Peer Review File

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Review comments

Reviewer A

Comment 1:
Sachdeva et al are reporting about current endoscopic surveillance and therapy approaches for esophageal neoplasms. The authors are shortly describing the different approaches and techniques used for diagnostic and surveillance of Barrett's esophagus and its subtypes like non-dysplastic and indefinite Barrett's esophagus as well as low- and high grade dysplasia. Limitations and strategies are dysplayed in detail. They as well discuss technologies and sampling techniques and lastly biomarkers and the role of AI. A similar approach is taken for esophageal carcinoma types.

The paper has a high relevance and the authors are in detail explaining chances and challenges of each approach in a logical manner.

I would normally say, accept as is but it is a bit long with 5000 words. So shortening it would help raise interest. Otherwise, great job!

Reply 1: Thank you for your feedback. We appreciate your positive evaluation of our paper on current endoscopic screening and surveillance approaches for esophageal neoplasms. We have made efforts to provide a comprehensive overview of the different diagnostic and surveillance techniques for Barrett's esophagus as well as esophageal squamous dysplasia. We have also highlighted the role of biomarkers and artificial intelligence. We understand your concern about the length of the paper and have shortened it to enhance reader interest while maintaining its valuable content.

Reviewer B

Comment 1:
Esophageal cancer continues to have a poor prognosis due to detection at advanced stages after the onset of symptoms. The authors have described the application of guidelines and techniques for early detection of neoplastic lesions of the esophagus. The manuscript would be interesting for the readers of the Journal and its publication is suggested.

Reply 1: Thank you for your insightful comment. We agree that esophageal cancer is often diagnosed at advanced stages, leading to poor prognosis. In our manuscript, we have extensively discussed the application of guidelines and techniques aimed at early

detection of neoplastic lesions in the esophagus. We believe that our findings will be of great interest to the readers of the Journal, and we appreciate your suggestion for its publication.

Reviewer C

In this review the authors adequately summarize current strategies regarding the detection and surveillance of neoplastic lesions of the esophagus. The review covers the relevant topics in this moving topic. It is easy to read and I expect this article to be of interest for the readers. A few minor comments:

Major
None

Minor
Comment 1:
1. The main problem in BE esophagus is that the progression rate even in known BE is very low, this means we are overtreating the majority of the patients. The only possibility to push the field forward is i) to better define who is at very low-risk for progression and ii) to identify those at high-risk which may be amenable for preventive EET even before the progression to HGD/EAC. this should be highlighted in the part biomarkers as adjuncts to dysplasia detection (column 354)

Reply 1: You bring up an important point regarding the challenge of low prevalence of EAC and concern for over treating the majority of patients with Barrett's esophagus (BE) due to the low progression rate. It is crucial to focus on identifying the subset of patients at very low risk for progression who may not require aggressive interventions. We reiterated this point in the biomarkers as adjuncts to dysplasia detection section along with the strategies to define the population at high risk for progression. Thank you for emphasizing this important perspective.

Comment 2:
2. Column 262: The authors should highlight the limitations of pathology in risk stratifiying Barrett's esophagus and include the study by Duits et al demonstrating that an increasing number of experts confirming LGD increases the risk of progression.

Reply 2: Thanks for your comment. We highlighted the challenges associated with histopathological diagnosis and prognostication particularly with LGD and referenced Duits et al. findings in our review.

Comment 3:
3. Column 370: Subsequently, Frei et al (published in AmJGastro) demonstrating that TissueCypher outperforms majority of pathologists should be cited as an example

how to overcome limitations of pathology review

Reply 3: Thank you for bringing up this point. We did mention the role of Tissuecypher as a potential risk stratification tool for progression prediction. However, its role to "overcomes limitations" of standard pathological analysis and its use for BE diagnosis as a sole entity by itself is not recommended by the society guidelines. We refrain from including that perspective in this article at this time per Reviewer 4's recommendation.

Comment 4:
4 Table 3: Where is the recommendation to perform EUS/PET-CT in T1a cancer coming from? Due to the verly low risk for lymph node metastasis these tumors usually will not be fully staged in most expert center.

Reply 4: The information was derived from the following source: Iyer PG, Kaul V. Barrett esophagus. In Mayo Clinic Proceedings 2019 Sep 1 (Vol. 94, No. 9, pp. 1888-1901). Elsevier. Current guidelines recommend staging only in selected cases of T1a. We removed the management aspect of T1a and T1b cancer from the table per recommendations from reviewer 4.

Reviewer D

Comment 1:
Thank you very much for your comprehensive review. We appreciate your expertise and dedication to writing this excellent review article.

I agree with comments from our reviewers---well written, helpful, and informative. For the incorporation of the prior reviewers' comments, I would suggest shortening the length of the paper by incorporating many of the novel techniques (confocal, tissue cypher, FISH etc) into a table.

Text and images can focus on and provide guidance on techniques that are commonly utilized in practice (i.e., clear cap attachment, seattle protocol, NBI/i-scan, risk factors related to dysplasia and cancer, and annual risk of malignant transformation). Please consider showing pictures of long segment barrett's, both smooth and nodular---and emphasizing how RFA is better suited for eradicating smooth barrett's, and endoscopic resection for nodular.

Reply 1: Thank you for your feedback. We acknowledge your concern regarding the paper's length and will take into account shortening it by incorporating use of tables, images to make it more engaging for readers while preserving its valuable contents.

Comment 2:

Reviewer 3 appropriately points out the challenge of interobserver variability between pathologists on diagnosing and designating the grade of dysplasia, and this is worth mentioning.

However, for point 3—while it is acceptable to mention Tissue Cypher as a potential promising solution--- I disagree it "overcomes limitations" and would not recommend incorporating that perspective into this review.

Reply 2: We agree with the need to highlight the histopathological diagnostic challenges due to inter-observer variability and reiterated this point in the role of biomarkers as adjuncts to dysplasia detection. We believe that its potential to overcome limitation and replace standard pathological analysis still needs to be proven and refrain from including that perspective in this article at this time.

Comment 3:
Re: point 4, I agree T1a will not typically require a PET/CT, and many expert endoscopists will consider surveillance, at most by EGD/EUS. You could consider removing the T1a section, as endoscopic resection of neoplastic lesions of the esophagus will be covered in detail in another review.

Reply 3: The information was derived from the following source: Iyer PG, Kaul V. Barrett esophagus. Current guidelines recommend staging in selective cases of T1a In Mayo Clinic Proceedings 2019 Sep 1 (Vol. 94, No. 9, pp. 1888-1901). Elsevier. We removed the management aspect for T1a EAC