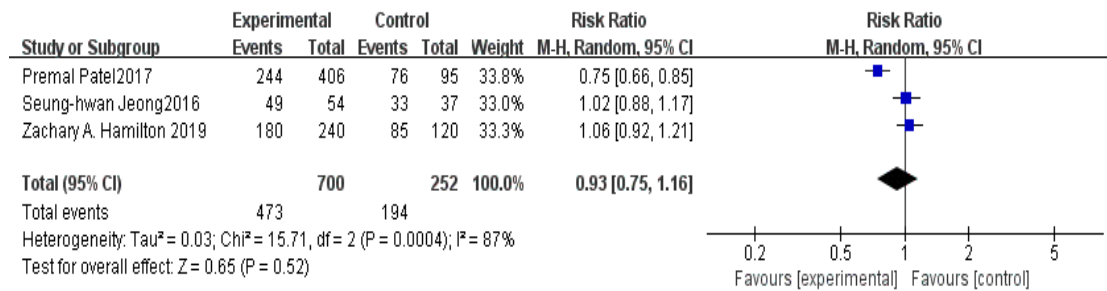


Fig. 5 Forest plot of RFS rates between PN and RN

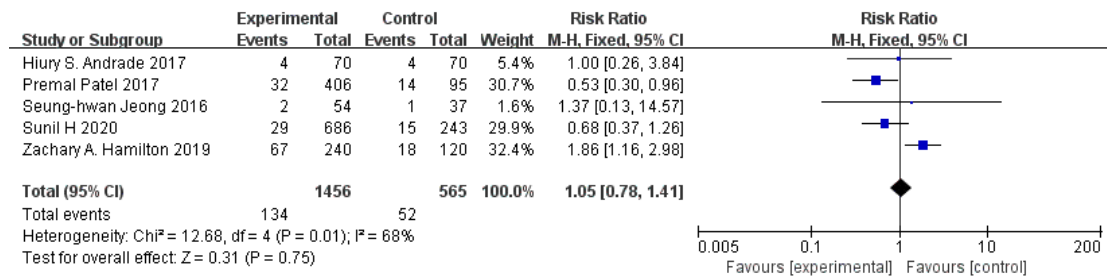


Fig. 7 Forest plot of Positive surgical margin between PN and RN

Comment 5: In the results section the Authors include 13 articles but in the flowchart figure (fig. 1) there are only 8 studies reported. Please clarify this point

Reply 5: Dear reviewer, due to negligence, we have typed the number of articles incorrectly. We have added another article to the meta analysis, including a total of 9 pieces

Changes in the text:

Features of included literature

According to the inclusion and exclusion criteria, a total of 9 articles were included in this study¹⁷⁻²⁵ (Fig. 1). The characteristics of the studies are showed in Table 1.

A total of 3391 patients were included, 1278 patients in the PN group, 2113 patients in the RN group, of which 2 studies compared PN and RN tumor-specific survival rates^{19,22}, and 5 studies performed PN and RN overall survival rates¹⁸⁻²², and 2 studies performed PN and RN CSM^{17,20}. 3 studies performed PN and RN RFS^{18,23-24}. 3 studies performed complications^{20,22,25}. 5 studies performed positive surgical margin^{18,20,22-24}. The baseline characteristics of included studies were shown in Table 2.

Studies	Ye Si Study ar ze Type	Intenve ntion	Outcome EENAL score	Quality score	Age
Jens Hansen ^[17]	20 95 Retrospe 12 4 ctive	RN,PN	CSM NA	7	64

Zachary A. Hamilton ^[18]	20 36 19 0	Retrospe ctive	RN,PN	RFS,OS RN:7.8 PN:7.7	8	60.7
Christopher J ^[19]	20 20 10 3	Retrospe ctive	RN,PN	CSS,OS NA	8	64
Sunil H ^[20]	20 92 20 9	Retrospe ctive	RN,PN	CSM,OS RN:8.81 PN:9.9	7	63
Brigitte K ^[21]	20 19 55	Retrospe ctive	RN,PN	OS RN:7.3 PN:7.3	8	67.9
Hiury S. Andrade ^[22]	20 14 17 0	Retrospe ctive	RN,PN	CSS, OS RN:8 PN:8	8	62.4
Premal Patel ^[23]	20 50 17 1	Retrospe ctive	RN,PN	RFS NA	7	63.2
Seung-hwan Jeong ^[24]	20 91 16	Retrospe ctive	RN,PN	RFS RN:7.5 PN:7.6	8	58.6
Julia Mühlbauer ^[25]	20 15 20 8	Retrospe ctive	RN,PN	OS RN:10 PN:8	9	67.0

Table 1 Basic situation of 9 documents

Comment 6: In the lines 33-34 and 39-40 the sentences “It is the most lethal tumor among urinary tract tumor” and “It is insensitive to conventional tumor treatment methods such as radiotherapy and chemotherapy” are debatable. It would be necessary to better specify the correlation between pathological characteristics and radio- and chemio- sensibility. Moreover, related bibliography is needed

Reply 6: Dear reviewer, we have changed “It is the most lethal tumor among urinary

tract tumor” into “It is the lethal tumor among urinary tract tumors”. And we have deleted “It is insensitive to conventional tumor treatment methods such as radiotherapy and chemotherapy”

Comment 7: In line 113 there is a typing error: “srudies”. Please correct

Reply 7: Dear reviewer, we have changed “srudies” into “studies”

Reviewer B

Comment 1: First, the outcomes measures were limited to survival (overall and cancer specific), whilst another key parameter to be considered when comparing PN versus RN is the complications' rate.

Reply 1: Dear reviewers, we have re added the content of complications to the original text. Three studies performed complications. Complications include secondary bleeding and wound infection. Meta analysis found that the complications rate difference between PN and RN was not statistically significant.(RR =0.78, 95%CI =0.50~1.23)(Fig.6).

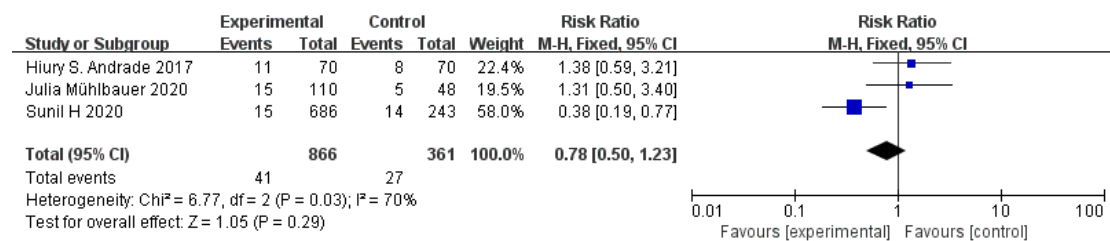


Fig. 6 Forest plot of complication between PN and RN

Changes in the text: Three studies performed complications. Complications include secondary bleeding and wound infection. Meta analysis found that the complications rate difference between PN and RN was not statistically significant.(RR =0.78, 95%CI =0.50~1.23)(Fig.6).



Fig. 6 Forest plot of complication between PN and RN

Comment 2: There is a recent study by Mühlbauer et al that was missed. (Mühlbauer J, Kowalewski KF, Walach MT et al. Partial nephrectomy preserves renal function without increasing the risk of complications compared with radical nephrectomy for renal cell carcinomas of stages pT2–3a. *Int. J. Urol.* 2020; <https://doi.org/10.1111/iju.14326>.) The authors retrospectively analyzed 158 patients

who underwent RN or elective PN for pT2–pT3a renal cell carcinoma (RCC) carried out by experienced surgeons at a single institution.¹ The authors concluded that, in selected cases of large/locally advanced RCC, PN can be carried out with comparable complications to RN, while conferring better functional preservation.

Reply 2: Dear reviewers, we have included the articles recommended by the reviewers in the meta analysis.

Comment 3: It is debatable that groups were based on pathological instead of clinical stage. Concerns exist that outcomes of pT3a tumors might not analogously apply to cT3a tumors. Indeed, the pT3 group will be heterogeneous.

This is because the final pathology usually upstages some cT1 tumors. The authors should have included a subgroup analysis of patients with tumor size >7.0 cm.

Reply 3: Dear reviewers, we have analyzed patients with tumor size >7.0 cm. Jens Hansen¹⁷ made a regression analysis of patients with tumor size >7.0 cm and found tumor size had no statistical significance (HR 0.67, 95%CI 0.30-2.17). So the outcomes of pT3a tumors could apply to cT3a tumors.

Comment 4: I strongly disagree that the PN approach can be universally suggested in any case of pT3 RCC.

Partial nephrectomy for pT3 is a challenging intervention and requires experience. The authors should stress this concept and avoid misleading conclusions. Please delete the suggestion in the conclusion. Enrich discussion by including papers reporting about the use of advanced technologies to aid in sparing the kidney when trying a nephron sparing approach. (see "Expanding the indications of robotic partial nephrectomy for highly complex renal tumors: urologists' perception of the impact of hyperaccuracy three-dimensional reconstruction. *J. Laparoendosc. Adv. Surg. Tech. A.* 2019; 29: 233–9.).

Reply 4: We delete the inductive statement in the conclusion part. And it was discussed again.

CONCLUSION

There were no differences in the CSS, OS, CSM, RFS, complications and positive surgical margin of the patients between RN and PN group. In pT3a RCC, RN did not provide a better survival benefit compared to PN. Considering PN has a good tumor control effect and reducing the risk of postoperative chronic renal insufficiency, we found partial nephrectomy is a good choice for pT3a RCC. Partial nephrectomy for pT3 is a challenging intervention and requires experience. In the future, further large-sample, studies are needed.

Riccardo Bertolo³² assessed the role of three-dimensional (3D) reconstruction in aiding

preoperative planning for highly complex renal tumors amenable to robotic partial nephrectomy (RPN). After viewing the respective 3D reconstructions, in 148 cases the responders changed their idea: indication to RPN raised in 404 cases (74.5%) ($P < .001$). The opinions changed regardless of the surgical experience. The use of this technology might translate into a larger adoption of nephron-sparing approach. More advanced technologies are needed in the future.