

Peer Review File

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Review Comments

Reviewer A

Dear Authors,

I read with interest your manuscript about your centre step-by-step technique of robotic radical nephroureterectomy.

The title is clear, the abstract is well structured, the body of the study is precise and accurate in every subpoint.

The article is well written, it is understandable in every point.

I think there are no major revision-limitation and the article can be published with some small changes:

- The overview of advancing surgical technology and standard operative approaches in RNU/BCE is interesting but it is not entirely clear the search strategy and the literature database that was used. It would also be interesting to be able to view the filters used to ensure reproducibility of the search.

Reply: Thank you for your recommendation. As this manuscript is essentially a review of our technique, no dedicated literature review was performed. Manuscripts included as references were those known in the literature to us previously and felt important to include for perspective on the development of this technique over the years.

Changes in text: None.

-More citations from this publishing house would be recommended. I suggest discussing the following:

° Pure retroperitoneoscopic extravesical standardized seeable (PRESS) excision of distal ureter and bladder cuff in radical nephroureterectomy: step-by-step technique; Zhenjie WU; Minerva Urology and Nephrology.

° Time to safety omit bladder cuff removal for low-risk upper tract urothelial carcinoma; Alberto Abrate et al; Minerva Urology and Nephrology.

° Neoadjuvant systemic therapy in patients undergoing nephroureterectomy for urothelial cancer: a multidisciplinary systematic review and critical analysis.

° Single-stage Xi robotic radical nephroureterectomy for upper tract urothelial carcinoma: surgical technique and outcomes; Alessandro Veccia et al; Minerva Urology and Nephrology.

Reply: We have updated the manuscript to include these recommended references, with the exception of the PRESS article as our focus is robot-assisted NU and that article discusses a laparoscopic (retroperitoneoscopic) approach and the Veccia et al article because it was already referenced in the manuscript (see table).

Changes in text:

Abrate et al: Referenced in last paragraph of introduction.

Wu et al: Referenced in second paragraph of section 3.1 Pre-operative evaluation.

Reviewer B

Excellent narrative on the authors' experience and approach to robotic nephroureterectomy. However, it will be helpful to have some photos to aid beginners to better understand:

1) patient positioning

2) port placement

Reply: We have added a photo demonstrating the standard transperitoneal port placement for RNU/BCE. A HIPAA compliant photo of a patient in the flank positioning described is not available and thus not included,. The description of this positioning is comprehensive in the text, however.

Changes in text: Added figure to Section 3.3 Abdominal Insufflation and Port Placement

A surgical video will be a fabulous adjunct as well.

Reply: A step-by-step surgical video has previously been put together by our team. Please see: Pathak RA, Crain NA, Hemal AK. Radical robotic nephroureterectomy with bladder cuff excision: overview of surgical technique. Urology Video Journal 2021:100119. This article is referenced in this paper.

Changes in text: None.

Reviewer C

This is a very detailed manuscript describing robotic RNU/BCE/LND, step-by-step and refined over many years and procedures. It is generally well written and provides good detail that most readers should be able to understand, visualize, and potentially repeat. It occasionally seems overdetailed, risking loss of attention from the reader – more detail is better than less, but it may benefit from review and exclusion of any statements that may be extraneous. There are also other descriptions of technique in the literature, so ensuring the reader knows why this publication is different is important. On quick review it appears LND may not be as commonly described in complete procedure descriptions.

This manuscript would greatly benefit from figure or photos of positioning, port placement, and some intraoperative steps. Additionally, discussion of some outcomes would be interesting as robotic RNU used in the setting of higher risk disease (T3+,N+) is not commonly recommended and historically has led to concern for recurrences in abnormal locations like port sites.

Comments: Thank you for your insightful feedback. We added a photo of port placement. Our team has previously published a detailed surgical video regarding other steps. This manuscript is a more up-to-date review of current approach with data summarized in the table regarding other similar approaches/outcomes. We also

made a point to comment on the procedure optimization over the last two decades. We are preparing a manuscript (to be published) that reviews outcomes as you have recommended and those data are not yet immediately available for publication in this manuscript.

Ref: Pathak RA, Crain NA, Hemal AK. Radical robotic nephroureterectomy with bladder cuff excision: overview of surgical technique. Urology Video Journal 2021:100119.

Below are some detailed comments that the authors should consider:

Abstract

Lines 29-31: This sentence does not make sense to me

Updated sentence in referenced text to improve readability.

Lines 32-34: Needs to be rewritten it uses the word review 3 times in an awkward fashion

Updated sentence in referenced text to improve readability.

Lines 43-46: Would consider excluding the sentence “This surgical technique...due to imperative indications” as it seems a little random in the abstract conclusions

Introduction

This is a point we wanted to make at the outset – surgery is generally safe and reliable in elderly patient and those with advanced co-morbidities if needed for.

Updated the sentence in referenced text to improve readability.

Line 66: What specifically about renal pelvis tumors vs other upper tract locations makes RNU gold standard?

Segmental ureterectomy/reconstruction may be an option in those with non-renal pelvis (ie, ureteral) tumors. I've updated the sentence to remove gold standard as this could be misleading.

Line 93: Use of “honed” is a little awkward sounding here would consider refined or something similar

Changed to “improved” in the referenced text

Main Body

3.1 Is there data for bowel prep?

This is included here to describe all aspects of our approach. A discussion of the data surrounding bowel prep is outside the scope of this manuscript.

3.2 Would benefit from illustration or pictures of positioning

A HIPAA compliant photo of a patient in the flank positioning described is not available and thus not included,. The description of this positioning is comprehensive in the text, however.

3.3 Would benefit from illustration or pictures of port placement with diagram of which robotic instruments are where for the renal dissection vs the bladder cuff.

A photo of port positioning has been added with a detailed description of the renal dissection and bladder cuff in the referenced text.

3.6

This is interesting that clips are used in addition to staplers as many people feel clips create risk for difficulty with stapling – any comment on this? Are there instances where they require over-sewing of the vessels?

Based on surgeon experience this practice had been adopted over time. The clips are placed away from the surgical stapler so as not to interfere with the stapling.

Is there any data regarding atherosclerosis and associated failure of stapling in the elderly population?

Based on surgeon experience – not aware of data specifically addressing this.

There is comment regarding non-adrenal-sparing if concern for local tumor invasion – do they have many in their series that have had clinical or pathologic T3+ disease and do they know if they have any abnormal recurrence outcomes as it is not recommended in guidelines at this time to perform MIS RNU when there is concern for invasion.

Long-term outcomes data to be published in forthcoming manuscript, which is in the process of being developed. In general, indication for RNU/BCE in advanced disease would be for symptomatic control (eg obstruction/infection/gross hematuria).

3.8

Ultrasound for localizing the lesion is interesting

A series of photos showing steps of bladder cuff excision and closure would be helpful as this is one of the most nuanced parts in my opinion.

A photo of using ICG for localization would be helpful.

No photo available for ICG however described comprehensively in the text. Please see reference for video of approach (this was included as a reference in this review).

Ref: Pathak RA, Crain NA, Hemal AK. Radical robotic nephroureterectomy with bladder cuff excision: overview of surgical technique. Urology Video Journal 2021:100119.

3.10

Illustration of template would be of benefit

Again, any odd recurrences? Some people use a bag each time for node extraction vs directly through the port.

Photo of template can be seen in the below reference as previously published.

Outcomes to be published as described above.

Ref: Pathak RA, Crain NA, Hemal AK. Radical robotic nephroureterectomy with bladder cuff excision: overview of surgical technique. Urology Video Journal 2021:100119.

3.13

Line 407: HALNU initialism is not necessary since it is never repeated

Thank you for catching this – updated in the line referenced above in-text to remove this reference.

Reviewer D

In their review "Refined step-by-step technique of robotic radical nephroureterectomy in the management of upper tract urothelial carcinoma" Timothy et al. nicely describe their experience in treatment of UTUC. The study is well written, easy to understand and relevant to the reader.

However, I have some minor comments:

1. An "Abbreviation section" is missing, please add.

Added as page following title page.

2. I would recommend to include the following citations in the introduction part to show international trends for treatment of UTUC as well as MIBC; e.g. in Germany robotic approach is rapidly increasing and more radical approach is also seen in elderly patients:

Herout R, Baunacke M, Flegar L, et al. Upper tract urothelial carcinoma in Germany: epidemiological data and surgical treatment trends in a total population analysis from 2006 to 2019. *World J Urol.* 2023;41(1):127-133. doi:10.1007/s00345-022-04219-5

Flegar L, Kraywinkel K, Zacharis A, et al. Treatment trends for muscle-invasive bladder cancer in Germany from 2006 to 2019. *World J Urol.* 2022;40(7):1715-1721. doi:10.1007/s00345-022-04017-z

Comments: Citations added along with a brief note of international adoption of robotic surgery

Changes in text: Added to introduction, end of paragraph 1

Reviewer E

We thank the Authors for providing a step by step technique on robotic radical NU for UTUC.

The description of the technique is clear and seems feasible, however, I have some concerns about the structure of the paper.

Abstract:

In the background and objective section the objective of the study is not mentioned.

Reply: Thank you for bringing this oversight to our attention.

Changes in text: The structure of the abstract has been revised to ensure the objective is clearly stated in that section.

Methods in the abstract are written in a confusing way for the reader. Moreover, the word review is redundant (3 times). Please write again.

Reply: Thank you for bringing this to our attention.

Changes in text: Sentence structure revised as recommended to improve readability. This suggestion had been made by another reviewer as well.

Introduction:

This section is too long.

Subheading in the introduction is confusing for the reader.

Comment: Thank you for your suggestions. We felt it very important to provide a historical perspective for the robot-assisted approach and to include reference to seminal articles over the years. This frames the article.

Changes in text: None

Methods:

Seems this is a review of internal cases plus a narrative review of literature? This is not mentioned in the title. Moreover, authors should choose for a systematic review according to Prisma guidelines.

Reply: The purpose of this manuscript was to serve as a descriptor of surgical technique and brief review of seminal articles in the literature that have impacted the development of this technique over time. This is not intended to be a systematic review.

Changes in text: None

Main body

Authors should describe how many patients were performed with this technique in their center table 1 of the perioperative characteristics of the cohort would enhance this paper.

Reply: We are analyzing data at our center for all cases to produce a forthcoming manuscript. These data are not immediately available to include in this review.

Changes in text: None

The discussion section is missing

Comment: Thank you for bringing this oversight to our attention.

Changes in text: The subheading for the final section prior to the Conclusions section has been updated as "Discussion" rather than including it in the main body.