

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

Pankaj Garg

Corresponding Author, on behalf of all authors

Reviewer's comments

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The title could reflect the content if there was included a specific section on acute and chronic treatment of this kind of fistula. The abstract resume correctly the aim of this guidelines paper. Although they are mentioned in other chapters, creating a bit of confusion specific sections should be created to order the work - A section of various treatment options . Also should be indicated different options of treatment depending on the different etiopathogenesis features. - A section on ultrasound diagnosis is mandatory in the diagnostic process. - A diagnostic and treatment flow chart should be included The images are good even if the captions should be integrated.

Ans: Thanks a lot for valuable comments. The implementation of these recommendations has tremendously enhanced the value of the manuscript. The treatment part has been added in detail as per the Levels of Evidence for Therapeutic Studies developed by Centre for Evidence-Based Medicine (Page-10,11,12,13,14,15,33). A section of transrectal ultrasound (TRUS) has been added in the diagnostic process with proper references (Page-7,8,11). However, the captions could not be integrated as they have been written as per the journal style.

Treatment part (as per 'level of evidence' and 'grade of recommendation' has been described on Page-12-15

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: High anal fistula is challenging in both diagnosis and

treatment, and there is a lack of recognized guidelines for diagnosis and treatment. In this manuscript, supralelevator, suprasphincteric, extrasphincteric, RIFIL and high intrarectal fistulas were clearly described and are collectively referred to as peri-levator high-5 anal fistulas. The anatomical structure diagram and MRI images presented in this paper are of great significance for the diagnosis and treatment of high anal fistula and have reference value for clinical practice. Pros 1. Enough cases and clear diagrams help the reader to understand. 2. Different types of anal fistulas are clearly defined and described.

Ans: We would like to thank the esteemed reviewer profusely for encouraging comments.

Cons 1. Since the results of MRI are dependent on the imaging physician to some extent, how to avoid the effect of individual differences leading to the judgment of fistula course is a problem **2.** Lack of introduction and advice on treatment. **3.** As a guideline for diagnosis and treatment, this article lacks some necessary items, and it is recommended to improve the content by referring to Tools of Appraisal of Guidelines for Research and Evaluation (AGREE II), Reporting Items for Practice Guidelines in healthcare (RIGHT) , International centre for globed Health Evidence (ICAHE) and global Rating Scale.

Ans: We would really obliged to the reviewer for these recommendations. We have completely revised the manuscript as per these recommendations and this has made the manuscript much more comprehensive and scientific.

The treatment part has been added in detail. We studied the recommended guidelines (GRADE, RIGHT, AGREE) and subsequently, the manuscript has been revised as per the Levels of Evidence for Therapeutic Studies developed by Centre for Evidence-Based Medicine (Page-10,11,12,13,14,15,33).

Methodology has been included on Page-10,11 & Tables (Page-33)

METHODS USED TO FORMULATE MANAGEMENT GUIDELINES

A search was performed on MEDLINE, PubMed, EMBASE, and the Cochrane Database of Collected Reviews from January 1975 to September 2021. Keyword combinations using MeSH terms included supralelevator, suprasphincteric, extrasphincteric, intrarectal, abscess, fistula, fistula-in-ano, anal, rectal, perianal, perineal, seton, fistula plug, fibrin glue, advancement flap, tuberculosis, Crohn's disease, ligation of intersphincteric tract, LIFT, FPR, fistulectomy with primary sphincter repair, TROPIS and stem cells.

Various guidelines such as GRADE^[50, 51], RIGHT^[52] AGREE^[53] were evaluated but considering the rarity of the disease condition (Hi-5 fistulas) in the study, the Levels of Evidence for Therapeutic Studies developed by Centre for Evidence-Based Medicine, <http://www.cebm.net>. (Oxford, UK) (Table-1) and Grade

Practice Recommendations recommended by American Society of Plastic Surgeons (Table-2) were utilized^[54]. Each diagnostic and therapeutic intervention was assigned a 'level of evidence' from 1A to 5 (1 A being the strongest evidence and 5 being the weakest) (Table-1) and then a 'grade of recommendation' was awarded ranging from 'A' to 'D' ('A' being a strong recommendation and 'D' being a weak option) (Table-2).

Authors (PG, VDY) reviewed all English language articles and tabulated all the evidence available and allotted the level of evidence. After that, the grade of recommendation was decided with consensus of all the authors.

Treatment part (as per 'level of evidence' and 'grade of recommendation' has been described on Page-12-15

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Accept in current form

Ans: We would like to thank the esteemed reviewer profusely for such wonderful and encouraging comments.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Thank you for inviting me to review this interesting manuscript regarding the management of perianal fistulae. In fact these types of fistulae are quite challenging to both the patient and the surgeon and difficult to treat. My main concern regarding this manuscript, this is not a guideline following a proper methodological way for development of guideline such as the GRADE or any other equivalent, nor a systematic review of literature. so I suggest to delete "guidelines" from the title as this might be confusing to the reader and instead it could be a review article. please provide a statement regarding the incidence of these fistulae, and percentage of healing to each technique proposed.

Ans: We would extremely thankful to the reviewer for these suggestions. We have completely revised the manuscript as per these suggestions and this has made the manuscript much more scientific. We totally agree that without these recommendations, the article was looking more like a review article.

The treatment part has been added in detail. We studied the recommended guidelines (GRADE, RIGHT, AGREE) and subsequently, the manuscript has been revised as per the

Levels of Evidence for Therapeutic Studies developed by Centre for Evidence-Based Medicine (Page-10,11,12,13,14,15).

Methodology has been included on Page-10,11& Tables (Page-33)

METHODS USED TO FORMULATE MANAGEMENT GUIDELINES

A search was performed on MEDLINE, PubMed, EMBASE, and the Cochrane Database of Collected Reviews from January 1975 to September 2021. Keyword combinations using MeSH terms included supralelevator, suprasphincteric, extrasphincteric, intrarectal, abscess, fistula, fistula-in-ano, anal, rectal, perianal, perineal, seton, fistula plug, fibrin glue, advancement flap, tuberculosis, Crohn's disease, ligation of intersphincteric tract, LIFT, FPR, fistulectomy with primary sphincter repair, TROPIS and stem cells.

Various guidelines such as GRADE^[50, 51], RIGHT^[52] AGREE^[53] were evaluated but considering the rarity of the disease condition (Hi-5 fistulas) in the study, the Levels of Evidence for Therapeutic Studies developed by Centre for Evidence-Based Medicine, <http://www.cebm.net>. (Oxford, UK) (Table-1) and Grade Practice Recommendations recommended by American Society of Plastic Surgeons (Table-2) were utilized^[54]. Each diagnostic and therapeutic intervention was assigned a 'level of evidence' from 1A to 5 (1 A being the strongest evidence and 5 being the weakest) (Table-1) and then a 'grade of recommendation' was awarded ranging from 'A' to 'D' ('A' being a strong recommendation and 'D' being a weak option) (Table-2).

Authors (PG, VDY) reviewed all English language articles and tabulated all the evidence available and allotted the level of evidence. After that, the grade of recommendation was decided with consensus of all the authors.

Treatment part (as per 'level of evidence' and 'grade of recommendation' has been described on Page-12-15

Incidence of various fistulas has been included on Page-7

Incidence

In recently published large cohorts, the prevalence of these high-5 fistulas has been highlighted^[18, 32]. The incidence of these fistulas in a cohort of 419 consecutively operated patients over a two year period were RIFIL – 10% (42/419), supralelevator- 9.5% (40/419), suprasphincteric- 5.5% (23/ 419) and extrasphincteric- 0^[18, 32].

Once again, we thank the reviewers and editorial team of World Journal of Gastrointestinal Surgery for their kind consideration of our manuscript. Please let us know if you feel any issue has not been adequately addressed or if you have any further queries

Yours sincerely,

Pankaj Garg