

Peer Review File

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Reviewer A

This is a manuscript on retroperitoneal robot-assisted nephrectomy. Although the manuscript is very well written, their retroperitoneal approach and technique are not novel at all. The other weak point is the small number of patients included in this study.

Major

Comment 1: Line 166: Do you really dissect the psoas muscle? Do you maybe remove flank pad and cut the fascia lateroconalis instead of cutting the psoas muscle?

Reply 1: The psoas muscle itself was not dissected, rather the perinephric fat was dissected off of the psoas muscle. This has been changed in the text

Changes in text: page 7, line 183

Comment 2. Line 221: You can simplify and summarize the medical history of patient #7. The patient's detailed record of treatment for heart failure or AMI is not necessary.

Reply 2: The postoperative course of patient #7 has been simplified

Changes in text: page 10, lines 246–251.

Comment 3. The discussion part is too long. Please simplify and revise the whole section.

Reply 3: The discussion has been shortened as where possible. Several other reviewers, however, asked for additional text be added to the discussion. We have attempted to satisfy all reviewer requests as much as possible.

Changes in text: Discussion section

Minor

Comment 1. Line 82: cell carcinoma (RCC) → renal cell carcinoma (RCC)

Reply 1: This has been changed

Changes in text: page 3, line 82

Comment 2. Line 87: remove “and”

Reply 2: The redundant “and” has been removed

Changes in text: Page 3, line 87

Reviewer B

I read with delight and curiosity your work about the technique and outcomes of robotic-assisted Retroperitoneal Radical Nephrectomy in order to increase the literature about this approach.

Overall I consider this paper very interesting; to follow my personal peer review:

- The abstract is clear and endearing. The aim of the study as well as materials and methods, results and conclusion are well-written.
- The introduction provides a complete and clear summary of what literature currently comprehends.
- Material and Methods, including preoperative outcomes, are well-defined.
- Surgical Technique, part of the article which personally liked most, is described appropriately and exhaustive. I think this part could inspire other centre.
- The results are very detailed for each outcomes.
- Discussion and conclusions offer some foods for thought, in order to, maybe increase the literature about this kind of technique.

However I suggest you to clarify some points:

Comment 1: In introduction it would be better specify that nephrectomy for upper tract urothelial cell carcinoma comprehends also ureterectomy, therefore for that kind of tumor a nephroureterectomy will be performed not only a nephrectomy.

Reply 1: In the introduction we have included that nephrectomy for upper tract urothelial cancer includes ureterectomy

Changes in text: page 3, lines 83-84.

Comment 2: It would be interesting, in my personal opinion, add the experience of surgeons mentioned in "Materials and Methods" in order to consider also the learning curve of young surgeon to reach the same outcomes.

Reply 2: The training and experience of the surgeons has been added to the methods section

Changes in text: page 5, lines 126-127.

Comment 3: In "Results" I'd like to know what is the median operative time (for those surgeons) in case of trans peritoneal approach.

Reply 3: Unfortunately we are unable to obtain the average operative times for transperitoneal nephrectomy for these surgeons as those cases are not included in the database used for this surgery. However in the discussion, published operative times of transperitoneal and retroperitoneal robotic partial nephrectomies are discussed so that the reader may extrapolate that information to radical nephrectomy

Changes in text: None

Comment 4: The sources sought includes interesting articles, nonetheless I suggest including the following papers in order to have a strong and multinational bibliography:

- Robot-assisted partial nephrectomy: 7-year outcomes. CARBONARA U. et al.
- Comparison between minimally-invasive partial and radical nephrectomy for the treatment of clinical T2 renal masses: results of a 10-year study in a tertiary care center. AMPARORE D. et al.
- Robot-assisted versus open surgery for radical nephrectomy with level 1-2 vena cava

tumor thrombectomy: a French monocenter experience (UroCCR study #73). VUONG N-S. et al.

Reply 4: These citations have been added

Changes in text: Citations 4, 5, and 6

Reviewer C

General Comments:

The manuscript is intriguing and relevant to current surgical practice with regard to the safety and feasibility of robotic retroperitoneal nephrectomy. The study addresses an important aspect of utilizing the retroperitoneal approach in patients with prior abdominal surgery. Overall, the study highlights the potential benefits of rRN and contributes valuable insights to the field. However, there are a few points that I believe require further discussion and consideration to strengthen the manuscript.

Specific Comments:

Surgical Technique:

Comment 1: The manuscript provides a clear description of the surgical technique employed for rRN. A supplementary video on the technique used could provide clear insight to readers.

Reply 1: A supplementary video has been added

Comment 2: The authors mention that different surgeons employed variations in the surgical technique. It would be beneficial to elaborate on these variations, providing a rationale for their choices and discussing potential implications on patient outcomes. Sharing tips and tricks from experienced surgeons would be highly valuable to readers.

Reply 2: The primary difference in technique was how one gained initial entry into the retroperitoneal space. Some surgeons used a laparoscopic trocar with a visual obturator and entered under direct vision, while other entered bluntly with a clamp and then performed finger dissection. A sentence has been added to discuss the difference in technique

Changes in text: page 6, lines 149-151.

Outcome Measures:

Comment 3: The study reports important outcome measures, such as operative time, estimated blood loss, length of stay, and complications. However, it would be beneficial to also include functional outcomes, such as postoperative renal function and overall patient satisfaction, as these factors are crucial when evaluating the success of the procedure.

Reply 3: Change in renal function postoperatively has been added to Table 3. We were unfortunately unable to capture patient satisfaction derived directly from the surgery. As the indication for surgery was varied in this patient population (ie some for cancer, some for chronically infected kidneys), it would be difficult to

control for other factors that could contribute to patient satisfaction levels after surgery.

Changes in text: Table 3 and page 10, lines 235-236.

Comment 4: Complications in Patient 7: Elaborating more on the cause of the complications with regard to the retroperitoneal approach can help readers maneuver their surgical technique in selected patients. Did the surgeons in your study rectify the same for future avoidance of this complication in patients who undergo retroperitoneal approach? If yes, needs to be mentioned.

Reply 4: While one patient did experience a small hydropneumothorax after surgery that did not require chest tube placement, it is not clear whether this was directly related to the patient's surgery or due to her underlying medical comorbidities. The published rate of pneumothorax following minimally invasive renal surgery is ~1%, and therefore we did not think any specific changes to our surgical technique were required.

Changes in text: None

Comparative Analysis:

Comment 5: While the study provides valuable data on rRN, it would be beneficial to compare the outcomes of rRN with other approaches, such as transperitoneal robotic nephrectomy or open nephrectomy. Discussing the advantages and disadvantages of the retroperitoneal approach in comparison to alternative techniques within the same study or multi-institutional external validation would offer readers a more comprehensive perspective on the topic.

Reply 5: There have been no direct comparisons of rRN to transperitoneal or open RN. We have, however, included a meta analysis of transperitoneal RN in the discussion and demonstrate that the perioperative outcomes of rRN in our study are comparable to what has been published regarding transperitoneal RN.

Changes in text: Page 15, lines 392-399.

Discussion:

Comment 6: The discussion section could be expanded on the potential impact of rRN on postoperative pain, recovery time, and cosmesis compared to other approaches would be of great interest to the readers.

Reply 6: On page 12 of the discussion we have included text postulating potential impacts of rRN on postoperative pain and recovery time (small muscle-splitting extraction incision, decreased visceral pain and ileus due to pneumoretroperitoneum rather than pneumoperitoneum). We do not feel that there is any difference in cosmesis as the number of ports are similar and the patient still requires an extraction incision).

Changes in text: Page 12, lines 303-306.

Comment 7: Addressing the limitations of the study, such as potential selection bias or the retrospective nature of the analysis, would enhance the transparency of the research.

Furthermore, discussing strategies to mitigate these limitations or proposing areas for future research would be valuable.

Reply 7: Limitations including selection bias and the retrospective nature of the review have been added to the limitations paragraph. The conclusion proposes future prospective studies to assess long-term outcomes.

Changes to text: Page 15, lines 408-409 and Page 16, lines 433-435.

Conclusion:

Comment 8: The conclusion should provide a concise summary of the study's main findings and their clinical implications. It would be helpful to emphasize the potential benefits and limitations of rRN, highlighting its role in the surgical management of patients with prior abdominal surgery.

Reply 8: A concise summary of the study's main findings has been added to the conclusion, as has a comment emphasizing the potential benefits in patients with prior abdominal surgery.

Changes in text: Page 15, lines 430–433.

In summary, the manuscript presents valuable findings on the safety and feasibility of robotic retroperitoneal nephrectomy. Addressing the points mentioned above, including visual aids in the form of a surgical video, and expanding the discussion section will further strengthen the manuscript. Sharing insights from experienced surgeons and comparing outcomes with alternative approaches will provide a well-rounded perspective on the topic. Overall, the study contributes to the growing body of knowledge in robotic renal surgery and will be of interest to robotic surgeons and urologists alike.

Reviewer D

Interesting paper with very detailed technical description, despite the limited number of cases.

Comment 1: I would like to have more infos concerning the previous experience of each surgeon fit rRPN or even open retroperitoneal approaches:

Reply 1: The training and experience of the surgeons has been added to the methods section

Changes in text: page 5, lines 126-127.

Comment 2: What are the author thoughts concerning reproducibility of such technique? (add some comments in the discussion)

Reply 2: We feel that rRRN is reproducible, however surgeons should first become adept at rRPN before attempting rRRN. This has been added to the discussion section.

Changes in text: Page 15, lines 420-423.

Comment 3: What are the advantages of the robotic platform over laparoscopy? Considering the narrow retroperitoneal space the high dexterity and degree of freedom of robot should represent an asset: expand the comment on this behalf, referring to other published comparisons of robotic vs laparoscopic approaches to nephrectomy (10.1089/end.2021.0026; 10.1001/jama.2017.14586; 10.1097/TP.0000000000004618)

Reply 3: The part of the discussion section which discusses benefits of robotic nephrectomy over laparoscopic nephrectomy has been expanded and the reviewer's points have been incorporated. The first recommended citation has been added (citation 27). The second recommended citation is already present (citation 2). We feel that the third recommended citation is outside the scope of this manuscript as it is regarding laparoscopic versus robotic donor nephrectomy. Changes to text: Page 14, lines 364-371 and citation 27

Comment 4: Last, could you provide a short video as a supplement? It would be really appreciated by readers

Reply 4: A supplementary video has been added

Reviewer E

I read with interest your manuscript entitled: "Technique and Outcomes of Robotic-assisted Retroperitoneal Radical Nephrectomy".

Comment 1: First, English should be revised as there are grammatical errors, e.g., transpeitoneal in the abstract.

Reply 1: This error has been fixed

Changes in text: Page 2, line 39

Comment 2: The study is very interesting because there is still much debate in the literature about the retroperitoneal approach, which is mainly intended for selected cases. However, the retroperitoneum is the surgical space that characterizes the urologist and therefore should always be a surgical asset to ensure that the patient can choose the best approach regardless of technique confidence. In this regard, in support of the surgical feasibility and noninferiority of the technique I recommend reading and citing in the discussion this paper:

- Carbonara U, Crocerossa F, Campi R, Veccia A, Cacciamani GE, Amparore D, Checcucci E, Loizzo D, Pecoraro A, Marchioni M, Lonati C, Sundaram CP, Mehrazin R, Porter J, Kaouk JH, Porpiglia F, Ditunno P, Autorino R; YAU-EAU Kidney Cancer Working Group. Retroperitoneal Robot-assisted Partial Nephrectomy: A Systematic Review and Pooled Analysis of Comparative Outcomes. *Eur Urol Open Sci.* 2022 Apr 26;40:27-37. doi: 10.1016/j.euros.2022.03.015. PMID: 35515269; PMCID: PMC9062267.

Reply 2: We appreciate the reviewer's recommendation and agree that this article is a valuable addition to the literature. It has been added to the manuscript.

Changes in text: Citation 37

Comment 3: The most important thing to pay attention to in this paper is the substantial difference between retroperitoneal partial or radical nephrectomy versus nephroureterectomy. This is because the surgical technique for nephroureterectomy has a different indication (UTUC) and is obviously a more complex procedure and difficult to compare with the others. That's why I recommend that you evaluate this work:

- Veccia A, Carbonara U, Derweesh I, Mehrazin R, Porter J, Abdollah F, Mazzone E, Sundaram CP, Gonzalgo M, Mastroianni R, Ghoreifi A, Cacciamani GE, Patel D, Marcus J, Danno A, Steward J, Satish Bhattu A, Asghar A, Reese AC, Wu Z, Uzzo RG, Minervini A, Rha KH, Ferro M, Margulis V, Hampton LJ, Simone G, Eun DD, Djaladat H, Mottrie A, Autorino R. Single-stage Xi® robotic radical nephroureterectomy for upper tract urothelial carcinoma: surgical technique and outcomes. *Minerva Urol Nephrol.* 2022 Apr;74(2):233-241. doi: 10.23736/S2724-6051.21.04247-8. Epub 2021 Mar 29. PMID: 33781022. The retroperitoneoscopic technique also allows considerable advantages for associated lymphadenectomy as can be seen in this article:

- Wu Z, Li M, Wang J, Veccia A, Xu Y, Zhang C, Ren J, Yin L, Chen M, Wang J, Xu D, Zhang Z, Liu B, Yang B, Xie L, Qu L, Wang L. Pure retroperitoneoscopic extravesical standardized seeable (PRESS) excision of distal ureter and bladder cuff in radical nephroureterectomy: step-by-step technique. *Minerva Urol Nephrol.* 2021 Jun;73(3):392-400. doi: 10.23736/S2724-6051.20.03711-X. Epub 2020 Apr 10. PMID: 32284528.

Therefore, I recommend revising the paper with the advice given: correcting some grammatical errors, implementing the discussion also with the work that was recommended, and differentiating well retroperitoneoscopic partial or radical nephrectomy from retroperitoneoscopic nephroureterectomy as they have different indications, different patients, and different surgical techniques.

Comment 3: Thank you for the comments. We agree that there are specific differences between nephroureterectomy and radical nephrectomy. We have added a comment discussing the use fo the robotic platform for performing nephroureterectomy and have added the two suggested citations.

Changes in text: page 15, lines 389-390. Citations 31 and 32.

Reviewer F

The Authors performed a descriptive, retrospective analysis of a cohort of 12 patients scheduled for robot-assisted radical nephrectomy, simple nephrectomy, or nephroureterectomy, all performed with a retroperitoneal approach. The topic is of interest considering the paucity of similar studies available in literature.

Comment 1: Results: please consider adding a brief description of the recommendations for surgery in the text (for example for renal cancer the median diameter of the lesions, the location ...).

Comment 1: The specific indications for surgery have been added to the first paragraph of the results section

Changes in text: page 9, lines 214-218.

Comment 2: Please consider adding more details on the previous surgeries received by the patients (which kind of surgery did they receive and why?....). I suggest to add these details in Table 1 which is very limited with the few variables reported.

Comment 2: Details on the previous surgeries has been added to Table 2, as this is the table where the indication for a retroperitoneal approach is listed

Changes in text: Table 2

Comment 3: In the materials and methods, the authors reported that complications were scored according to Clavien Dindo, but they were simply described in the results section. Please provide the number of complications in the text also according to Clavien Dindo classification.

Reply 3: The specific Clavien Dindo grades of each complication has been added to the results section and has been added to Table 2

Changes in text: Page 10, lines 245, 251, and 253. Table 2

Comment 4: Discussion, line 260: "Thus, we felt this robotic approach reduced overall incision pain and morbidity". Being only a descriptive analysis, please consider rephrasing this sentence because these outcomes were not addressed except from a descriptive point of view.

Reply 4: We agree that this study did not specifically assess postoperative pain. However it has been reported and is widely accepted that minimally invasive kidney surgery results in decreased levels of postoperative pain compared to open kidney surgery. For patients like the ones in this cohort, where minimally invasive nephrectomy via a transperitoneal approach would be extremely challenging, retroperitoneal robotic nephrectomy is an attractive option as these patients would otherwise have to undergo an open procedure. We have rephrased the sentence and have added a citation supporting decreased pain for minimally invasive nephrectomy compared to open nephrectomy.

Changes in text: Page 12, lines 302–306.

Comment 5: Discussion: I believe that one of the most important points is the selection of eligible patients. Please consider adding a paragraph related to this aspect. Second, I would stress more the benefit of this approach on the standard transperitoneal.

Reply 6: Indications for a retroperitoneal approach is listed in the first paragraph of the introduction and include hostile abdomens from previous abdominal surgery, the presence of a urinary or intestinal diversion, the presence of a peritoneal dialysis catheter, morbid obesity, and pregnancy. Benefits of the retroperitoneal approach are mentioned throughout the manuscript, both in the introduction and discussion. These include avoidance of peritoneal cavity structures, more direct access to the renal hilum, and avoidance of the large abdominal pannus in morbidly obese patients.

Changes in text: None

Comment 6: Consider adding the lack of oncological outcomes among limitations.

Reply 6: This has been added to the text

Changes in text: Page 16, lines 417-418.

Comment 7: The tables are too limited and they are not adding a lot of information to the text. For example, in table 2 I would specify which type of prior abdominal surgery ... in table 3 (perioperative results) I would report the median postoperative renal function, postoperative Hb, rate of conversion, intraoperative and postoperative complications according to Clavien Dindo, positive surgical margins, the median follow up ...

It doesn't make so much sense to report a table with only 3 variables.

Reply 6: The type of prior abdominal surgery has been added to Table 2. Postoperative complications according to Clavien Dindo grade are listed in Table 2. Final pathology including margin status is listed in Table 2. Change in renal function postoperatively and change in Hgb has been added to Table 3. Only one patient underwent a "conversion" (conversion from partial to radical nephrectomy due to intraoperative tumor spillage). As this is explained in the results section and we did not feel it was necessary to include in table format

Changes in text: Table 2 and Table 3

Comment 8: How was the surgical experience of the 3 surgeons involved?

Reply 8: The training and experience of the surgeons has been added to the methods section

Changes in text: page 5, lines 126-127.

Comment 9: I would report the STROBE statement as supplementary material.

Reply 9: The STROBE checklist has been submitted with the manuscript as instructed

Comment 10: Could you please add some details regarding the postoperative surgical drain?

Reply 10. A surgical drain was placed only if there was suspected leak after bladder cuff closure when performing a nephroureterectomy or if performing a simple nephrectomy for a chronically infected kidney. This has been added to the text.

Changes in text: Page 9, lines 210-211.

Reviewer G

I applaud the authors for this case series in which they present their retroperitoneal approach for nephrectomy.

In this paper authors extensively describe the retroperitoneal technique and present perioperative outcomes of patients treated with this approach at their institution.

Some points need to be clarified by the authors:

Comment 1: Despite the ten years period taken into account within the case series authors managed to include a limited sample size which hampers the quality of the results

Reply 1: We agree that the small sample size is a notable limitation and this has been added to the manuscript.

Changes in text: Page 15, lines 408-409.

Comment 2: In my opinion a clear definition of inclusion and exclusion criteria within the materials and methods paragraph would make easier for the reader to understand the population addressed in this study

Reply 2: Inclusion criteria has been added to the methods section.

Changes in text: Page 5, lines 128-131.

Comment 3: Authors may consider adding also functional post-operative outcomes (post-operative creatinine, eGFR) for greater completeness of the results

Reply 3: Change in renal function postoperatively has been added to Table 3. We were unfortunately unable to capture patient satisfaction derived directly from the surgery. As the indication for surgery was varied in this patient population (ie some for cancer, some for chronically infected kidneys), it would be difficult to control for other factors that could contribute to patient satisfaction levels after surgery.

Changes in text: Table 3 and page 10, lines 235-236.

Comment 4: As stated by the authors occasionally opening of the peritoneum could occur, I would suggest to mention how many times this happened, in which stage of the surgical procedure and if it was due to any particular anatomical condition encountered during the surgery.

Reply 4: More details regarding this portion of the procedure and the number of patients in which a peritoneal hole was made has been added.

Changes in text: Page 6, lines 161-165.

Reviewer H

The authors presented an interesting article on Retroperitoneal Robotic Radical Nephrectomy.

The study is well designed, methods are well described and reproducible.

I have few comments to add:

Comment 1: although literature is poor on the topic I think the sample size presented is very limited (12 cases in ten years!) and this can reflect a scarce reproducibility of the technique, as also an impossible learning curve's estimate.

Reply 1: We agree that the indications for this technique are relatively uncommon, which lead to the small sample size in this study. The small sample size has been

added as a limitation. Regarding reproducibility, we feel that rRRN is reproducible, however surgeons should first become adept at rRPN before attempting rRRN. This has been added to the discussion section.

Changes in text: Page 15, lines 408-409. Page 16, lines 420-423.

Comment 2: Following the previous comment, to better estimates the feasibility of the technique a prospective and multi-institutional study would be more helpful in order to standardize the technique and to show its real pro/cons.

Reply 2: We agree with the reviewer, and have added that further prospective, multi-institutional studies are needed.

Changes in text: Page 16, lines 433-435.

Comment 3: I really appreciate the tips and tricks on ports' placement to avoid instruments' clashing, however I think the authors must also report limitations of the technique (reduced working space, unfamiliar landmarks/anatomy).

Reply 3: In the introduction section we discuss the anatomic unfamiliarity among surgeons and the smaller working space in the retroperitoneum. In the discussion section we also have added that while we believe this technique to be reproducible, we recommend surgeons first become adept at rRPN before attempting rRRN.

Changes in text: Page 15, lines 420-423.

Comment 4: A pain-score analysis would be helpful to strength the advantage of avoiding peritoneum and all the issues correlated with pneumoperitoneum and bowel irritation.

Reply 4: While we agree with the reviewer's comment, unfortunately systematic pain scores were not obtained postoperatively for these patients. We do discuss that minimally invasive kidney surgery is associated with less pain compared to open surgery.

Changes in text: None

Comment 5: Which is your Co2 set-up (pneumoperitoneum level) during retroperitoneal surgery?

Reply 5: AirSeal was used and pneumoretroperitoneum was established at 12 – 15 mm Hg. This has been added to the text.

Changes in text: Page 7, lines 170-171.