

Peer Review File

Article information: <https://dx.doi.org/10.21037/amj-23-233>

Review Comments:

Reviewer A

The authors should be congratulated for their effort in making a narrative review in RAPN. The topic is not very new but the manuscript is well written and summarize all the main debated topics on RAPN.

I have some concerns:

-There are some errors during the text like “renal nephrectomy” in the abstract and more others in the text, please correct them

Response:

Thank you for pointing this out. We have addressed this issue.

- I feel that a short chapter on the new robotic platforms should be added (HUGO both transperitoneal PMID:36847815 and retroperitoneal PMID: 37328354, Hinotori..) to make the manuscript more appealing and actual.

Response:

Thank you for the suggestion. As the reviewer pointed out, we also thought describing the new modalities used in the RAPN was necessary. Based on this point, we have added the following to the manuscript.

(Introduction)

“In the 2000s, robot-assisted PN (RAPN) was first performed using daVinci robot systems and has been done with new modalities such as HUGO and Hinotori (8–10)

Gallioli A, Uleri A, Gaya JM, et al. Initial experience of robot-assisted partial nephrectomy with Hugo™ RAS system: implications for surgical setting. *World J Urol* 2023;41:1085-91.

Miyake H, Motoyama D, Matsushita Y, et al. Initial experience of robot-assisted partial nephrectomy using Hinotori Surgical Robot System: single institutional prospective assessment of perioperative outcomes in 30 cases. *J Endourol* 2023;37:531-4..”

- Please include and discuss this paper in the multiple lesions RAPN chapter (PMID: 36847584)

Thank you for the introduction to the paper. We have revised the entire chapter using the paper you mentioned.

(RAPN for multiple ipsilateral tumors)

Reports of RAPN for multiple ipsilateral renal tumors have been seen since around 2009 (35). The feasibility of the unique clamping technique of sequentially blocking segmental renal arteries for multiple ipsilateral renal tumors in 11 patients was demonstrated (36). There were reported good results with renal function preservation or oncological outcomes (insignificant reduction of postoperative eGFR (9.3%), no PSM, and no recurrence or metastasis during a follow-up period of 5.4 months).

A study of 61 patients with multiple ipsilateral renal masses reported acceptable results concerning complications, WIT, EBL, and PSM by preoperative simulation for hilum management using 3D construction from images and intraoperative use of TilePro (Life360; San Francisco, CA, USA), indocyanine green fluorescence and intraoperative ultrasound. (Three (4.8%) intraoperative complications occurred, all classified as grade-1 according to EAUiaiC. Postoperative complications were reported in 14 (22.9%) cases with 2 Clavien-Dindo grade >2 complications. The median WIT was 17 (12-24) minutes, the median EBL was 200 (100-400) mL, and PSM was 6.56%) (37).

In a study in which 50 patients who underwent RAPN for ipsilateral multiple renal masses (mPN) were matched with 146 patients who underwent RAPN for a single renal mass (sPN), there were no significant differences in complications, renal function outcomes, and EBL. However, ipsilateral multiple renal masses were associated with increased operative time (mPN:174.6 vs. sPN:156.4 minutes, $p = 0.008$) and WIT (mPN:17.0 vs. sPN15.3 minutes, $p = 0.032$) (38).

mPN is more challenging than sPN because the optimal anatomic approach for each tumor is different. Limitations in the range of motion and rotation of the kidney during RAPN also contribute to the difficulty. It has been reported that mPN increases operative time and WIT (38). Inexperienced surgeons, with the employment of the currently available technologies and surgical techniques, mPN may guarantee optimal outcomes.

B Buffi N, Uleri A, Paciotti M, et al. Techniques and outcomes of robot-assisted partial nephrectomy for the treatment of multiple ipsilateral renal masses. *Minerva Urol Nephrol* 2023;75:223-30.

Biebel MG, Hill H, Patel B, et al. A Multi-Institutional matched-pair analysis of robotic partial nephrectomy for single vs multiple ipsilateral renal masses. *J Endourol* 2023;37:781-5.

- please include and discuss these 2 paper PMID: 37714966; PMID: 36631353

Response:

Thank you for the suggestion. As the reviewer pointed out, we should focus on the renal function after RAPN. We have added the following to the manuscript regarding estimation of renal function after RAPN, citing the proposed literature.

5.3 Estimation of renal function

Concerning postoperative renal function, there is a trade-off between PN and RN. Therefore, estimating postoperative renal function may provide clinicians with

insights into whether it is worth accepting the potentially higher surgical risks associated with complex PN compared to RN. The Fundació Puigvert model, using machine learning and data from 568 patients undergoing minimally invasive partial nephrectomy between 2005 and 2022, identified key predictors of chronic kidney disease progression post-surgery. A c-index of 0.75 highlights the importance of perioperative renal function in recovery, offering a tool to improve patient management and minimize renal function decline post-operation (92). A systematic review of available prediction models for estimating postoperative renal function, 21 prediction models were assessed from 18 studies on estimating mid- to long-term postoperative renal function after surgery for renal masses, focusing on preoperative or modifiable intraoperative factors. Patient-, kidney-, surgery-, tumor-, and provider-related factors were included among the predictors in 95%, 86%, 100%, 61%, and 0% of the models, respectively. However, most were not yet suitable for routine clinical use, indicating a need for further validation and assessment of clinical utility (93). Thus, at this time, there is no robust predictive model of postoperative renal function, which is an unmet clinical need.

Uleri A, Baboudjian M, Gallioli A, et al. A new machine-learning model to predict long-term renal function impairment after minimally invasive partial nephrectomy: the Fundació Puigvert predictive model. *World J Urol* 2023;41:2985-90.

Pecoraro A, Campi R, Bertolo R, et al. Estimating postoperative renal function after surgery for nonmetastatic renal masses: a systematic review of available prediction models. *Eur Urol Oncol* 2023;6:137-47.

Reviewer B

The authors drafted a comprehensive overview of “surgical choices” in RAPN. It’s okay written and overall a pretty interesting read for those seeking a scoping review. Although overall it has little nuance and some statements are not correct. Please see discussed below more in detail.

Content:

3 Focus and title of the article are not clear. Article focuses on T1b and T2 renal masses, however this focus is nowhere mentioned in the title, introduction or methods. Please make this focus more clear.

Response:

Thank you for the suggestion. As the reviewer pointed out, we have revised the title and introduction.

(Title)

“A narrative review of optimal treatment choices in robot-assisted partial nephrectomy **focusing on indication and surgical procedure**”

(Introduction)

“**While RAPN is widely used for tumors with challenging characteristics, such as larger (T1b and T2) and complex tumors, and diverse patient backgrounds, it is**

essential to distinguish between the technical feasibility of the procedure and whether the surgery has been effectively performed”

25 ‘focused on specific topics’: vague: please clarify

Response:

Thank you for pointing this out. We apologize for the confusing description. We also found it vague; therefore, we have removed this description.

31 ‘In older patients, RAPN is a feasible and safe treatment option’: more nuance needed. For each mass? For each patient? Other treatment modalities are available. For slowly growing masses other modalities might even be the preferred treatment option (active surveillance, thermal ablation (either radiofrequency ablation or cryotherapy), SBRT...) because of less morbidity and decent outcomes, especially for T1a and smaller T1b lesions.

Response:

Thank you for pointing this out.

We have understood the nuances of the reviewer, and in response to the peer reviewer’s opinion, we have made the following revisions.

RAPN for older patients

In a study evaluating overall survival (OS) with propensity score matching of 4457 patients with T1a aged 70 years or older who underwent partial nephrectomy (PN) or non-surgical treatment (NST; treatment details unknown), the PN group had better OS than the NST group in both patients aged 70-79 years and 80 years or older (70-79 years old; PN 158 months vs. NST 75 months. Over 80 years old; PN 158 months vs. NST 59 months). In multivariate analysis, treatment (PN vs NST) and age (70-79 vs 80 years) were independent prognostic factors. Although there may be patient selection bias, this study demonstrates the benefit of partial nephrectomy for elderly patients with T1a. However, age is a prognostic factor, and the indication for partial nephrectomy in older people should be carefully considered (45)

RAPN is known to have fewer complications and better operative outcomes than open partial nephrectomy or laparoscopic partial nephrectomy (46) If partial nephrectomy is the procedure of choice in older patients, RPAN is the preferred.

In a study, the median patient age was 74 (Interquartile range, 72–76.5) years, and most of the patients (67.3%) had low PADUA scores (48). The complication rate was 15.4%. The trifecta achievement rate was 71.2%. The disease-free, overall, and cancer-specific survival were 89.33%, 90.06%, and 94.4%, respectively. These results demonstrated that RAPN was a feasible and safe treatment for elderly patients and had good oncological outcomes.

In another study comparing RAPN with robot-assisted radical nephrectomy (RARN) in older patients with large renal masses, the mean ages were 71.3 years and 73.0 years, and the mean scores were 9.6 points and 8.6 points for the RARN and RAPN groups, respectively. EBL (200 vs. 100 mL; $p < 0.001$) and rate of overall complications (38% vs. 23%; $p = 0.05$) were higher in the RAPN group (49). There was no significant difference in major complications between the groups ($p = 0.678$).

Higher eGFR levels (55.4 ± 22.6 vs. 45.7 ± 15.7 mL/min; $p=0.016$) and lower eGFR variation (9.7 vs. 23.0 mL/min; $p<0.001$) at the final follow-up were observed for RAPN. The procedure type was not associated with progression-free survival (PFS) (hazard ratio [HR], 0.47 ; $p=0.152$) or OS (HR, 0.22 ; $p=0.084$).

In another study comparing perioperative, oncological, and renal outcomes of cryotherapy and RAPN in elderly patients (>75 years) using propensity score matching, the overall complications rate was higher for RAPN (31% vs. 9% ; $P = 0.007$), but no difference was found in major (Clavien III-IV) complications (6% vs. 1.5%). No significant differences were found in cancer-specific and overall survival, but recurrence-free survival was higher for RAPN (RAPN vs. cryoablation, 100% vs. 83% , $P = 0.02$). Renal function was comparable between the groups (51) (Table 6).

In a meta-analysis of Minimally invasive partial nephrectomy (MIPN; RAPN and LPN) and focal therapy (FT; radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA), irreversible electroporation, non-thermal [irreversible electroporation (IRE)] ablation, and stereotactic body radiation therapy (SBRT)) for 4,420 patients with small renal masses (SRMs), Renal function of FT was significantly lower decrease and FT possessed lower risk in minor complications (Clavien 1–2) ($P = 0.023$) and overall complications ($P = 0.008$).

Finally, there is no obvious difference between FT and MIPN in local recurrence, distant metastasis, and major complications (50).

Considering the above literature, RAPN for older people is technically sound and has an acceptable safety profile. However, the outcomes of RAPN and other focal therapies are presumed to be comparable. Especially for small renal tumors, the treatment choice should be carefully considered depending on the patient's comorbidities and general condition.

Tang Y, Wu K, Hu X, et al. Survival benefit stratification of partial nephrectomy versus non-surgical treatment in elderly patients with T1a renal cell carcinoma. *Cancer Med* 2023;12:7974-81.

Luciani LG, Chiodini S, Mattevi D, et al. Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: results from a prospective cohort study. *J Robot Surg* 2017;11:333-9.

Bertolo R, Garisto J, Armanyous S, et al. Perioperative, oncological, and functional outcomes after robotic partial nephrectomy vs. cryoablation in the elderly: a propensity score matched analysis. *Urol Oncol* 2019;37:294.e9–15.

Dong L, Liang WY, Ya L, Yang L, Qiang W. A Systematic Review and Meta-Analysis of Minimally Invasive Partial Nephrectomy Versus Focal Therapy for Small Renal Masses. *Front Oncol.* 2022 May 26;12:732714. doi: 10.3389/fonc.2022.732714. PMID: 35692758; PMCID: PMC9178090.

32 ‘Enucleation may lead to a higher rate of positive surgical margins’: This statement is not supported by other literature e.g. recent meta-analysis. Please

comment and adapt as suited. <https://pubmed.ncbi.nlm.nih.gov/37182118/>

Response: Thank you for the suggestion. As the reviewer pointed out, systematic review presented demonstrated that enucleation did not increase a rate of PSM. Based on this point, we have edited this point.

(4.1. Standard resection vs. enucleation)

“In other words, the dilemma in the choice of surgical procedure between standard resection and enucleation lies in the fact that enucleation involves cutting the interface between the parenchyma and pseudo capsule. However, a systematic review supported that enucleation does not contribute to increased PSM (56).”

”

34 ‘Transperitoneal and retroperitoneal... choice between them should be based on the surgeon’s preference and experience’: this should also be based on localization of the renal mass, patient (surgical) history...

Response: Thank you for pointing this out. We have added this point to the manuscript.

(Abstract)

“The transperitoneal and retroperitoneal approaches lead to similar treatment outcomes, and the choice between them should be based on the surgeon’s preference and experience, tumor location, and surgical history.”

36 ‘Regarding renal function preservation... do not demonstrate a clear advantage’: different studies show favorable short-term renal function advantages, however not long term. Please nuance this accordingly.

Response: Thank you for the suggestion. As the reviewer pointed out, we changed the nuance of the text.

(Introduction)

“The currently available data do not demonstrate a clear advantage of unclamped or super-selective clamping in RAPN over standard clamping regarding short-term renal function preservation.”

69 ‘considered the mainstream technique’: please nuance: in developed countries and if robotic surgery is available

Response: Thank you for the suggestion. As the reviewer pointed out, we changed the nuance of the text.

(Introduction)

“RAPN is currently a widely spread technique for performing PN...”

95 ‘predominant technique’: see comment for line 69

95 ‘because of its advanced surgical approach’: this is vague, please clarify or

remove this line.

Response to the above two suggestions:

Thank you for the suggestion. As the reviewer pointed out, we changed the nuance of the text.

“Patient selection of robot-assisted partial nephrectomy

RAPN is currently the most **widely used technique** for PN because of **the development of robotic technology and its introduction into surgery.**”

98 ‘RAPN is considered the standard treatment for clinical T1a renal tumors’: this is not true, the EAU guidelines e.g. state that partial nephrectomy is the gold standard (but not necessarily robotic, although it does have some advantages). Please also nuance that other treatment modalities are available for small renal masses.

Response: Thank you for pointing this out. I understand your intention and have revised the relevant part of the sentence to note that RAPN is one of some standard treatments for T1a tumors.

“Patient selection of robot-assisted partial nephrectomy)

RAPN is considered **one of** the standard treatments **and a widely spread treatment** for clinical T1a renal tumors because of these advantages.”

100 ‘T1b and T2 tumors, which are large and complex renal tumors’: false, T1b and T2 tumors are large renal tumors (T-stage only based on size), but not necessarily complex tumors

Response: Thank you for pointing this out. The text has been revised for accuracy.

“Patient selection of robot-assisted partial nephrectomy

Here, we discuss the indications for RAPN in **T1b and T2 tumors. Furthermore, we would like to consider more challenging cases (high-complexity tumors, multiple ipsilateral tumors, tumors in a solitary kidney, and tumors in elderly patients).**”

117 ‘When the anatomical location allows...’: other important factors include tumor complexity, patient,...

Response: Thank you for pointing this out. We have revised the text following your feedback.

“RAPN for T1b tumor

When the **tumor location, complexity, and general condition of the patient** allow for a feasible procedure, RAPN **is a sufficient treatment option for T1b tumors.**”

129-131: nuance needed, based on retrospective data, so there is selection bias. There is no RCT available for T1b-T2 lesions, only for small renal masses <5cm, and this actually showed better survival following radical nephrectomy.

<https://pubmed.ncbi.nlm.nih.gov/21186077/>

Response: Thank you for pointing this out. We understand your concerns, but we believe the evidence you have presented is over ten years old and may not provide meaningful information to our readers. We believe that some patients can benefit from RAPN if carefully selected (e.g., solitary kidney patients, patients with bilateral renal

tumors, patients with CKD, etc.).

However, we have considered your feedback and made the following revisions to the text.

“RAPN for T2 tumor

There is no RCT available for T2 lesions, only for renal masses <5cm. It shows that survival after radical nephrectomy (RN) is higher than survival after partial nephrectomy (PN) (18). This RCT is evidence published more than 10 years ago, and there is an urgent need to build the evidence from RCTs about PN for T2 tumors.

The guidelines mentioned the indications for T2 tumors as follows: the risks and benefits of PN should be discussed with patients with T2 tumors. In this setting, PN should be considered, if technically feasible, in patients with a solitary kidney, bilateral renal tumors, or CKD with sufficient parenchymal volume preserved to allow sufficient postoperative renal function (22).

Van Poppel H, Da Pozzo L, Albrecht W, 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.

Ljungberg B, Albiges L, Bedke J, et al. *EAU Guidelines on Renal Cell Carcinoma 2023*.

147: The authors do not expand upon extra surgical possibilities for RAPN in highly complex tumors: e.g. the use of cold ischemia for prolonging ischemia times (peri-renal ice slush, cold saline surface irrigation, retrograde cooling through ureter or this novel intra-arterial cooling technique [https://www.euroscience.europeanurology.com/article/S2666-1683\(23\)01799-8/fulltext](https://www.euroscience.europeanurology.com/article/S2666-1683(23)01799-8/fulltext)) or even kidney auto-transplantation with on bench resection of the tumor. It would be interesting to have an additional paragraph on this.

Response: Thank you for pointing this out. We understand your concerns, but including a discussion on kidney auto-transplantation in a review may confuse the reader. However, considering your feedback, we will add a note stating, “patients need to be informed of the possibility of conversion to nephrectomy or kidney auto-transplantation.” Thank you for the introduction to advanced technology. We will incorporate a note on this in the manuscript.

“RAPN for high-complexity tumor

In RAPN for high-complexity tumors, WIT tends to be longer. Therefore, a unique surgical technique was reported to provide a solution to long WIT and to protect renal function. After incising the renal artery and vein, 4°C heparinized saline is administered intravascularly through a Fogarty catheter to maintain renal hypothermia while performing RAPN. The median warm and cold ischemia times were 4 min (interquartile range [IQR] 3–7 min) and 60 min (IQR 33–75 min), respectively. The

median rewarming ischemia time was 10.5 min (IQR 6.5–23.75 min). The median pre- and postoperative estimated glomerular filtration rate values at least 1 mo after surgery were 90 ml/min (IQR 78.35–90 ml/min) and 86.9 ml/min (IQR 62.08–90 ml/min), respectively (34).

An attempt to expand the feasibility of minimally invasive nephron-sparing surgery for highly complex renal masses has been made in this way.

De Backer P, Vangeneugden J, Berquin C, et al. Robot-assisted partial nephrectomy using intra-arterialrenal hypothermia for highly complex endophytic or hilar tumors: case series and description of surgical technique. *Eur Urol Open Sci* 2023;58:19-27.

211 ‘better oncological outcomes’: as compared to?

Response: Thank you for pointing this out.

The sentence pointed out has been removed to allow for other revisions.

227-228: ‘OPN is considered the standard treatment for tumors in solitary kidneys’: Is this true? Why open and not robotic? Reference? Or do you mean that PN is considered ... which is the case (imperative indication).

Response: The wording has been revised to address any potential confusion.

“RAPN for tumor in a solitary kidney

Nephron-sparing surgery is a good indication for tumors in solitary kidney patients. When performed by an expert, laparoscopic partial nephrectomy (LPN) is minimally invasive, and the WIT will not be prolonged. However, open partial nephrectomy (OPN) would be the first choice. if the surgeon lacks expertise and is considering renal function-sparing

In a study for tumors in solitary kidneys comparing 169 OPN cases with 30 LPN cases, there was no difference in renal function at 3 months postoperatively between LPN and OPN. The WIT of LPN was 9 minutes longer than OPN ($p < 0.0001$), and the chance of postoperative complications of LPN was 2.54-fold higher than OPN ($p < 0.05$). OPN might be the preferred nephron-sparing approach at this time for these patients at high risk for chronic kidney disease (39). However, the above was a long time ago, and with the rise of robotic surgery, RAPN has replaced OPN.”

In a retrospective comparison study for tumors in solitary kidneys between RAPN and OPN on perioperative and functional outcomes, 68 (45%) patients in the RAPN group and 82 (55%) in the OPN group were included. It was reported that postoperative renal function was comparable between the 2 groups ($p = 0.45$). Trifecta was achieved in 40% of the patients in the RAPN group and 33% in the OPN group ($p = 0.42$). A significant difference was observed for the length of stay, 5 days for the robot group versus 9 days for the open surgery group ($p < 0.0001$). The surgical approach did not modify functional results, and RAPN is a safe and efficient

method for managing tumors in solitary kidneys (42).

Focal therapy has emerged, as well as RAPN. However, studies of focal therapy for tumors in the solitary kidney are limited. A study comparing cryotherapy with PN for tumors in solitary kidneys showed no significant differences concerning postoperative renal function and OS. However, the recurrence rate was higher with cryotherapy (29% vs. 3.2%, $P=0.005$) (44). As mentioned above, there is a lack of evidence about focal therapy for tumors in a solitary kidney. RAPN is less invasive than OPN, and tumors in solitary kidneys are considered to be a good indication of RAPN at the moment.

Lane BR, Novick AC, Babineau D, et al. Comparison of laparoscopic and open partial nephrectomy for tumor in a solitary kidney. *J Urol* 2008;179:847-51.

Benichou Y, Audenet F, Bensalah K, et al. Partial nephrectomy in solitary kidneys: comparison between open surgery and robotic-assisted laparoscopy on perioperative and functional outcomes (UroCCR-54 study). *World J Urol* 2023;41:315-24.

Beksac AT, Corrigan D, Abou Zeinab M, et al. Long-term comparative outcomes of partial nephrectomy and cryoablation in patients with solitary kidneys: a single-center analysis. *Minerva Urol Nephrol* 2022;74:722-9.

233: please also nuance other treatment modalities in older patients here.

Response: Thank you for pointing out. Please follow the revision of line 31.

253: ‘Older age may not be a reason for avoiding RAPN’: please nuance. What about comorbidities? Anesthesiology? Other treatment options? If patients have a life expectancy <10 years and it is a slowly growing T1a mass, active surveillance is the therapy of choice in my opinion as 5-10 year outcomes are excellent (99% CSS).

Response: Thank you for pointing out. Please follow the revision of line 31.

281: ‘enucleation is associated with benefits such as avoiding renal artery clamping’: please clarify, arteries are often still clamped during enucleation

Response: Thank you for the suggestion. Satkunasivam R et al. detailed the technique for minimal-margin PN performed for procedures without renal artery clamping, which meant enucleation. Satkunasivam R et al. (2015) described an anatomic PN technique aimed at tumor-specific devascularization to eliminate global ischemia to the renal remnant. Therefore, a Systematic Review mentioned that enucleation is associated with benefits such as avoiding renal artery clamping, but this does not seem to be a generalization (Bertolo R et al., 2023). Therefore, we have supplemented it in the manuscript as follows.

(4.1. Standard resection vs. enucleation)

“Regarding nucleation to avoid arterial clamping, the concept of nucleation by tumor-specific devascularization aimed at eliminating global ischemia with a renal remnant,

according to Satkunasivam R et al. (57).”

Satkunasivam R, Tsai S, Syan S, et al. Robotic unclamped “minimal-margin” partial nephrectomy: ongoing refinement of the anatomic zero-ischemia concept. *Eur Urol* 2015;68:705-12.

Bertolo R, Pecoraro A, Carbonara U, et al. Resection techniques during robotic nephrectomy: a systematic review. *Eur Urol Open Sci* 2023;52:7-21.

286: ‘higher rate of PSM’: see comment for line 32

Response: Thank you for the suggestion. As the reviewer pointed out, the systematic review demonstrated that enucleation did not increase the rate of PSM. Based on this observation, we have revised this point.

(4.1. Standard resection vs. enucleation)

“In other words, the dilemma in the choice of surgical procedure between standard resection and enucleation is that enucleation involves cutting the interface between the parenchyma and pseudo-capsule. However, a systematic review supported that enucleation does not contribute to increased PSM (56).

301-323: one study shows shorter operative times in transperitoneal group, the other shorter operative times in retroperitoneal group, please discuss these different results.

Response: Thank you for the suggestion. As the reviewer pointed out, reports vary regarding operative time. A prospective study (RECORD2 project) found that the retroperitoneal approach required longer surgical times. Conversely, systematic reviews have shown that the retroperitoneal approach results in shorter surgical times. However, from the standpoint of generalizability, we believe that systematic reviews hold more weight. The retroperitoneal approach allows for a faster procedure because it reduces the time needed to secure the renal artery and eliminates steps such as avoiding bowel mobilization. However, in the case of veteran surgical skills, we believe that the advantage in terms of operative time might be less. Taking this into account, we have added the following to the manuscript:

(4.2. Transperitoneal vs. retroperitoneal approach)

“The reason why the operative time varied depending on the reports may be because of surgical skills. However, the retroperitoneal approach generally reduces operative time because the time required to secure the renal artery is reduced, and steps such as avoiding bowel mobilization are no longer necessary.”

378-381: please nuance and discuss that all studies regarding ‘selective clamping or no clamping’ were conducted on healthy patients with bilateral kidneys, small renal masses only (no or few T1b-T2), good renal function, no 3D (perfusion zone) models were used, often cross-over in RCT arms (e.g. CLOCK trial)... also

there were some positive results regarding benefit for short-term renal function outcomes.

Response: Thank you for the suggestion. As the reviewer pointed out, caution should be exercised in interpreting the results because the studies presented were clinical studies.

(4.3. Clamping vs. no-clamping)

“The crossover was observed in 14% and 43% of the on- and off-clamp arms. The study found no significant differences between the two groups regarding renal function outcomes despite a crossover, indicating that both approaches were comparable in patients with normal kidney function and two kidneys (68).”

“Clinical studies on selective clamping or off-clamping presented were conducted on patients with bilateral kidneys, small renal tumors (little to no T1b-T2), and good renal function. Thus, caution is required in interpreting the results.”

383: ‘inner’ and ‘outer’ renorrhaphy terms are not used. ‘Single layer’ might be confusing as it is not clear if this describes the inner or outer renorrhaphy. Please correct.

Response: Thank you for the suggestion. Since the presented systematic review used single- or double-layer renorrhaphy words, we have included them in the manuscript. We apologize for the confusing descriptions. We have added its explanation to the manuscript.

(4.4. Renorrhaphy vs. without renorrhaphy)

“Single-layer renorrhaphy is generally a technique in which medullary and cortical layers are sutured together in one layer, while double-layer renorrhaphy is a technique in which medullary and cortical layers are sutured separately in two layers.”

413 adjuvant therapy: only the KEYNOTE study is mentioned, no other studies (eg PROSPER, CHECKMATE... - al be it negative studies) are mentioned, but they should be to add nuance.

Response; Thank you for suggestion. We have added text as follows.

(Adjuvant therapy)

Several clinical trials have been conducted but failed to demonstrate the benefit of postoperative adjuvant therapy (83, 84) .

Motzer RJ, Russo P, Grünwald V, et al. Adjuvant nivolumab plus ipilimumab versus placebo for localised renal cell carcinoma after nephrectomy (CheckMate 914): a double-blind, randomised, phase 3 trial. *Lancet*. 2023;401:821-32.

Pal SK, Uzzo R, Karam JA, et al. Adjuvant atezolizumab versus placebo for patients with renal cell carcinoma at increased risk of recurrence following resection (IMmotion010): a multicentre, randomised, double-blind, phase 3 trial. *Lancet*. 2022;400:1103-16.

413 Neo-adjuvant treatment is not discussed. This could be an even more interesting paragraph as this actually might increase the indications for partial nephrectomy or help in patients with solitary kidney and large renal mass (imperative indication) ? (e.g.

<https://www.hindawi.com/journals/au/2021/6674637/>)

Response; Thank you for your interesting suggestion. However, the topic of this review is RAPN and is intended for patients with localized renal cell carcinoma. The mention of presurgical setting and Neo-adjuvant for patients with advanced and metastatic renal cell carcinoma confuses the reader.

The level of evidence for presurgical setting and neo-adjuvant for RAPN in existing articles is low, and mentioning them may discredit your journal, so we will refrain from mentioning neo-adjuvant in this review. We would be happy to contribute to your journal if you would like to include a special issue on the treatment of metastatic renal cell carcinoma. However, we had included the following statement in consideration of the reviewers' intentions.

(RAPN for T2 tumor)

In T2 renal masses cases, the indication for systemic neoadjuvant therapy is discussed. Several small studies (25, 26) have demonstrated a potential benefit of systemic neoadjuvant therapy (mostly with VEGFR-TKIs), including a modest reduction in tumor size and possible facilitation of locally advanced tumor resection and complex partial nephrectomy.

However, no randomized controlled trials support the use of neoadjuvant therapy. At this point, there is no indication for neoadjuvant therapy before planned surgical resection of the primary kidney tumor outside the context of a clinical trial (27)

Lane BR, Derweesh IH, Kim HL, et al. Presurgical sunitinib reduces tumor size and may facilitate partial nephrectomy in patients with renal cell carcinoma. *Urol Oncol* 2015;33:112.e15-21.

Lebacle C, Bensalah K, Bernhard JC, et al. Evaluation of axitinib to downstage cT2a renal tumours and allow partial nephrectomy: a phase II study. *BJU Int* 2019;123:804-10.

Canil C, Kapoor A, Basappa NS, et al. Management of advanced kidney cancer: Kidney Cancer Research Network of Canada (KCRNC) consensus update 2021. *Can Urol Assoc J* 2021;15:84-97.

Spelling/style/other:

14 inconsistent use of abbreviations

Response: We apologize for this point. We have edited them throughout the article.

21 'procedure choice': the article focuses on RAPN (not directly comparing it with RARN). 'Procedure' = RAPN or RARN. I think what you mean here is the surgical resection technique (enucleation/enucleoresection/...) or surgical approach (trans/retroperitoneal). Maybe 'surgical technique'.

Response: Thank you for the suggestion. As the reviewer pointed out, we changed the procedure choice to surgical technique.

(Abstract)

“This narrative review addresses the surgical precision dilemma by examining patient selection, **surgical technique**, and postoperative adjuvant therapy.”

30 ‘renal nephrectomy’: radical nephrectomy

Response: We apologize for this point. This was a misprint. We have changed it.

(Abstract)

“suggesting outcomes comparable with those of **radical nephrectomy**”

38 ‘of RAPN’: in RAPN

Response: Thank you for pointing this out. We have changed it.

(Abstract)

“**in RAPN** over standard clamping”

60 ‘overall survival’: add ‘(OS)’, which is now done in 130

Response: Thank you for pointing this out. We have changed it.

(Abstract)

“when RN is performed, there is a decrease in **overall survival (OS)**”

77 ‘procedure selection’: see 21

Response: Thank you for the suggestion. As the reviewer pointed out, we changed procedure choice to surgical technique.

(Introduction)

“We focused on patient selection, **surgical technique**, and postoperative adjuvant therapy”

103 (and throughout article): citations should be placed at the end of the sentence (before punctuation) and not in the middle of the sentence

Response: Thank you for the suggestion. As the reviewer pointed out, we changed them.

105 ‘collection system’: collecting system

Response: Thank you for pointing this out. We have changed it.

130 ‘overall survival’: see 60

Response: Thank you for pointing this out. We have changed it.

131, 133 inconsistent use of citation brackets throughout article (squared vs rounded brackets)

Response: We apologize for this point. They were misprints. We have changed them.

138-140 inconsistent use of comma's and 'for' when describing results of different T-stages

Response: We apologize for this point. They were misprints. We have changed them.

158: inconsistent use of 'PADUA' vs 'Padua' throughout article

Response: We apologize for this point. They were misprints. We have changed to PADUA throughout the article.

187-188: 'their initial experience in RAPN in 24 tumors from the ipsilateral kidney in nine patients': unclear

Response: Thank you for pointing this out.

We have revised the entire chapter you pointed out and deleted the expressions.

189, 193, 216...: MEDIAN values? Specify

Response: Thank you for pointing this out, I added 'median.'

288 inconsistent use of 'vs', 'vs.' and 'versus' throughout entire article

Response: We apologize for this point. They were misprints. We have changed them.

379 and other: 'superselective clamping' usually describes selective clamping of a tertiary branch or higher, otherwise 'selective clamping' is enough

Response: We apologize for this confusing description. We have changed them.