

To the Reviewers,

We thank you for taking the time to read our manuscript and offer suggestions for improvement. Below is a list of the stated concerns with an explanation of how they were addressed in the manuscript.

Reviewer 2:

This is a comprehensive review of the application status of HRM and PH measurement in gastroesophageal reflux disease. The writing is great, and the documentation is comprehensive and representative. two questions:

1) In the "Manometry and Motility Testing" section, "While there is limited data to support mandatory pre-operative manometry testing, the ACG still recommends HRM to specifically rule out achalasia and scleroderma [5]". However, in reference 5, Manometry but not HRM is recommended by ACG. I think HRM is a kind of manometry, but it cannot replace it. I tend to use "manometry", which is more precise.

The sentence was edited to more clearly define “manometry” instead of “HRM” as a tool to rule out motility disorders.

2. Does Reference 6 equal to "Surg Endosc (2010) 24:2647–2669, 10.1007/s00464-010-1267-8"? Does Reference 44 equal to "Surg Endosc (2012) 26:296–311, DOI 10.1007/s00464-011-2017-2"? If yes, citing the corresponding papers will make it easier for reading.

The suggested references were the correct articles. The citations were edited accordingly

Reviewer 3:

The authors performed literature review about preoperative esophageal assessment for GERD patients, especially by HRM and MII-pH. The manuscript is well-written. I have some comments for the manuscript as below.

Major comments:

1. Table 1. To make the table easy to understand, the listed diseases should be classified with broader disease concepts, then go on to specific diseases as it is. “Weak Acid Reflux”, “Functional heartburn” and “Reflux hypersensitivity” should be a part of GERD. Similarly, “Achalasia”, “Distal Esophageal Spasm”, Hypercontractile Esophagus”, and “EGJ outflow obstruction” should be within the spectrum of esophageal motility disorders.

Table 1 was reorganized to include broader categories as suggested by the reviewer

2. GERD was never defined in the manuscript. Does “GERD” in the manuscript mean patients with reflux symptoms or a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications as in Montreal classification?

A sentence was added in the introduction to clarify what we are considering GERD in our review.

3. Figure 4. MII-pH is also important to detect supragastric belching.

An addition was made to Figure 4 to include the utility of pH impedance studies for supragastric belching.

4. Page 7-8. In “Manometry and Motility Testing” section, it should describe that HRM can measure the size of hiatus hernia precisely. (United European Gastroenterol J. 2018 Aug;6(7):981-989.)

Additions were made to highlight the utility of HRM for patients with hiatal hernia.

5. Page 9, line 15-17. The main indication of HRM prior to anti-reflux surgery is rule out major esophageal motility disorder not only achalasia or scleroderma because abnormal esophageal contraction itself can underlie reflux symptoms. Additionally, assessing esophageal peristalsis is also important to predict post-operative dysphagia.

This sentence was edited to clarify that HRM is beneficial for all major motility disorders and not just achalasia or scleroderma.

6. Page 9, line 15-17, 28. HRM can speculate scleroderma by absent peristalsis but cannot diagnose it. Additionally, achalasia is unlikely to have gastroesophageal reflux. However, achalasia can manifest itself as reflux symptoms. Probably the esophageal pressurization or contraction, or the to-and-fro movement of bolus inside the esophagus underlie those reflux symptoms.

This sentence was edited to clarify that HRM can detect absent peristalsis which is consistent with scleroderma, but cannot specifically diagnose scleroderma.

7. Page 10, line 13. “Scleroderma” is not a term of esophageal motility disorder in Chicago classification. It would be good to replace it with “absent peristalsis”, which paragraph explains scleroderma is often accompanied by that motility disorder.

This section was renamed “Absent peristalsis” to better fit with the underlying motility issues discussed.

8. Page 12, line 26, 27. What did RDC improve the sensitivity and specificity of HRM to diagnose?

Additions were made to clarify how RDC improved the sensitivity and specificity of diagnosing esophageal dysmotility.

9. Page 14, line 8, 9. Supragastric belching (SGB) is not necessarily more common in FD than in GERD. In fact, approximately 40% of NERD and reflux hypersensitivity showed pathological SGB (Clin Gastroenterol Hepatol. 2020 Apr 6;S1542-3565(20)30440-7.).

This sentence was edited to clarify that SGB can be seen in FD, but can also be seen in other disorders and is not necessarily more common.

10. Page 14, line 12, 13. SGB can induce gastroesophageal reflux, which means LES relaxation can be triggered by SGB.

This sentence was edited to clarify that HRM can identify specific subtypes of SGB that only release esophageal air and do not involve gastric air or the LES.

11. Page 14, line 27~Page 15, line 2. ARS might be a potential option for rumination. However, it should be stressed that psychological intervention such as cognitive behavioral therapy is the first-line treatment for rumination.

A sentence was added to clarify that cognitive behavioral therapy remains the first line treatment for patients with rumination and that a subset might benefit from anti-reflux surgery.

Minor comments:

1. Page 4, line 26. The sentence “Another important aspect of the patient’s history it to assess their response to PPI therapy,” should be corrected.

This sentence was corrected.

2. Page 11, line 11. “Opioid Induced-Opioid induced esophageal dysfunction (OIED)” should be corrected.

This sentence was corrected.

3. Figure 1B. There seem many acid refluxes other than ones indicated by stars. The remaining ones also should be indicated.

Figure 1B was edited to highlight the multiple reflux events present.

4. Page 12, line 20 and 22. Figure 1 and 2 do not seem to fit statements.

These figure citations were erroneously included. They have been deleted.

We again thank the reviewers for the time and the suggestions they offered. Please let us know if we have adequately addressed all concerns. Thank you.

Sincerely,

A handwritten signature in black ink, appearing to read 'M. Yodice', with a stylized flourish at the end.

Michael Yodice