REVIEW ARTICLE

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Guidance on performance and reporting of high-resolution oesophageal manometry and ambulatory pH monitoring in Singapore

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ABSTRACT

Introduction: We aimed to provide a practical and evidence-based guide on the indications, performance and reporting of high-resolution oesophageal manometry (HRM) and ambulatory pH monitoring (PHM) in adult patients in Singapore.

Methods: The guideline committee comprised local gastroenterologists from public and private sectors with particular expertise in aspects of HRM and PHM, and it was tasked to produce evidence-based statements on the indications, performance and reporting of these tests. Each committee member performed literature searches to retrieve relevant articles within the context of domains to which they were assigned.

Results: Twelve recommendation statements were created and summarised.

Conclusion: Standardising key aspects of HRM and PHM is imperative to ensure the delivery of high-quality care. We reported the development of recommendations for the performance and interpretation of HRM and ambulatory reflux monitoring in Singapore.

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Keywords: Gastro-oesophageal reflux disease, GERD, high-resolution oesophageal manometry, oesophagus, pH testing

INTRODUCTION

High-resolution oesophageal manometry (HRM) and ambulatory pH monitoring (PHM) are essential for evaluating oesophageal symptoms. Guidelines in this article were created to provide practical and evidence-based guidance on the indications, performance and reporting of oesophageal physiological tests in adult patients in Singapore. This document is therefore aimed at healthcare professionals treating patients with these symptoms. Guidance on these tests is available in Western countries.[1,2] However, at the time of writing, there was a notable lack of Singapore guidance despite these physiological tests being used widely. Therefore, there was a need to establish local guidance to limit variations in practice. The coronavirus disease 2019 (COVID-19) situation also allowed us to reflect on our institutional practices and resulted in changes in practice that we have reflected in these guidelines.

METHODS

The creation of these guidelines was commissioned by the Chapter of Gastroenterologists of the College of Physicians, Singapore, under the auspices of the Academy of Medicine, Singapore. The guideline committee comprised local gastroenterologists from public and private sectors with particular expertise in aspects of HRM and PHM, and it was tasked to

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CLINICAL IMPACT

What is New

- These are the first Singapore guidelines for the performance and interpretation of high-resolution oesophageal manometry and ambulatory reflux monitoring.

Clinical Implications

- Performance of these physiological tests varies widely.
- Guidelines in this study were created to provide practical and evidence-based guidance on the indications, performance and reporting of oesophageal physiological tests in adult patients in Singapore.
- This guidance is aimed at healthcare professionals treating patients with these symptoms.

produce evidence-based statements on the indications, performance and reporting of these tests. These statements were formulated using the population, intervention, comparator and outcome format to guide the search for evidence. Each committee member performed literature searches to retrieve relevant articles within the context of specific questions and domains to which they were assigned. The written segments from each member were then consolidated by the main author and circulated to the entire committee for further review. This document was externally reviewed and endorsed by the Specialty Board of the Chapter of Gastroenterologists, Council of the College of Physicians and Council of the Academy of Medicine, Singapore.

Each recommendation statement has an associated assessment of the quality of evidence and strength of recommendation based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system, which specifically separates the strength of the evidence from the strength of a recommendation.[3] All members of the committee were asked to rate each statement using a 5-tier system: A+: strong agreement; A: agree with reservation; U: undecided; D: disagree with reservation; and D+: strongly disagree. The wording of recommendations that did not reach at least 80% substantial agreement (A+, A) was modified, and further online voting was undertaken until substantial agreement was attained. The guidelines were crafted using the Reporting Items for Practice Guidelines in Healthcare to ensure quality and completeness.[4]

RESULTS

Statement 1: Patients undergoing high-resolution oesophageal manometry or ambulatory pH monitoring should have a prior oesophagogastroduodenoscopy, with oesophageal biopsies if indicated (e.g. eosinophilic oesophagitis), to exclude structural and mucosal causes.

GRADE evidence: High

Strength of recommendation: Strong

Level of agreement: 100% strongly agree

Statement 2: Patients with obstructive oesophageal symptoms without mechanical causes should undergo high-resolution oesophageal manometry.

GRADE evidence: Very low

Strength of recommendation: Strong

Level of agreement: 83% strongly agree, 17% agree with reservation

Patients should have an oesophagogastroduodenoscopy performed prior to HRM or PHM, especially if the indication is dysphagia, as endoscopy allows evaluation o f oesophageal structural abnormalities that may potentially increase complication risk during catheter insertion. Additionally, oesophageal biopsies should be obtained, particularly if eosinophilic oesophagitis is a differential diagnosis.[1] Likewise, endoscopy also can evaluate reflux symptoms to objectively diagnose pathological gastro-oesophageal reflux disease (GORD) in the presence of high-grade erosive oesophagitis, Barrett's oesophagus or peptic strictures. However, despite its high specificity, oesophagogastroduodenoscopy has a low sensitivity for the diagnosis of GORD[5] and therefore cannot conclusively exclude GORD.

Barium imaging can be considered if endoscopy is not possible. A static contrast study can diagnose majority of lesions within the oesophagus, while a timed barium oesophagram is useful in the evaluation of oesophageal motility disorders.[1] However, barium imaging is a suboptimal screening modality for dysphagia with 69% sensitivity and 50% specificity in detecting oesophageal motility disorders.[6] Patients with obstructive symptoms without a mechanical cause may harbour an oesophageal motility disorder; therefore we recommend that an HRM be performed since it is useful in diagnosing oesophageal motility disorders such as achalasia and ineffective oesophageal motility.[7]

Statement 3: Patients with symptomatic gastro-oesophageal reflux disease not responding to proton pump inhibitor therapy (compliant with 20mg omeprazole equivalent for 8–12 weeks) should undergo ambulatory pH monitoring.

GRADE evidence: Very low

Strength of recommendation: Strong

Level of agreement: 67% strongly agree, 33% agree with reservation

Patients with symptoms from suspected GORD should first undergo a therapeutic trial of a proton pump inhibitor (PPI) since this is cheaper, less invasive and more widely available than PHM. The equivalent of 20mg of omeprazole taken appropriately for 8–12 weeks would be deemed a therapeutic trial of PPI.[1] However, symptoms, PPI response and low-grade erosive oesophagitis (Los Angeles Classification grades A and B) on endoscopy are not conclusive evidence for GORD and also do not always correlate with abnormal reflux burden on PHM performed off PPI therapy.[8] Hence, these constitute unproven GORD and require PHM before escalation of management.[8]

Patients being planned for laparoscopic anti-reflux surgery should undergo preoperative PHM to confirm pathological acid exposure time (AET), an association between symptoms and reflux episodes, or both, as preoperative pathological AET and positive symptom scores[9] lead to better long-term patient satisfaction and less symptoms post surgery. Many extraoesophageal symptoms have been associated with GORD.[10] PHM allows demonstration of association between symptoms and reflux episodes, and therefore enables the diagnosis or exclusion of pathological GORD. Patients who demonstrate increased acid exposure and associated symptoms are more likely to respond to acid suppression therapy, and thus PHM can be used to optimise pharmacological treatment of these patients.[11] Indications for HRM and PHM are summarised in Table 1.

Statement 4: Patients should be fasted adequately prior to high-resolution oesophageal manometry, or ambulatory pH monitoring, or both. Adequate instructions regarding medications to be stopped should be provided. Written informed consent should be obtained and documented clearly.

GRADE evidence: High

Strength of recommendation: Strong

Level of agreement: 100% strongly agree

Patients undergoing oesophageal physiological tests should fast for at least 6 hours prior to the test to reduce the risk of vomiting during catheter insertion or during endoscopic-guided insertion of the wireless capsule. However, if achalasia is highly suspected, a longer fasting period of 12 hours may be considered.[12] During the monitoring period, patients are encouraged to continue with regular activities and food during regular times, and avoid carbonated beverages. A diary of mealtimes, symptoms and recumbence periods has been advocated to improve diagnostic accuracy and analysis of symptoms occurrence.[13]

Medications that alter oesophageal motility function such as nitrates, calcium channel blockers, opiates, prokinetics and anticholinergic drugs should be stopped for 48 hours pre-procedure as tolerated.[12] If PHM is to be done off acid suppression medications, PPIs should be stopped for 7 days and histamine-2 receptor antagonists stopped 3 days before the study.[1] Patients on antiplatelet and anticoagulant drugs should be informed about a small increased risk of bleeding, particularly from the nose during catheter insertion. Based on published literature and existing guidelines, there is insufficient evidence to support withholding of antiplatelet and anticoagulant drugs routinely.[1] However, the bleeding risk should be tailored to the individual; and for patients on warfarin, it is prudent to ensure that the international normalised ratio is not above therapeutic range.

Table 1. Indications for high-resolution oesophageal manometry and pH monitoring

High-resolution oesophageal manometry	Ambulatory pH monitoring
Obstructive oesophageal symptoms (dysphagia, chest pain)	Evaluation of gastro-oesophageal reflux disease (heartburn, regurgitation, extra-oesophageal symptoms)
Evaluation of gastro-oesophageal reflux disease, especially prior to catheter placement for pH monitoring	Belching disorders
Anti-reflux surgery pre-evaluation	Anti-reflux surgery pre-evaluation
Symptoms post anti-reflux surgery	Symptoms post anti-reflux surgery
Rumination syndrome	Evaluation of lung transplantation candidates

HRM and PHM are generally regarded as low-risk procedures and can be conducted in a standalone medical clinic. Major complications are rare, but there exists in the literature a case report of oesophageal perforation[14] and finding of decrease in oxygen saturation with increased heart rate.[15] Although wireless PHM is generally well tolerated, some subjects may experience throat discomfort, dysphagia, chest discomfort and foreign body sensation.[16] Standard risks of upper endoscopy apply if wireless PHM is applied.[17] In addition, risks specific to wireless PHM include premature detachment, poor data transmission, failure to detach, failure to attach, capsule aspiration, capsule retention, mucosal tears, bleeding and perforation.[16] Patients should also be informed about magnetic resonance imaging (MRI) compatibility of the attached device, and specific precautions should be taken based on the manufacturer's recommendations. A screening X-ray should be undertaken to ensure that the capsule has passed if an urgent MRI examination is required.[1]

The procedure, along with risks mentioned above, should be explained to the patient appropriately and written informed consent obtained and documented clearly.

Statement 5: Symptomatic patients with suspected GORD should undergo ambulatory pH monitoring off acid suppression if there is no previous objective evidence of GORD.

GRADE evidence: Moderate

Strength of recommendation: Strong

Level of agreement: 83% strongly agree, 17% agree with reservation

In patients with no previous evidence of GORD, PHM should be performed off acid suppression therapy to quantify reflux and maximise chances of diagnosing significant symptom reflux association.[18] Those with high GORD probability should undergo the study on twice daily PPI, as few patients have persistent abnormal acid exposure on twice daily PPI.[18] This allows better phenotyping of refractory non-erosive reflux disease and functional heartburn.[19]

Statement 6: High-resolution oesophageal manometry should be performed using 10 swallows of 5mL with 20–30 seconds between each swallow, in the supine position. A minimum of 7 evaluable swallows is recommended for meaningful interpretation. The use of adjunctive testing provides additional information and improves the sensitivity of detecting clinically relevant oesophageal dysmotility, and consideration for use should be individualised.

GRADE evidence: Moderate

Strength of recommendation: Strong

Level of agreement: 83% strongly agree, 17% agree with reservation

The HRM procedure should be performed according to published Association of Gastrointestinal Physiologists guidelines.[20] This is performed using 10 water swallows of 5mL with a rest period of 20–30 seconds between each swallow and conventionally performed while supine. Although current classification algorithms are based on 10 water swallows in the supine position, studies have shown that interpretation is possible if at least 7 swallows are adequate.[21]

As these standardised manoeuvres are not representative of normal physiology, adjunctive swallows using provocative measures in the upright-seated position may be used. Adjunctive tests include multiple rapid swallows (5 water swallows of 2mL, 1–2 second apart),[22] rapid drink challenge (free drinking of 200mL of water with a straw),[23] the use of viscous solutions,[24] a solid bread bolus[25] and a solid test meal.[26] Although certainly useful for clinical investigation, provocative measures are refined specific measures whose universal adoption may be impractical, and the application of these manoeuvres should be individualised.

Statement 7: We recommend manual review of high-resolution oesophageal manometry tracings and reporting according to the Chicago Classification. The report should include (1) reasons for referral; (2) diagnosis based on Chicago Classification; and (3) summary of results including the mean and median integrated relaxation pressure, mean distal contractile integral, and distal latency values.

GRADE evidence: High

Strength of recommendation: Strong

Level of agreement: 50% strongly agree, 33% agree with reservation, 17% undecided

Reporting of HRM

General information

The following items should be in the procedure report: reason for referral, clinical diagnosis, summary of results, tabulated results and communication to referring provider.[27] Mandated documentation of recommendations for follow-up evaluation and treatment was considered inappropriate since HRM is a diagnostic aid to be used in concert with other clinical information. Any symptoms reported during the HRM study and their correlation with the HRM findings should be included.

Interpretation

Published manufacturer-specific normal values should be used, as data have suggested that catheter-specific "normal" data are required for correct diagnosis according to the Chicago Classification.[28] If utilised, the form of adjunctive testing undertaken should be included with appropriate normal values. There should be a manual review of the entire HRM tracing, with the aim of providing a clinically interpretable summary. All HRM studies must be interpreted according to a formally validated scheme, and the scheme used should be documented. We have agreed that analysis and reporting of manometry should be performed according to the Chicago Classification, which is the version 3.0 classification at the time of writing.[7] Key information required in the report includes the median reading of 10 integrated relaxation pressure values, the mean value of the distal latency, and the mean distal contractile integral values for 10 single water swallows of 5mL. An HRM diagnosis according to the Chicago Classification should be given whenever possible, although it is emphasised that the final diagnosis for an individual patient should be based on a careful consideration of clinical features, and radiological or endoscopic findings, or both, in addition to the HRM findings.

Statement 8: A minimum period of 16 hours is recommended for catheter-based monitoring and at least 48 hours of extended monitoring is recommended for wireless capsule monitoring.

GRADE evidence: High

Strength of recommendation: Strong

Level of agreement: 83% strongly agree, 17% agree with reservation

An international consensus has recommended a minimum of 16 hours of monitoring (excluding meal times) to obtain clinically meaningful data.[29] As there can be considerable day-to-day variability in oesophageal acid exposure and symptom reporting, a prolonged period of 48 hours of wireless PHM can potentially produce a higher sensitivity for reflux detection and associated symptom events.[30]

Statement 9: Details in the ambulatory pH monitoring report should include (1) reasons for referral; (2) diagnosis; and (3) summary of results including acid exposure time, number of reflux episodes and symptom association profiles. Additional impedance parameters (mean nocturnal baseline impedance, post-reflux swallow-induced peristaltic wave index) are useful adjunctive tests and the reporting of these parameters can be individualised.

GRADE evidence: Low

Strength of recommendation: Strong

Level of agreement: 50% strongly agree, 33% agree with reservation, 17% undecided

Statement 10: Automatic analysis of pH monitoring is adequate, provided that the recordings are checked for accurate mealtimes, posture changes and symptom reporting. A manual review of the 2-minute time window prior to a reflux event and symptom event is suggested to obtain accurate reflux quantification and symptom association analysis.

GRADE evidence: Moderate

Strength of recommendation: Conditional

Level of agreement: 50% strongly agree, 33% agree with reservation, 17% disagree

Reporting of PHM

General information

The report should include patient identification details, date of the test, indications for procedure and a list of current medications, particularly whether acid-suppressing drugs were stopped or continued during the study.

Interpretation

Data are analysed using proprietary software and interpreted by the reporting physician. The following parameters should be included for acid exposure: percentage of total time at pH<4, percentage of upright time at pH<4, percentage of supine time at pH<4, and number of episodes at pH<4 for >5 minutes. The symptom index and symptom association probability of the patient's symptoms during the study should be included.

The pH recordings in healthy volunteers and patients were manually edited to remove episodes of spurious acid reflux caused by ingestion of food or drinks by excluding mealtimes from the automated pH analysis. Comparison of the results showed a close agreement in all pH parameters for distal oesophageal pH recordings.[31] Thus, it is important to manually check patients' recordings for artefacts, meal periods and symptom events to allow a reliable assessment of the AET using the automated analysis. However, automated analysis overestimates non-acidic reflux events and provides inaccurate symptom association analysis in up to 20% of patients.[32] On the other hand, manual analysis of the entire 24-hour monitoring period for

reflux events and reflux symptom association is time-consuming, and individual physicians have to decide on the balance between automated and manual analysis.

Oesophageal PHM variables

Oesophageal AET is defined as the percentage of total recording time at pH<4 in the distal oesophagus 5cm above the lower oesophageal sphincter. AET is extracted from both pH and pH-impedance data and is the most reproducible metric and most useful single discriminator to define oesophageal acid burden.[33] Based on current consensus,[8,29] total AET<4% is consistently physiological and AET>6% is consistently pathological. AET readings of 4–6% require additional diagnostic tests.

The wireless PHM device is associated with marginally increased 95th percentile AET values compared with those of healthy controls (4.4–5.3%)[34], but similar thresholds can be applied for both the catheter- and wireless-based PHM devices. The number of reflux episodes measured on PHM can be used as an adjunct in predicting treatment outcomes.[35]

Symptom association analysis

The symptom index and symptom association probability are the most commonly used parameters to establish the reflux symptom association profile. However, only episodic symptoms with a finite onset and offset, such as heartburn, acid regurgitation, cough and chest pain, can be subject to evaluation of the symptom reflux association. It is crucial for patients to accurately record symptom events by pressing the symptom button in the symptom diary at the immediate onset of symptoms as any delay may render the symptom index, symptom association probability, or both, negative. Careful instruction to patients is essential for accurate recording.

Adjunct metrics

Oesophageal baseline impedance correlates inversely with mucosal integrity and oesophageal acid burden. It has been shown that GORD patients with pathological AET had lower average baseline impedance readings than did patients with functional heartburn and healthy controls.[36] A simplified method to measure baseline impedance using the mean nocturnal baseline impedance has been proposed.[37] This is obtained from measuring baseline impedance over 3 periods of 10 minutes at 3cm and 5cm above the lower oesophageal sphincter during the nocturnal sleep period in the absence of swallowing or reflux episodes.[38,39] A mean nocturnal baseline impedance threshold of <2,292Ω identified patients with erosive reflux disease with 91% sensitivity and 86% specificity; among pH-positive GORD patients, the sensitivity and specificity was 86%.[38] Further prospective studies are required to better define the role of baseline impedance and mean nocturnal baseline impedance in GORD evaluation.

Following a reflux episode, a post-reflux swallow-induced peristaltic wave (PSPW) demonstrated on pH-impedance monitoring is observed in healthy volunteers and represents chemical clearance of the oesophagus.[38] A PSPW is defined as a 50% drop in impedance relative to the pre-swallow baseline originating from the proximal to distal impedance sites, followed by >50% return to baseline in the distal impedance sites. The PSPW index is calculated manually by counting the number of reflux episodes that are followed by a PSPW within 30 seconds, and dividing by the total number of reflux episodes. The PSPW index is significantly lower in patients with reflux oesophagitis or with non-erosive reflux disease than in patients with functional heartburn and healthy controls,[38] and may potentially be more accurate than AET and mean nocturnal baseline impedance in predicting PPI responsiveness.[39] More studies are required before these novel pH-impedance parameters can be applied for routine GORD evaluation.

Statement 11: High-resolution oesophageal manometry and pH monitoring should be performed and interpreted by individuals who have achieved competency and have been given privileging rights by their institution's clinical privileging system.

GRADE evidence: Low

Strength of recommendation: Strong

Level of agreement: 50% strongly agree, 50% agree with reservation

The quality of the individual performing and interpreting the study was considered to be integral to HRM, and the technician and interpreting physician should show competency in HRM.[27] The performance of catheter-based PHM is similar to that of HRM catheter insertion and is often done in the same sitting by the same individual. Therefore, we would take both into account. The recommendations regarding minimum procedural volume required for competency[27] are included in Table 2.

Case volume by itself, however, should not be the sole determinant of competency in interpreting these studies. We suggest that once competency is established, it is up to their local clinical privileging

Table 2. Minimum case volume required for establishing competency

Performance of high-resolution oesophageal manometry, catheter-based ambulatory reflux monitoring, or both	Perform 20 to establish competency
Interpret high-resolution oesophageal manometry	Interpret 50 to establish competency
Interpret ambulatory reflux monitoring	Interpret 25 to establish competency

systems to determine the rights for continued interpretation of these procedures.

Statement 12: During the COVID-19 pandemic, all gastrointestinal motility laboratory staff should undergo training for standard infection control and proper usage of personal protective equipment.

GRADE evidence: Moderate

Strength of recommendation: Strong

Level of agreement: 50% strongly agree, 50% agree with reservation

For detailed guidance on the practice of these oesophageal tests during the COVID-19 pandemic, we refer readers to the Asian Neurogastroenterology and Motility Association statements.[40] Several key points that are worthy of inclusion have been incorporated in our guidelines.

DISCUSSION

Risks of procedures and actions taken to mitigate risks

All elective and non-urgent HRM and PHM are considered high-risk procedures and deferment should be considered if there is a high risk of COVID-19 transmission within the community,

All staff involved in performance of these procedures have to abide by the institution infection policy: standard, droplet and airborne precautions with full personal protective equipment are highly recommended, and the procedure should be performed in negative-pressure rooms whenever possible. All staff involved should undergo training for standard infection control and the proper usage of personal protective equipment.

Triage of patients prior to procedure

All patients should be triaged and screened for fever and respiratory symptoms (shortness of breath, runny nose, cough, sore throat and anosmia), history of close contact with confirmed or suspected COVID-19 cases, and travel history to high COVID-19 prevalence area within the last 14 days. There should also be a recalling system in place to proactively prioritise rebooking of patients for procedures when deemed safe to resume normal activities.

Follow-up of patients for contact tracing

Patients who have undergone these procedures should be given advice to contact the motility laboratory staff if they develop COVID-19 within 14 days. Staff should contact the patient by phone on day 7 and day 14 to ask about the development of COVID-19 symptoms or presence of any recent diagnosis of COVID-19. Any patient suspected of having COVID-19 should be guided to seek medical opinion immediately. Contact tracing should be performed for possible patients and staff exposed to suspected or confirmed cases.

Areas for future research

The guideline development process has highlighted areas for future research. An HRM study may be compromised in the hands of an incompetent technician or an interpreting physician, regardless of technology quality. It appears that there are marked variations in practice quality in Singapore. Also, studies have shown that trainees who achieved competency did so at differing case volumes. Moreover, the majority of trainees failed to demonstrate competency in HRM even after interpreting 50 HRM cases. These results suggest that using a minimal case volume to assess oesophageal HRM competency is inaccurate; furthermore, most trainees need to interpret more than 50 cases to achieve competency. Therefore, some of the key areas to pursue include a formal determination of what constitutes competency in performing HRM or PHM; and a more structured training programme for trainees to establish competency in HRM and PHM interpretation.

Limitations

Our guidelines were written by a few individuals who were all gastroenterologists, and we therefore had minimal input from other disciplines. There may be potential bias in such a small steering group, and the cost or resources, along with preferences of the endusers, may not have been sufficiently considered.

CONCLUSION

Standardising key aspects of HRM and PHM is imperative to ensure the delivery of high-quality care. We reported the development of recommendations for

the performance and interpretation of HRM and PHM in Singapore. Despite substantial agreement on these recommendations, variations in practice existed even among our panel of 6 experts, highlighting the role of future research on training and competency evaluation.

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