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January 24, 2016

Dear Sir/Madam

Please note that all of the editor's queries have been addressed and reconciled.

Accompanying this letter is a point by point response to the reviewer comments. The manuscript is highlighted yellow to reflect these changes.

Syed M Jafri 1/29/16

Name: Syed M Jafri

Signature: Date: 1/29/16

Name: David Qi

Signature: Date: JAN 27/2016

Response to Reviewer #1

The paper is a review over treatment modalities for patients having 'a small renal mass'. The whole focus is on preservation of renal function after treatment. Based on papers including two kidneys or one kidney respectively, the conclusion of the review is that thermal ablation is better than partial or radical nephrectomy regarding preservation of renal function in the post treatment period. The topic was evaluated by follow-up studies after months to years. The thermal ablation procedure seems especially relevant in patients with preexisting renal - and/or cardiovascular disease. This analysis of renal function after treatment is interesting.

However, the paper lacks central information about the nature of 'small renal masses'. In the last paragraph of the information, it is suggested that the paper is about small renal tumors with low grade, a slow growth rate and low metastatic potential. Information about the type of tumor must be given in the review for each paper reviewed. In addition, it should be stressed that the information is not based on RCT's but on observational studies. The problem regarding survival should also be discussed in the review. It goes without saying that renal function after treatment is important, but survival is more important. Information about this aspect should be added to the review. I suggest that the title is clarified by using 'small renal tumors' instead of 'small renal masses', if the context of the paper is about renal tumors.

We appreciate the reviewer's thoughtful commentary and would like to provide the following responses.

- 1. The discussion of small renal masses is quite an extensive topic that can encompass an entire review amongst itself. The intent here was to focus on one particular aspect of kidney tumor management that would be particularly relevant for a Nephrology journal. As such, a more detailed review of small renal mass biology is limited. The introduction has been amended to include references regarding the biology of SRMs.**
- 2. We have now included a sentence to highlight that the data are based on observational studies and not RCT.**
- 3. There are a number of manuscripts written about the oncologic efficacy or thermal ablation compared with partial and radical nephrectomy. Furthermore, several have compared cryoablation and RFA. We agree that oncologic outcomes are important. However, it would require an entire review article to address the oncologic outcomes comparing ablation and other modalities. Given the target audience, we believe that the kidney function outcomes are**

most important to highlight. We have added several references to further aid the reader interested in oncologic outcomes and relevant studies.

4. We appreciate the reviewer's comments regarding terminology. The American Urologic Association recommends the term small renal masses as the term of use according to their 2010 AUA Small Renal Mass Guidelines statement. We would respectfully argue to maintain this name due to convention.

Reviewer #2

Dr. Raman and his colleagues reviewed the renal function outcome of RN, PN and thermal ablation (RFA and CA) in the management of small renal mass. They focused on the renal function outcome of thermal ablation and its advantages in managing patients with solitary kidney. It is a well written review and ready for publication. I have some minor suggestions to improve the quality:

1. In "Renal function following surgical extirpation", authors stated "deterioration of renal function dose occur in a significant percentage of patients following PN". Would you provide us a detail number (how many percentage) regarding the issue?

We appreciate the reviewer's comments. To address this percentage we have included a reference to a 2015 systematic review article which highlights a 20% decline in renal function in the affected kidney.

2. Is there any different of tumor outcome between PN and RN ? How about the tumor outcome of RFA/CA when compared to PN. Please summary the data when possible. I think patients treated with renal mass worry about tumor outcome more than the renal function decline, as renal dysfunction is treatable, while the tumor recurrence should be a disaster.

The reviewer has a good point regarding the oncologic effectiveness of thermal ablation, partial, and radical nephrectomy. In short, this question has been actively debated throughout the literature, particularly when considering thermal ablation and extirpation. Furthermore, adequate discussion merits and entire review article to itself. Given the focus of the target journal, our goal was to investigate the kidney function outcomes as opposed to oncologic outcomes. We have, however, provided a more extensive reference list for the interested reader to further investigate the oncologic efficacy between therapies.

3. I suggest author revise the tile "Renal ablation and kidney function changes" to "Renal function changes after renal ablation", which match other two sub-titles "Renal function following surgical extirpation", "Kidney function changes in a solitary kidney model".

We concur and have changed this title

4. "Subequently" on page 7 should be "subsequently"

Thank you. We have corrected.

5. In the introduction authors stated “ablative therapies as an alternative to extirpative surgical intervention for select patients.(10, 11)”. Is there any guideline or consensus on which group of patient (“ selected” patients except these solitary kidney)will be benefited from RFA/CA therapy or how to select suitable patient for the RFA/CA treatment. Adding this information will make the review more constructive.

The best consensus statement for the use of thermal ablation originates from the American Urologic Association Small Renal Mass guidelines. This is now extrapolated to a greater degree in the Introduction.

Reviewer #3

Article "Kidney function outcomes following thermal ablation of small renal masses" by Raman JD et. al. according to my opinion, is acceptable for publication but after revisions. This article is interesting for persons involved in the field of kidney cancer. In the text there is need for some revisions: a) In the section "Renal ablation and kidney function changes" authors stated: Furthermore, patients undergoing radical and partial nephrectomy were 34.3 and 10.9 times more likely, respectively, to develop stage 3 CKD compared to RFA counterparts. According to previous text it is not more times but percentage (%).

We appreciate the reviewers comments. The manuscript from Lucas and colleagues specifically reported on two factors. Firstly, they looked at the % of patients developing new onset CKD. Secondly, they reported on the increased likelihood of developing CKD. The above mentioned numbers of 34.3 and 10.9 are fold increases for CKD compared to thermal ablation and are not percentage increases. We hope this clarifies the reviewers comment and certainly review of the Lucas et al. article would further support this explanation.

b) The literature is not written in the unique and consistent way. For example The Journal of Urology is The journal of urology, The Journal of urology and J Urol.

We appreciate the reviewers comments and have uniformly formatted this manuscript using Endnote. We hope this will maintain consistency in names of journals.