Reply to the reviewer's comments

Reviewer number 1

All statements on oncological and functional outcomes have yet to be validated in the literature. There are no prospective randomized trials but only meta-analysis and retrospective multicentric works. At this time it is not possible to claim that the TaTME could be the gold standard for oncologic resection of low rectal cancers. Prospective randomized studies between TaTME and laparoscopic TME are required. The international TaTME registry assemble many cases also of centers with little experience and therefore the conclusions reported have low scientific evidence. At present it can only be said that the technique is safe and feasible.

We agree with the reviewer. The results have been tempered to highlight that outcomes reported are short and mid term, and no large RCT studies have been completed to make definitive statements from.

The references are many and complete. However, the work represents the evolution of the surgical technique rather than a review on the TaTME.

We agree, and have titled the work as such.

Reviewer number 2

1. There were plenty reviews and meta-analysis about the TaTME these several years. And not much of new opinion were given in this article leading to the lack of innovation.

We regret that this reviewer did not see value in our work and appears biased and disparate from the other reviewers. Although many systematic reviews and meta-analyses have been published, this review uniquely provides updated data on outcomes, explores functional as well as oncologic outcomes, the structured education and training movement, and offers possible future directions and expanded indications from high volume TaTME surgeons. We thank the reviewer for considering the revision with all comments from the reviewer addressed.

2. Only advantages of the TaTME were listed. But the indications and the disadvantages were not discussed.

New sections discussing the indications for and disadvantages of TaTME were added to the manuscript.

There are no completed large RCT studies in this field, and the results of the present researches are not sufficient to make such definitive conclusion on the superiority of the TaTME

The results have been tempered to highlight that outcomes reported are short and mid term, and no large RCT studies have been completed to make definitive statements from.

3. There should be tables to list the reviewed articles and their main results when presenting the performance of the TaTME.

As highlighted by the reviewer, there are no controlled trials completed yet, which would warrant the evidence-based comparative table.

Reviewer number 3

This is a well written and interesting paper and more balanced than previous similar publications. I have a few minor corrections and requests for expansions.

We thank the reviewer for the favorable appraisal of our work.

Some of the authors by their email addresses are part of the AIS Channel which has been promoted in the review and as such should be mentioned in the potential "Conflict- of- interest statement."

The conflict of interest statement was revised to include the relation of the authors with the AIS channel.

The authors wisely in the document have stated the need for controlled clinical trials as the next step as has been done in laparoscopic and robotic rectal cancer surgery. This should be reiterated in the conclusions.

The need for controlled clinical trials to further validate the utility of TaTME in treatment of rectal cancer was added to the conclusion as suggested.

Mention of who will lead these and when these trials may start would be relevant particularly with the learning curve mentioned as being 20 cases and that the largest pooled review of the international database is only more than 700 cases?

A statement about who will lead the trials and the proper timing to start them was added to the manuscript.

The 10% quoted urethral injury rate is really quite concerning and what do the authors think is acceptable as this is close to zero in other techniques such as open or laparoscopic trials? Given this extremely concerning figure the authors should also raise the concern of urethral sphincter damage and risks of incontinence and urinary dysfunction which would go inherently with any procedure that has this concerning full injury rate.

The acceptable complication rate would be close to zero, as with other approaches. As expected, with new procedures, new procedure-specific complications may arise, but we expect the incidence of urethral injury would decline after adequate experience. As stated in the manuscript,

adequate training and mentoring, meticulous dissection in the anterior plane, and intra-operative identification of the urethra using fluorescent imaging may minimize the risk.

The authors should discuss what would be the primary and secondary outcomes of a future or planned controlled trial as it is not ethically justified to start a new technique for a common cancer with such potential positive and negative outcomes without this trial?

Suggestions of the primary and secondary outcomes of future controlled trials on TaTME were added to the manuscript.

For those that have been doing the technique the importance of the pursestring cannot be underestimated as the risk for leakage of cancer cells and liquid stool is a major concern for most. Can the authors give some data on techniques to minimise risk and is there any published incidence of leakage during the procedures? Similarly can the authors also discuss the potential for implantation of cancer cells and/or bacteria inherent in a transanal dissection platform presacral spaces? As the move is towards higher rectal cancers and higher dissection and transections the platform is operating for several hours thru a segment of anus and lower rectum that is opened. While vigorous irrigation is the defence we don't know the efficacy of this and this should be mentioned in a balanced assessment of the pros and cons of this technique.

The risk of leakage of cancer cells and liquid stool as well as possibility of translocation during the transanal approach was highlighted in the technical section of the manuscript. There are no published studies reporting the incidence of leakage of cancer cells with this emerging technique. However, as will be highlighted, long-term outcomes are pending. Techniques to minimize the risk include rectal irrigation with cytocidal solution, standard manipulations and appropriate case selection (*Sun et al, Analysis of 116 cases of rectal cancer treated by transanal local excision. World Journal of Surgical Oncology. 2014; 12:202).* This has been included in the text.

Page 6 the sentence referencing the ACOSOG and ALaCaRT trials is not references given 22 and 23?

The in-text reference citation was revised and proper citation of the ACOSOG and ALaCaRT in the manuscript was done

Page 8 line 19 “md” should be “mid”.

The typographic error was corrected.

Page 12 line 8 “Studies show the ….” Only one study is referenced 95?

The sentence was revised in accordance with the reviewer’s comment.

Page 13 Line 12 “TaTME had longer CRM…’ do you mean wider??

The word “longer” was replaced with “wider” as suggested.

Page 13 Line 19 TaTME decreases the number of permanent stomas…” Needs a reference.

Since there is no conclusive evidence on this statement, the sentence was revised for the potential of TaTME to decrease the number of permanent stomas.

Page 15 Line 18-19. “This will help safe expansion of the technique and mitiat the safety issues”. This is a bit bold and not justified so a “may” in there might be better?

The sentence was revised in accordance with the reviewer’s suggestion.