Dear Editor-in-Chief

We would like to thank you and the reviewers for taking precious time to review the manuscript and suggest excellent recommendations. The implementation of these recommendations has markedly enhanced the quality of the manuscript tremendously.

We have revised the manuscript as per the suggestions of the esteemed reviewers. However, if there are some shortcomings or any further new suggestions, kindly do let us know. We would be delighted to carry out the changes.

The changes have been highlighted in yellow colour in the revised manuscript and have been included here along with the response to the questions.

Thanking you once again

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Reviewer's comments

Reviewer #1:

The manuscript is an excellent guide for understanding both procedures. Usually there are not comparing procedure papers so easy to understand but this one does. Even though you mention other sphincter preserving procedures It would be very interesting to compare these 2 procedures to FLAP procedures, since these 2 procedures are less comlicated than Flaps, but you can get nearly same sucess rates than LIFT and TROPIS. Also the other new methods you mentioned are quite expensive and for developing countries TROPIS seems to fit quite well for Universal treatment. I liked the way you oriented the paper since fistula is one of the most challenging diseases for the Colorectal surgeon due to preservation of continence and even though I do not have much experience with TROPIS I do believe is the road to follow for its simplicity and very good succesful rates. The only ortographic mistake I found was in page 5, in the last lane: you missed the I in LIFT and you wrote LFT. You may correct it. Congratulations

Ans: I would like to thank the esteemed Reviewer profusely for such nice and wonderful comments. I am really encouraged and motivated. Thanks once again.

Reviewer #2:

The author of the article has strong personal biases.

①In the article, the author overemphasized the difficulty and the indications of the LIFT procedure. Usually, dissected the fistula in the intersphincteric space along the medial edge of the external sphincter, you usually do not enter the submucosal space or the anal canal.

Ans: I would thank the esteemed Reviewer for this point. The manuscript has been modified accordingly and this technical point has been added. The point would be quite helpful to the readers.

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In LIFT procedure, a useful trick to avoid entering the submucosal space is to dissect the fistula in the intersphincteric space along the medial edge of the external sphincter.

②On the other hand, TROPIS procedure is easy to learn and reproduce. However, based on my experience, the proposed success rate and the continence of anal sphincter after postoperative are questionable.

Ans: I thank the reviewer for raising this query. The doubts regarding success rate and incontinence after TROPIS procedure in the esteemed reviewer's mind are also expected to come in most reader's mind as well. Therefore, answering these would significantly enhance the quality of the manuscript.

Regarding success rate (healing rate), the following paragraph has been added on **Page-7,8**

In TROPIS procedure, the infected crypt glands are thoroughly destroyed as the fistula tract in the intersphincteric space is laid open and the resultant opened up intersphincteric space is completely cauterized with electrocautery. The complete removal of infected crypt glands also happens in LIFT procedure but the difference is that healing in LIFT occurs by primary intention whereas in TROPIS, the healing of wound occurs by secondary intention. In presence of infection, the healing by secondary infection is preferred and this could be the reason for high healing rate(80-93%) by TROPIS in complex fistulas.[27-29, 37] In the single largest study of TROPIS in 408 patients suffering from high complex fistulas (all fistulas involving >1/3 of EAS), the reported healing rate was 86% at a median follow-up of 30 months.[37] The data of 408 patients in this study[37] included 325 patients reported in earlier study[29]. The study had several strong points. Apart from a large cohort with a fairly long follow-up, pre-operative MRI was done in all the patients and all 408 patients were documented to be high (involving >1/3 of EAS) on clinical as well

as on MRI assessment.[37] Additionally, the clinical fistula healing in postoperative period was also documented on postoperative MRI assessment in majority of cases.[37] So, from the evidence available so far, the healing rate of TROPIS seems better than LIFT in high complex fistulas. But, an important point to consider is that LIFT has been performed, studied and published from far more centers across the globe than the TROPIS procedure. Therefore, TROPIS would be considered highly successful in high complex fistulas only when its high success rate is replicated in much more centers in different regions of the world. For translation into practical guidelines, comparative prospective studies of LIFT and TROPIS in complex fistulas need to be done.

Regarding incontinence after the TROPIS procedure and its subsequent improvement with Kegel exercises, the detailed explanation and results of a recent study (under submission in World J Gastro) has been included in the manuscript on **Page-8,9**

In a recent study, the efficacy of Kegel exercises (KE) in improving incontinence was evaluated in 102 complex anal fistula patients in whom TROPIS procedure was performed.[44] There were 65 recurrent fistulas, 92 had multiple tracts, 42 had associated abscess, 46 had horseshoe fistula and 34 were supralevator fistulas.[44] All were MRI-documented high fistulas (>1/3 EAS involved). The incontinence was evaluated objectively by Vaizey's incontinence scores [a score of 0 (minimum score) implies no continence problem while score of 24 (maximum score) implies total incontinence].[45] The scoring was done once in the immediate postoperative period before commencement of KE [Pre-KE Group] and on long-term follow-up at 18 months after surgery [Post-KE Group]. The incontinence scores in both groups were compared to evaluate the efficacy of KE. Overall incontinence occurred in 31% patients (Pre-KE Group) with urge and gas incontinence accounting for the majority of cases (28.3%).[44] The mean incontinence scores in the Pre-KE Group were 1.19± 1.96 (in 31 patients, solid=0, liquid=7, gas=8, urge=24) and in the Post-KE Group were 0.26 ± 0.77 (in 13 patients, solid=0, liquid=2, gas=3, urge=10) (p=0.00001, t-test).[44] Division of the IAS led to mainly urge incontinence.[44] However, regular Kegel exercises led to significant reduction in incontinence (both in the number of affected patients and the severity of scores in these patients).[44]

The IAS is primarily responsible for maintaining resting anal pressures. Division of the IAS leads to decrease in resting anal pressure. Normally, the anal canal is free of fecal matter and only when the IAS relaxes during the act of defecation, feces enter the anal canal. The human mind is tuned to associate the presence of fecal matter in the anal canal with impending passage of feces.[44] Therefore, in patients with a

divided IAS and decreased resting anal pressure, feces when present in the lower rectum passes unrestricted into the anal canal giving the feeling that 'feces are about to pass out of the anus' (urge incontinence). That's why the urge incontinence was seen in significant number of patients after TROPIS procedure but it improved substantially with Kegel exercises. [31]

③The disadvantage of TROPIS is partially internal sphincter should be divided, and lead to some deterioration in continence. Except for two small sample reports from China, the cases reported in refs. 30 and 31 were reported by the author, and the author should clarify whether the 408 patients in the ref. 31 included 325 patients in ref. 30.

Ans: Thanks for raising this point. This should have been clarified earlier to avoid confusion. This point has been clarified now on **Page-7**

The data of 408 patients in this study[37] included 325 patients reported in the earlier study[29].

Additionally, the point that the evidence of success rate of TROPIS is limited as compared to LIFT has also been highlighted on **Page-7,8**

But, an important point to consider is that LIFT has been performed, studied and published from far more centers across the globe than the TROPIS procedure. Therefore, TROPIS would be considered highly successful in high complex fistulas only when its high success rate is replicated in much more centers in different regions of the world. For translation into practical guidelines, comparative prospective studies of LIFT and TROPIS in complex fistulas need to be done.

On the other hand, the author emphasized that patients routinely recommend Kegel exercises after TROPIS procedure could prevent incontinence , this explanation is too reluctant.

Ans: Thanks for this comment. As mentioned in above comment no.2, the detailed explanation and results of the recent study which corroborates the efficacy of Kegel exercises in improving continence occurring due to division of IAS in TROPIS procedure have been included in the manuscript (**Page-8,9**).

④The author overemphasized that the TROPIS procedure completely removed the infected anal gland tissue between the sphincter, the relatively short incision resulted in poor drainage and prolonged healing time. In fact, the LIFT procedure separated and ligated the fistula between the intersphincteric space also has completely removed the infected anal gland

Ans: I totally agree with the opinion of the esteemed reviewer. The infected crypt glands are also completely removed in LIFT removed. We have added this in the manuscript on **Page-7.**

In TROPIS procedure, the infected crypt glands are thoroughly destroyed as the fistula tract in the intersphincteric space is laid open and the resultant opened up intersphincteric space is completely cauterized with electrocautery. The complete removal of infected crypt glands also happens in LIFT procedure but the difference is that healing in LIFT occurs by primary intention whereas in TROPIS, the healing of wound occurs by secondary intention.

Science Editor Comments

The manuscript describes an opinion review of "Comparison between two recent sphincter-sparing procedures for complex anal fistulas- LIFT vs TROPIS". The topic is within/ the scope of the WJG. The authors perform a good comparison of two different procedures(LIFT vs TROPIS) for the complex anal fistulas. As both procedures are primarily sphincter-sparing, they do not lead to deterioration in continence. The advantages and disadvantages, indications and contraindications of LIFT and TROPIS have been discussed in this opinion viewpoint as well as the role both these procedures are likely to play in future. However the author of the article may have strong personal biases. As a result, the conclusions of the two reviewers are completely inconsistent. We suggested that the author revises the manuscript according to the reviewers' suggestions and reviews the manuscript again. Recommendation : Major revision.

Ans: Thanks a lot for the comments. The manuscript has been revised as per the recommendations of the esteemed reviewers.