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British Society of Gastroenterology guidelines for oesophageal manometry and oesophageal reflux monitoring

Nigel J Trudgill,[1] Daniel Sifrim,[2] Rami Sweis,[3] Mark Fullard,[4] Kumar Basu,[5] Mimi McCord,[6] Michael Booth,[7] John Hayman,[8] Guy Boeckxstaens,[9] Brian T Johnston,[10] Nicola Ager,[8] John De Caestecker[11]

[1]Sandwell and West Birmingham Hospitals NHS Trust, West Bomwich, UK
[2]Centre of Gastroenterology Research, Queen Mary University London, London, UK
[3]University College London Hospitals NHS Foundation Trust, London, UK
[4]West Hertfordshire Hospitals NHS Trust, Watford, Hertfordshire, UK
[5]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
[6]Heartburn Cancer UK, Baingstoke, UK
[7]Royal Berkshire NHS Foundation Trust, Reading, UK
[8]Sandwell and West Birmingham Hospitals NHS Trust, West Bromwich, UK
[9]Gastroenterology, University Hospital, KU Leuven, Leuven, Belgium
[10]Department of Gastroenterology, Belfast Health and Social Care Trust, Belfast, UK
[11]University Hospitals of Leicester NHS Trust, Leicester, UK

Correspondence to
Dr Nigel J Trudgill;
nigel.trudgill@nhs.net

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ABSTRACT

These guidelines on oesophageal manometry and gastro-oesophageal reflux monitoring supersede those produced in 2006. Since 2006 there have been significant technological advances, in particular, the development of high resolution manometry (HRM) and oesophageal impedance monitoring. The guidelines were developed by a guideline development group of patients and representatives of all the relevant professional groups using the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool. A systematic literature search was performed and the GRADE (Grading of Recommendations Assessment, Development and Evaluation) tool was used to evaluate the quality of evidence and decide on the strength of the recommendations made. Key strong recommendations are made regarding the benefit of: (i) HRM over standard manometry in the investigation of dysphagia and, in particular, in characterising achalasia, (ii) adjunctive testing with larger volumes of water or solids during HRM, (iii) oesophageal manometry prior to antireflux surgery, (iv) pH/impedance monitoring in patients with reflux symptoms not responding to high dose proton pump inhibitors and (v) pH monitoring in all patients with reflux symptoms responsive to proton pump inhibitors in whom surgery is planned, but combined pH/impedance monitoring in those not responsive to proton pump inhibitors in whom surgery is planned. This work has been endorsed by the Clinical Services and Standards Committee of the British Society of Gastroenterology (BSG) under the auspices of the oesophageal section of the BSG.

SUMMARY OF ALL RECOMMENDATIONS

1. Oesophageal manometry, including high resolution manometry

Technical aspects of oesophageal manometry

1.1 In patients undergoing evaluation for dysphagia, high resolution manometry (HRM) is superior to standard manometry in terms of reproducibility, speed of performance and ease of interpretation
GRADE evidence: High
Strength recommendation: Strong

1.2 The addition of impedance to HRM can be a helpful adjunct to 'visualise' bolus movement and peristalsis effectiveness; however, its utility in clinical practice and impact on therapeutic decision making is not yet clear.
GRADE evidence: Moderate
Strength recommendation: Conditional/weak

1.3 Normal values for HRM are manufacturer and catheter specific.
GRADE evidence: High
Strength recommendation: Strong

1.4 Adjunctive testing (eg, larger volumes of water, solid/viscous swallows or a test meal) can provide additional information and unmask pathology not seen with standard water swallows, as they are more representative of normal swallowing behaviour and more likely to induce symptoms and, in turn, improve diagnostic yield.
GRADE evidence: High
Strength recommendation: Strong

Patients with dysphagia

1.5 Patients with dysphagia should preferably have an endoscopy with oesophageal biopsies to rule out and treat mucosal and structural disorders prior to manometry. Barium swallow should be considered where endoscopy is not possible and/or where structural disorders require further scrutiny.
GRADE evidence: Moderate
Strength recommendation: Strong

Patients with achalasia

1.6 In patients with achalasia, HRM provides information on achalasia subtype which is predictive of clinical outcome. Although also possible, subtyping achalasia with standard manometry requires expertise.
GRADE evidence: Moderate
Strength recommendation: Strong

Patients with major motility disorders other than achalasia (diffuse oesophageal spasm, hypercontractile oesophagus, absent peristalsis)

1.7 Among patients with major motility disorders other than achalasia (diffuse oesophageal spasm, hypercontractile oesophagus, absent peristalsis), HRM, compared with standard manometry, may provide increased diagnostic and functional information changing intervention.
GRADE evidence: Moderate
Strength recommendation: Conditional/weak

Patients undergoing catheter based reflux monitoring

1.8 Oesophageal manometry is the preferred method by which to localise the lower oesophageal sphincter (LOS) prior to catheter based pH sensor placement.

GRADE evidence: Moderate

Strength recommendation: Strong

Patients prior to antireflux surgery

1.9 Although there is currently no evidence to rule out or tailor antireflux surgery in patients with minor motor disorders, oesophageal manometry should be performed in advance of all patients being considered for surgery to rule out LOS dysfunction (ie, achalasia), as well as major motor disorders of the oesophageal body (eg, diffuse oesophageal spasm).

GRADE evidence: High

Strength recommendation: Strong

Symptomatic patients after antireflux surgery

1.10 HRM can provide useful diagnostic information not obtainable by standard manometry, among patients with dysphagia after antireflux surgery.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Patients with suspected rumination

1.11 Rumination syndrome can be confidently diagnosed clinically on the basis of a typical history, but if the diagnosis is unclear, the patient needs convincing of the diagnosis or objective evidence is required prior to therapy, HRM with impedance after a test meal can be utilised to identify diagnostic features. Simultaneous impedance provides additional confirmatory and diagnostic information.

GRADE evidence: Moderate

Strength recommendation: Strong

2. Catheter based oesophageal reflux monitoring, including pH and impedance monitoring

Technical aspects of reflux monitoring

2.1 Automatic analysis of oesophageal pH recordings and symptom association with acid reflux episodes is adequate for pH monitoring in patients, provided the recording is checked for artefacts and major technical issues and that times of meals and symptoms have been accurately recorded.

GRADE evidence: Low

Strength recommendation: Strong

2.2 Analysis of oesophageal pH/impedance recordings requires manual editing of reflux episodes and symptoms, to obtain accurate reflux quantification and reflux symptom association assessment.

GRADE evidence: Moderate

Strength recommendation: Strong

2.3 To enhance the chance of establishing a diagnosis of gastro-oesophageal reflux disease and a symptom association with acid reflux, patients undergoing pH monitoring should not take acid suppression.

GRADE evidence: Moderate

Strength recommendation: Strong

2.4. In patients with heartburn or acid regurgitation symptoms not responding to a proton pump inhibitor twice daily, if pH/impedance monitoring is required it should be undertaken on proton pump inhibitors if the patient has previous pathological endoscopic or pH monitoring findings, and the study should be performed off proton pump inhibitors if they have no previous such demonstration of pathological gastro-oesophageal reflux disease.

GRADE evidence: Low

Strength recommendation: Conditional/weak

2.5 In patients with heartburn, acid regurgitation or chest pain, symptom association with reflux episodes is best assessed with both the symptom association probability and symptom index.

GRADE evidence: Low

Strength recommendation: Conditional/weak

2.6 In patients with throat or respiratory symptoms, dual probe distal oesophageal and proximal oesophageal or pharyngeal pH monitoring has no advantage over single probe distal oesophageal pH monitoring.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease

2.7 Patients with symptoms suspected to be due to gastro-oesophageal reflux disease should undergo a therapeutic trial of a proton pump inhibitor as the initial diagnostic approach.

GRADE evidence: Moderate

Strength recommendation: Strong

2.8 Reflux monitoring with pH or pH/impedance is not recommended in patients with gastro-oesophageal reflux disease symptoms responsive to proton pump inhibitor therapy in whom antireflux surgery is not planned.

GRADE evidence: Moderate

Strength recommendation: Strong

2.9 In patients with heartburn or regurgitation not responding to twice daily proton pump inhibitors, reflux monitoring should be performed with pH/impedance monitoring. This technique allows diagnosis of increased acid exposure, association between symptoms and acid or non-acid reflux, and identification of phenotypes—ie, non-erosive reflux disease, hypersensitive oesophagus and functional heartburn.

GRADE evidence: Moderate

Strength recommendation: Strong

2.10 In patients with chest pain, throat or respiratory symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors, we recommend performing reflux monitoring with pH/impedance, as this enables the diagnosis of pathological gastro-oesophageal reflux and/or an association between symptoms and acid or non-acid reflux.

GRADE evidence: Low

Strength recommendation: Strong

Patients with idiopathic pulmonary fibrosis, cystic fibrosis and lung transplantation with suspected gastro-oesophageal reflux disease

2.11 Patients with idiopathic pulmonary fibrosis, cystic fibrosis or other pulmonary disorders that might require lung transplantation should have reflux monitoring with pH/impedance to detect pathological acid or non-acid gastro-oesophageal reflux prior to intensive proton pump inhibitor treatment or antireflux surgery.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease and antireflux surgery planned

2.12 Patients with symptoms suspected to be due to gastro-oesophageal reflux disease and responsive to a proton pump inhibitor should undergo oesophageal pH monitoring, rather than

pH/impedance, before antireflux surgery, to confirm excess oesophageal acid exposure and/or an association between symptoms and acid reflux episodes.

GRADE evidence: Moderate

Strength recommendation: Strong

2.13 Patients with heartburn or acid regurgitation, chest pain, throat or respiratory symptoms not responsive to a proton pump inhibitor should undergo oesophageal pH/impedance monitoring, rather than pH monitoring alone, before antireflux surgery, to confirm excess oesophageal acid exposure and/or an association between symptoms and acid or non-acid reflux episodes.

GRADE evidence: Low

Strength recommendation: Strong

Patients with recurrent or persistent gastro-oesophageal reflux symptoms following antireflux surgery

2.14 Patients with recurrent or persistent gastro-oesophageal reflux symptoms following antireflux surgery should undergo reflux monitoring by pH/impedance, rather than pH monitoring alone, as this can objectively confirm or reject persistent gastro-oesophageal reflux and exclude other causes for symptoms such as supragastric belching.

GRADE evidence: Low

Strength recommendation: Conditional/weak

3. Wireless oesophageal pH monitoring

Technical aspects of wireless pH monitoring

3.1 Wireless pH monitoring should be undertaken for at least 48 hours, as this increases the number of patients found to have excess acid exposure and the number of symptoms available for symptom association analysis.

GRADE evidence: High

Strength recommendation: Strong

3.2 Wireless pH monitoring can be undertaken for up to 96 hours, if the capsule has not detached and the results at 48 hours are indeterminate, but both 'worst day' and 'average' analyses should be undertaken to determine a diagnosis of gastro-oesophageal reflux disease.

GRADE evidence: Moderate

Strength recommendation: Conditional/weak

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors

3.3 Wireless pH monitoring should be undertaken in patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors who require pH monitoring but who have been intolerant of catheter based monitoring, leading to inconclusive results, or who would be very likely to be poorly tolerant.

GRADE evidence: Moderate

Strength recommendation: Strong

INTRODUCTION

Purpose and methods

The purpose of these guidelines is to provide a practical and evidence based guide to the indications for, performance and reporting of oesophageal manometry, oesophageal pH monitoring, both catheter based and wireless pH monitoring, and oesophageal impedance monitoring in adult patients. These investigations are undertaken in patients with symptoms potentially arising from motility disorders of the oesophagus (including dysphagia, regurgitation and chest pain) and from gastro-oesophageal reflux (including heartburn, acid regurgitation, chest pain, cough and throat symptoms). This document is therefore aimed at gastroenterologists, upper gastrointestinal surgeons, ear nose and throat surgeons, respiratory physicians, gastrointestinal physiologists and nurse practitioners for the benefit of the patients we care for. The role of oesophageal manometry and reflux monitoring in patients under the age of 18 years will not be addressed in these guidelines.

The previous British Society of Gastroenterology (BSG) guidelines on oesophageal manometry and pH monitoring were produced in 2006.[1] Since then there have been a number of advances in the technology available to enhance oesophageal manometry and reflux monitoring. The development of HRM and oesophageal impedance monitoring in particular have led to the need for new guidelines on the role of these technologies in the management of patients with oesophageal disorders. This guidelines update was commissioned by the Clinical Services and Standards Committee of the BSG, under the auspices of the oesophageal section of the BSG.

During the development of these guidelines, we systematically reviewed the medical and nursing literature to address any changes that were required to the previous guidance issued in 2006. These guidelines were developed in accordance with recommendations from the BSG and National Institute for Health and Clinical Excellence (NICE) and utilised the AGREE II (Appraisal of Guidelines for Research and Evaluation) instrument. The purpose of the AGREE II instrument is to provide a framework to: assess the quality of the guideline; provide a methodological strategy for its development; and inform the reporting process of the guideline.

The guideline development group (GDG) included patients and individuals who are representative of all the relevant professional groups: gastroenterologists with a particular expertise in aspects of oesophageal manometry or reflux monitoring, an upper gastrointestinal surgeon, and the Association of Gastrointestinal Physiologists (AGIP).

A systematic literature search strategy was developed with the aid of a librarian with extensive experience of conducting literature searches. We searched MEDLINE, EMBASE, CINAHL, US national guideline clearing house and the Cochrane Central Register of Guidelines, from 2000 to 31 October 2017 using the medical subject headings 'esophageal manometry', 'esophageal high resolution manometry', 'esophageal manometry impedance', 'esophageal pH monitoring', 'esophageal pH impedance monitoring', 'wireless esophageal pH' and 'wireless pH monitoring'. Reference lists of journal articles identified as being of potential value to the guidelines were also searched for relevant references. No language limits were applied. The search results were divided among three groups of at least two GDG members covering oesophageal manometry, oesophageal reflux monitoring and wireless pH monitoring. Each GDG member independently reviewed the abstracts of each paper relevant to their group. Studies were selected if they reported data on any aspect of oesophageal manometry and reflux monitoring relevant to the guidelines' scope and purpose. A series of guideline questions were developed in PICO (Problem/population, Intervention, Comparator, Outcome) format and relevant references from the search allocated. Further PICO questions were developed following the review of the search results.

The quality of included evidence was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system, which specifically separates the strength of the evidence from the strength of a recommendation. While the

Table 1 An overview of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system

GRADE—strength of evidence	GRADE—strength of recommendation
High quality Further research is very unlikely to change our confidence in the estimate of effect	*The trade-offs* Taking into account the estimated size of the effect for main outcomes, the confidence limits around those estimates and the relative value placed on each outcome
Moderate quality Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	*The quality of the evidence*
Low quality Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	*Translation of the evidence into practice in a particular setting* Taking into consideration important factors that could be expected to modify the size of expected effects
Very low quality Any estimate of effect is very uncertain	*Uncertainty about the baseline risk for the population of interest*

strength of a recommendation may often reflect the evidence base, the GRADE system allows for occasions where this is not the case—for example, where it seems sensible to make a strong recommendation despite the absence of high quality scientific evidence, such as large randomised controlled trials (table 1).

To achieve transparency and simplicity, the GRADE system classifies the quality of evidence in one of four levels—high, moderate, low and very low (table 1). Evidence based on randomised controlled trials begins as high quality evidence, but confidence in the evidence may be decreased for several reasons including: study limitations; inconsistency of results; indirectness of evidence; imprecision; and reporting bias. The GRADE system offers two grades of recommendations: 'strong' and 'conditional/weak'. When the desirable effects of an intervention clearly outweigh the undesirable effects, or clearly do not, guideline panels offer strong recommendations. On the other hand, when the trade-offs are less certain—either because of low quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced—conditional/weak recommendations become mandatory. In addition to the quality of the evidence, several other factors affect whether recommendations are strong or weak such as: uncertainty about the balance between desirable and undesirable effects, uncertainty or variability in values and preferences, and uncertainty about whether the intervention represents a wise use of resources.

Areas of disagreement on the wording of recommendations derived from the PICO questions and their GRADE strength and evidence grades were resolved by consensus among the GDG members of the three groups and the GDG chair. All members of the GDG were then asked to rate each recommendation using a five tier system: A+, strong agreement; A, agree with reservation; U, undecided; D, disagree with reservation; D+, strongly disagree. The wording of recommendations that did not reach at least 80% substantial agreement (A+ or A) was modified and further voting undertaken until substantial agreement was attained.

The provisional recommendations of the guidelines were externally reviewed by an independent international expert prior to presentation and public discussion of the draft guidelines at a 1 day BSG symposium on 7 March 2016.

Dissemination and implementation of guidelines

These guidelines have been written to be as practical as possible for both referring clinicians and clinicians undertaking and reporting the investigations. Dissemination will be achieved through publication in *Gut* and through presentation at national and regional BSG meetings. We do not anticipate any barriers or resource implications to the implementation of these guidelines as the techniques described are already in established clinical practice, with the possible exception of the cost of more widespread adoption of HRM and particularly oesophageal impedance monitoring.

It is anticipated that a review and updating of this guideline will be required in 5 years in order to account for new developments.

OESOPHAGEAL MANOMETRY INCLUDING HIGH RESOLUTION MANOMETRY

Equipment

Oesophageal manometry measures the pressure profiles of the oesophageal sphincters and oesophageal body muscle. Manometry systems are composed of a pressure sensing catheter and a recording device. Currently there are two main forms of manometric equipment, standard manometry (SM) and HRM, dependent on the number of pressure sensors on the manometry catheter. Each form has the option of two types of sensing/transducer device: water perfused or solid state.

Solid state catheters consist of pressure transducers mounted within the manometric catheter. They are reusable and must be sterilised according to local protocol and in line with manufacturer's instructions prior to and after every procedure.

Water perfused catheters comprise a bundle of microcapillary plastic tubes. The pressure in each tube is monitored by a transducer located at the perfusing pump. As the pressure transducer is located at an external position, the dynamic performance of these catheters is delayed in comparison to solid state catheters. Water perfused catheters are generally single use.

Standard manometry

SM catheters generally consist of 3–8 pressure sensors spaced along the length of the catheter. Due to the low number of pressure sensors a pull through technique is required to allow identification of the location and length of the LOS high pressure zone.

High resolution manometry

Miniaturisation of solid state pressure sensors has allowed the development of HRM, employing catheters with multiple sensors (up to 36).[2 3] This allows for simultaneous measurement across the whole oesophagus and oesophageal sphincters. HRM allows for topographical analysis with the generation of two- and three-dimensional contour plots.

Patient and equipment preparation

Patient preparation prior to the procedure

Patients should undergo endoscopy and appropriate oesophageal biopsies prior to referral for oesophageal manometry for symptoms of dysphagia, regurgitation or chest pain to rule out structural and mucosal causes for their symptoms including eosinophilic oesophagitis. Endoscopy also allows assessment of abnormalities (eg, oesophageal diverticula, pharyngeal pouch, varices, etc), which potentially increase the risk of insertion of a catheter into the oesophagus. Any medication known to affect oesophageal motor function should be stopped for 48 hours prior to the test if possible (eg, nitrates, calcium channel

blockers, opiates, anticholinergic drugs and prokinetics).[4] Patients should fast for 6 hours prior to the test. However, if achalasia is suspected a longer fast is advisable. This can be guided by the results of endoscopy. If there were considerable liquids and solids noted in the oesophagus at endoscopy then a 12 hour fast before manometry should be recommended. In some cases, a liquid only diet for 2–3 days might be also required. Informed consent should be obtained.

There is likely to be an increased risk of bleeding from the nose during oesophageal manometry in patients taking antiplatelet agents, such as clopidogrel, and anticoagulants such as warfarin or direct acting oral anticoagulants. In the absence of guidelines or data on this risk, we cannot make a categorical recommendation that these agents are discontinued for oesophageal manometry but suggest that patients should be warned about the small increased risk and in patients taking warfarin it is ensured that their international normalised ratio is within the therapeutic range (and not above) prior to testing. Individual practitioners may, however, wish to consider the individual risk of nosebleed balanced against the risk of discontinuing the anticoagulant/antiplatelet agent in each case.

Equipment preparation

Prior to the test the catheter must be cleaned in line with the manufacturer's guidelines and local procedure. The catheter should be calibrated and zeroed as per the manufacturer's guidelines.

Procedure

The procedure should be performed according to published guidelines. The previous BSG guidelines offered a comprehensive review of the test procedure for standard manometry.[1] The AGIP has recently provided guidelines on the performance of HRM studies.[5]

Any staff member performing HRM should either be fully trained and accredited by the AGIP in this procedure or supervised by a fully trained and accredited practitioner.

Oesophageal body motility is assessed using ten 5 mL room temperature wet swallows allowing for 20–30 s between swallows. This is conventionally undertaken in the supine position, although recent evidence suggests that for solid state (but not water perfused) manometry the more physiological upright position may be used.[6–8] Adjunctive testing should then be undertaken as it reproduces normal behaviour and is more likely to identify the cause of a patient's symptoms.[7 9] Adjunctive assessments include: drinking larger volumes of water (200 mL drunk freely (rapid drink challenge)) or 2 mL of water every few seconds (multiple rapid swallows), single solid or viscous bolus swallows or consuming a test meal. All adjunctive assessments are performed in the upright position, sat at 90° to the horizontal.

High resolution manometry parameters

The following parameters have been defined for HRM and recently clarified.[10]

Integrated relaxation pressure

The integrated relaxation pressure (IRP) is calculated as the lowest mean deglutitive oesophago-gastric junction (OGJ) pressure referenced to gastric pressure for 4 continuous or non-continuous seconds during a 10 s window after the onset of swallowing, measured from the start of upper oesophageal sphincter (UOS) opening. This provides information on the degree of OGJ relaxation during swallowing.[11 12]

Distal contractile integer

The distal contractile integer (DCI) is expressed as the product of the mean amplitude of contraction in the distal smooth muscle oesophagus (mm Hg) multiplied by both the duration of contraction (s) and by the length of the distal oesophageal segment (cm) from the transition zone to the proximal margin of the LOS. Peristaltic integrity is confirmed when the DCI is >450 and there are no peristaltic breaks of more than 5 cm within a 20 mm isobaric contour.

Contractile deceleration point

The contractile deceleration point (CDP) is the inflection point along the 30 mm Hg isobaric contour (or pressure greater than intrabolus pressure in instances of compartmentalised pressurisation) at which propagation velocity slows, demarcating peristalsis from ampullary emptying. The CDP must be localised within 3 cm of the proximal margin of the LOS.

Distal latency

Distal latency is measured from the beginning of UOS swallow induced relaxation to the CDP.

Reporting

General information

The report should include patient identification details, date of the test, indications for the procedure and a list of current medications. Any symptoms reported during the HRM study and their correlation with the manometric findings should be included in the report.

SM should be reported according to previously published guidelines.[1] Analysis and reporting of HRM should be in line with the most recent Chicago classification (currently version 3.0).[10] Published manufacturer specific normal values should be used. If utilised, the form of adjunctive testing undertaken should be included with appropriate normal values.

Interpretation

A meaningful summary should be provided. There should be a manual review of any automated reports with the aim of providing a clinically interpretable summary. A manometric diagnosis according to the Chicago classification should be given where possible, although it is important to emphasise that the final diagnostic formulation for an individual patient should be based on a careful consideration of clinical features, radiological and/or endoscopic findings, in addition to the manometric information.

Technical aspects of oesophageal manometry

1.1 In patients undergoing evaluation for dysphagia, HRM is superior to standard manometry in terms of reproducibility, speed of performance and ease of interpretation.

GRADE evidence: High

Strength recommendation: Strong

Although HRM is more expensive than SM, there are a number of potential advantages of HRM over SM. A study comparing patients undergoing HRM and water perfused SM reported that total procedure time was reduced from 42 min with SM to 31 min with HRM, with no significant difference in comfort scores.[13]

A number of studies have examined the quality of the information from HRM and its reproducibility. A study of endoscopy negative reflux disease and healthy controls compared HRM with SM line plots obtained at the same time.[14] HRM more

accurately measured bolus movement through the oesophagus than SM. HRM also detected disorders of oesophageal peristalsis and abnormalities of the LOS in patients with oesophageal spasm that were not seen with SM. The results of HRM studies in healthy volunteers 2 weeks apart were highly reproducible for most parameters examined, including UOS, pressure transition zone length, LOS length and pressure, and LOS relaxation.[15 16]

It is important that any new technique is readily learnt and applied in clinical practice and that the results are reproducible outside the research setting in everyday clinical practice. Medical students with no experience of oesophageal manometry were taught to interpret line plots used in SM and spatiotemporal plots used in HRM. Subsequent analysis was slightly more accurate (89% vs 86%, P=0.002) and faster (25 vs 31 s, P<0.001) with spatiotemporal plots.[17] A similar study of manometry novices found that HRM interpretation was significantly more accurate, particularly when assessing oesophageal apersistalsis, hypomotility and relaxation of the LOS.[18]

1.2. The addition of impedance to HRM can be a helpful adjunct to 'visualise' bolus movement and peristalsis effectiveness; however, its utility in clinical practice and impact on therapeutic decision making is not yet clear.

GRADE evidence: Moderate

Strength recommendation: Conditional/weak

The addition of multichannel impedance to the HRM catheter (HRIM) can contribute by measuring the direction of bolus movement within the oesophagus, without exposure to radiation.[19 20] This may be particularly relevant to those with dysphagia but with no dysmotility based on manometric measurements alone. This subset comprises up to 50% of referrals for oesophageal physiology testing with swallowing problems.[21–23] This technology has been used to assess bolus flow through the oesophageal body and across the OGJ.[22 24–27] Normative data using HRIM have been published with high interobserver and intraobserver reproducibility.[28 29]

HRIM provides a clear visual representation of bolus transport through the oesophagus, which graphically demonstrates when transport disruption or resistance occurs. This also allows the correlation of interrupted bolus transport with symptoms. However, the most recent report from the International Manometry Working Group does not include impedance in the classification of motor disorders. Rather it states that the addition of impedance might help 'complement the analysis of oesophageal function'.[10] Whether the addition of impedance to HRM will aid diagnosis and provide therapeutic guidance is not yet established.

1.3 Normal values for HRM are manufacturer and catheter specific.

GRADE evidence: High

Strength recommendation: Strong

Normal values for HRM of the oesophagus have been published, initially using the Manoview catheter comprising 36 solid state transducers at 1 cm intervals (Manoscan ESO, Given Imaging, Los Angeles, California, USA) in healthy volunteers.[2 3 11 30 31] These transducers measure intra-oesophageal pressure circumferentially, which is advantageous for asymmetric areas such as sphincters, whereas HRM using water perfused catheters and some solid state transducers such as Unisensor AG (Attikon, Switzerland) have unidirectional sensors.[32 33] However, for the Unisensor system, circumferential soft membranes filled with fluid cover the sensors. The luminal pressure acts on the membrane circumferentially and this pressure is transferred to the fluid, so the sensors actually perceive average luminal pressure. The values obtained using the Unisensor catheter are in a similar range to those reported using Manoscan, but differences in the upper limits of normal were found for IRP, OGJ resting pressure, UOS resting pressure and transitional zone length. In particular, the 4 s IRP, the accepted standard for measuring OGJ relaxation under the Chicago classification, is markedly higher using the Unisensor catheter.[34 35] In another study where Manoview and Unisensor catheters were compared in tandem studies in healthy volunteers, the Unisensor measurements, other than contraction front velocity (CFV), were consistently higher.[36] Furthermore, a study comparing two Manoscan catheters of differing diameters (4.2 vs 2.7 mm) reported higher IRP with the narrower catheter and higher UOS pressure and oesophageal body DCI with the thicker catheter.[37] For the Unisensor catheter, when volunteers had their studies repeated twice 1–2 weeks apart, the results were reproducible for 'anatomic' parameters (sphincter length, pressure and relaxation) although less so for contraction wave parameters. On the other hand, in this study, parameters obtained from conventional line tracings were poorly reproducible.[15] These data suggest that for solid state HRM, catheter specific 'normal' data are required for correct diagnosis according to the Chicago classification.

Water perfused catheters are cheaper and have been shown to be more comfortable for patients.[38] However, they are more time consuming and complicated to set up and operate. Furthermore, because of the hydrostatic pressure effect, results are most reliable when patients are studied supine. Solid state systems are easy to use and preferred by most operators; however, disadvantages include increased expense, catheter fragility and thermal drift in pressure measurement requiring correction. As solid state catheters allow for studies to be performed in the physiological upright position, normal values (particularly of OGJ relaxation, motility and smooth muscle response to bolus swallows) differ, as the impact of gravity is not excluded, as it would be with supine studies. Normal values for HRM in the upright position have been reported,[6 35 39] as have values using viscous boluses[39] and solid meals.[6] A comparative study during which solid state and water perfused HRM were performed in random order in healthy volunteers found moderate to good agreement in most parameters (especially CFV, distal latency, DCI and IRP) but poor agreement in some parameters, notably UOS measurements.[40] Two other studies using different water perfused systems found lower upper limits of normal for IRP than for solid state.[12 38]

1.4 Adjunctive testing (eg, larger volumes of water, solid/viscous swallows or a test meal) can provide additional information and unmask pathology not seen with standard water swallows, as they are more representative of normal swallowing behaviour and more likely to induce symptoms and, in turn, improve diagnostic yield.

GRADE evidence: High

Strength recommendation: Strong

Conventionally, manometry studies are performed using 5 mL water swallows in the supine position.[41] To replicate more physiological swallowing conditions, studies using HRM have been reported using 'adjunctive' techniques while sitting upright, which include rapid swallowing sequences (drinking) as well as swallowing viscous material, bread or a meal. When compared with single water swallows, adjunctive testing commonly uncovers new pathology and alters existing diagnoses, as well as reproducing relevant symptoms. Increasing the diagnostic yield of clinically relevant, symptomatic motility disorders, such as achalasia, OGJ obstruction and spasm, through adjunctive

testing is of clear clinical value. A growing number of studies describe how such adjunctive testing can positively influence patient management.[9 42–45]

The rapid drink challenge (RDC), also known as multiple water swallows, involves 200 mL of water drunk freely through a straw, such that the rate and number of swallows are determined by the patient.[9 46 47] With multiple rapid swallows (MRS), repetitive 2 mL volumes are administered at 1–2 s intervals with a syringe such that the rate and number of swallows are controlled by the examiner.[43 48] With either test, repetitive swallowing inhibits oesophageal body motility and causes relaxation of the OGJ ('deglutitive inhibition'), which is then followed by a clearing contraction.[49] RDC fills the oesophagus with water, making it more sensitive at measuring resistance to flow by measuring intrabolus pressure and IRP.[46 47] Ang *et al* found that RDC−IRP >12 mm Hg (IRP stretched across the entire length of the RDC sequence) accurately identified obstruction associated with achalasia, while RDC−IRP >8 mm Hg had optimal accuracy for 'all cause' OGJ obstruction. MRS, on the other hand, might be more sensitive at identifying peristaltic reserve in patients whose single water swallows were found to be fragmented or ineffective.[43 50]

The use of swallowed solids, such as bread, has long been known to provoke oesophageal motility disturbances and symptoms in patients with suspected dysmotility.[51] Including bread during SM studies increased the amplitude and duration of peristaltic contractions and slowed peristaltic front velocity in normal individuals.[52] However, non-conducted and non-peristaltic contractions also increased in healthy subjects with no symptoms, which explains why bread swallows have not been widely adopted during SM. With the advent of HRM, several studies have provided normative values and documented high interobserver agreement for both water and bread swallows in the supine and upright seated positions,[6 53] with findings not dissimilar to those of SM.[52] The oesophagus responds to the 'challenge' of position change and higher bolus consistency by increasing the coordination and vigour of peristaltic contractions.[6 54] Studies during single solid swallows, a test meal or the postprandial period, have been found to be more sensitive for clinically relevant dysfunction.[9] Solids can also help identify patients with peristaltic reserve, as is often seen in those with endoscopy negative gastro-oesophageal reflux disease, with hypotensive or even absent peristalsis with water swallows but peristaltic recovery with solids, thus excluding a major motor disorder.[55] Although no direct comparison is available, MRS can be considered as an alternative to solids to investigate peristaltic reserve.

A comparison of patients with reflux-like symptoms and healthy subjects reported that, compared with water swallows, inclusion of a standardised meal led to an altered manometric classification in 67% and a change in clinical diagnosis in 39% of patients. Furthermore, a test meal was better able to identify the cause of symptoms and guide effective management as determined by clinical outcomes at the 2 year follow-up.[9] In a recent large patient series, compared with water swallows, inclusion of a test meal doubled the diagnostic yield of a new 'major motor disorder'.[47] A standardised meal has also been shown to help define the aetiology behind symptoms in patients following antireflux surgery. Compared with water swallows, a test meal was able to detect more patients with dysmotility and dysphagia (30% vs 70%) as well as outlet obstruction (7% vs 26%).[44] Methodology and normal values have been described using a rice meal; achalasia or OGJ obstruction is defined when ≥2 swallows have an IRP of >25 mm Hg, spasm where ≥2 swallows have a distal latency of <4.5 s and hypercontractility were ≥2 oesophageal contractions have a distal contractile integral of >8000 mm Hg×s×cm.[8]

Minor disorders of peristalsis are defined in the Chicago classification of motor disorders with single water swallows as >50% with DCI <450 mm Hg ('ineffective oesophageal motility') or >50% swallows with breaks of >5 cm in 20 mm Hg isobaric contour ('fragmented peristalsis'); however, these findings are of uncertain clinical significance. Of 98 patients with minor motor disorders followed up for 5 years, 70% were found to be asymptomatic at follow-up, having exhibited spontaneous improvement.[56] It was concluded that the identification of minor disorders of motor function is a good prognostic indicator and they rarely progress over time. Furthermore, as already described, the relevance of many of these findings can be addressed by inducing challenge swallows with adjunctive testing.

It is not clear, as there have been no direct comparisons to date, whether standardised meals identify additional diagnoses and change management compared with RDC and MRS, but use of standardised meals should be considered among patients with dysphagia, if no major motility disorder has been discovered using water swallows and RDC/MRS. If a solid swallow is utilised, it is recommended that either the patient brings a culprit meal to reproduce his or her symptoms or a standard meal is provided (eg, a standard quantity of cooked rice).[8] However, further outcome studies would be useful to confirm the clinical value, especially the impact on treatment decisions, of this approach.

Patients with dysphagia

1.5 Patients with dysphagia should preferably have an endoscopy with oesophageal biopsies to rule out and treat mucosal and structural disorders prior to manometry. Barium swallow should be considered where endoscopy is not possible and/or where structural disorders require further scrutiny.

GRADE evidence: Moderate

Strength recommendation: Strong

Oesophago-gastro-duodenoscopy (OGD) is the preferred investigation in patients with oesophageal dysphagia, as it not only allows direct visual inspection of the oesophagus but also allows histological sampling.[57]Fifty-four per cent of a sample of 1649 patients presenting with dysphagia had a major abnormality at OGD, the yield being higher in men aged >40 years with heartburn, odynophagia and weight loss occurring in association with dysphagia.[58]Patients with dysphagia should undergo OGD and biopsy at two levels in the oesophagus to exclude eosinophilic oesophagitis in the absence of a mucosal or structural cause for their symptoms.[57 59]

Contrast radiology is a useful adjunct to endoscopic examination in the diagnosis of a patient with dysphagia. In countries where there are limited healthcare resource or in situations where a patient is unable or unwilling to undergo endoscopic examination, a contrast study can outline irregularities in the oesophageal lumen and diagnose the majority of stricturing lesions within the oesophagus.[60]

Patients with achalasia

1.6 In patients with achalasia, HRM provides information on achalasia subtype which is predictive of clinical outcome. Although also possible, subtyping achalasia with standard manometry requires expertise.

GRADE evidence: Moderate

Strength recommendation: Strong

Compared with the single sensor nadir pressure of SM (sensitivity 52%) and the 4 s nadir of HRM (sensitivity 69%), the 4 s IRP has a 98% sensitivity and 96% specificity for detecting achalasia.[11] HRM also measures pressurisation within the oesophageal body, so that the three subtypes of achalasia can be defined as: type II, pan-oesophageal compression in a non-dilated oesophagus; this is presumed to be the precursor to type I, the non-compression subtype in which the oesophagus is thought to have decompensated and dilated; type III is associated with persistent peristalsis with spasm (previously known as vigorous achalasia).[10 61–64] It is not clear if these represent different stages of the same disorder or if they are different phenotypic presentations of the same disease.

Studies have shown that compared with type I, type II has a better response to any form of therapy (botulinum toxin, pneumatic dilatation or myotomy) while type III has the poorest response to all treatments.[65–70] However, a recent retrospective analysis of patients who underwent cardiomyotomy found no difference in the outcome between type II and type I achalasia patients, while those with type III achalasia responded poorly.[71] There is insufficient evidence to recommend specific therapies based on subtype, especially between type I or type II achalasia.[62 69 70 72] Treatment decisions should therefore be based on local expertise, therapeutic availability and patient choice rather than subtype.[66 67 73–76]

Although achalasia subtyping is based on HRM criteria, it has been suggested that SM tracings can be reclassified to fit these phenotypes. To date, no studies have defined SM criteria for achalasia subtypes, but through reclassifying historical manometric data, studies have again reported that type II responds best to therapy followed by type I and type III, respectively.[69–71] However, such a reclassification requires considerable experience and expertise, as it is based on subjective interpretation of HRM based parameters.

Patients with major motility disorders other than achalasia (diffuse oesophageal spasm, hypercontractile oesophagus, absent peristalsis)

1.7 Among patients with major motility disorders other than achalasia (diffuse oesophageal spasm, hypercontractile oesophagus, absent peristalsis), HRM, compared with standard manometry, may provide increased diagnostic and functional information changing intervention.

GRADE evidence: Moderate

Strength recommendation: Conditional/weak

Diagnostic criteria for major motility disorders other than achalasia have evolved in recent years. Using SM, diffuse oesophageal spasm (DOS)—subsequently renamed 'distal oesophageal spasm'[77]—was defined on the basis of the results of 10 water swallows with at least two simultaneous contractions (defined by fast wave front velocity >8 cm/s) and normal peristalsis in at least 1 of the 10 swallows.[41] Minor criteria for DOS included high amplitude or multipeaked contraction waves, and high pressure and/or an incompletely relaxing LOS.[41] However, impaired OGJ relaxation should not be classified as DOS on the basis of some normal peristalsis. OGJ relaxation is less accurately measured by SM than HRM, and a randomised controlled trial comparing both techniques found that achalasia was diagnosed in 29% of patients studied with HRM compared with 12% undergoing SM.[78]

DOS is less commonly diagnosed by HRM compared with SM.[62 79 80] HRM can define patterns of OGJ obstruction, either mechanical (such as post-fundoplication dysphagia) or functional but not meeting the criteria for classical achalasia.[10 11 81] Functional OGJ obstruction needs to be differentiated from mechanical obstruction, and there is some evidence that the pattern of distal oesophageal motility can help to differentiate the two.[32] It has long been recognised that the pattern of DOS can occur with distal oesophageal obstruction,[82] so HRM can more confidently exclude this compared with SM.[11]

Using HRM, it has been recognised that the previous definition of simultaneous waves (contractile front velocity of distal peristaltic wave >8 cm/s) presenting in >20% of water swallows with amplitude >30 mm Hg,[83] is not specific for DOS.[10 84] Premature contractions, defined as a distal latency <4.5 s, is the best criterion for DOS.[10] Premature contractions can be measured by SM, although with more difficulty than with HRM. However, both OGJ relaxation and distal latency are more easily and reliably measured by HRM, which therefore has advantages over SM.

In patients with absent peristalsis, better termed 'absent contractility',[10] differentiating from type I achalasia is critical to management. HRM is superior in this regard, as OGJ relaxation is more reliably examined than with SM. Furthermore, adjunctive testing with MRS, RDC or a test meal can help identify such a diagnosis that may not have been evident from the standard water swallows of either HRM or SM.[46 47]

Hypercontractile oesophagus replaces the term nutcracker oesophagus, which was defined on the basis of SM as a mean distal contractile amplitude >180 mm Hg.[41] Originally, HRM DCI >5000 mm Hg.s.cm was taken to indicate hypertensive peristalsis, with a subgroup with DCI >8000 mm Hg.s.cm and repetitive contractions termed 'spastic nutcracker', invariably symptomatic in contrast with 'hypertensive peristalsis' defined by the lower threshold.[62] Hypercontractile disorders are differentiated from DOS by allowing <20% of swallows with a CFV >9 cm/s. The greatest DCI value observed after any water swallow among healthy subjects was 7732 mm Hg.s.cm, and a threshold of any swallow >8000 mm Hg.s.cm to define hypercontractile oesophagus was therefore proposed.[84] Three patterns of hypercontractile swallows were observed (in decreasing frequency): multi-peaked synchronised with respiration, multi-peaked not synchronised with respiration and not multi-peaked. The latter was more commonly associated with OGJ obstruction, while the former two were termed 'Jackhammer oesophagus'. Hypercontractile oesophagus defined in this way, and the particular variant of Jackhammer oesophagus, is rare, and may be associated with gastro-oesophageal reflux or OGJ obstruction, and treatment of these resulted in symptom relief in some patients.[84] Association with symptoms, in particular with dysphagia, was usual compared with individuals with DCI in the range 5000–8000 mm Hg.s.cm observed in earlier studies. Hypercontractile oesophagus is now defined as ≥20% of swallows with a DCI >8000 mm Hg.s.cm.[85]

Patients undergoing catheter based reflux monitoring

1.8 Oesophageal manometry is the preferred method by which to localise the LOS prior to catheter based pH probe placement.

GRADE evidence: High

Strength recommendation: Strong

Established convention is for the pH probe to be placed 5 cm above the manometrically determined upper border of the LOS, in order to prevent the probe inadvertently entering the stomach during the oesophageal shortening associated with swallowing.[86] The pH 'step-up' as the probe is withdrawn from the stomach into the oesophagus has been used for positioning.

However, a study comparing manometric placement to the step-up in pH method found that in 58% the step-up in pH did not accurately correlate with the position found at manometry.[87]

In a study of patients undergoing oesophageal pH monitoring, the pH probe was withdrawn such that it was positioned 5 cm above the manometrically determined LOS and its position checked by fluoroscopy.[88] It was found that 95% of pH catheters were positioned correctly in the oesophagus on fluoroscopy without kinks or bends. In the other 5%, the catheter was misplaced too proximally in the oesophagus but in the majority of these patients the catheter repositioned itself correctly when rechecked by fluoroscopy after the patient ate a meal. A combination of manometric localisation of the LOS, the step-up in pH in the oesophagus, along with being encouraged to eat straight after insertion of the pH catheter should result in correct placement.

Patients prior to antireflux surgery

1.9 Although there is currently no evidence to rule out or tailor antireflux surgery in patients with minor motor disorders, oesophageal manometry should be performed in advance of all patients being considered for surgery to rule out LOS dysfunction (ie, achalasia), as well as major motor disorders of the oesophageal body (eg, diffuse oesophageal spasm).

GRADE evidence: Moderate

Strength recommendation: Strong

Dysphagia is a potentially troublesome complication of antireflux surgery. A systematic review of studies examining 2453 patients reported an early dysphagia rate of 20% with 5.5% of patients experiencing dysphagia for more than 6 months after the surgery.[89]

Although there were initially some concerns about performing antireflux surgery in patients with abnormal oesophageal motility, to date there is no reliable evidence that these patients have an increased risk of postoperative dysphagia. There was no difference on SM in a cohort of 401 patients undergoing laparoscopic antireflux surgery between patients with and without postoperative dysphagia.[90] In patients initially without dysphagia, oesophageal motility preoperatively did not predict the likelihood of developing dysphagia after surgery. In a study of 103 patients who had undergone preoperative and postoperative SM, 8 of 15 with abnormal peristalsis before surgery regained normal peristalsis after surgery, while 13 of 88 initially with normal peristalsis developed abnormal peristalsis after surgery.[91] In 1354 patients who had undergone preoperative SM prior to laparoscopic fundoplication, primary peristalsis and distal contraction amplitude did not have a significant impact on postoperative dysphagia scores in patients undergoing laparoscopic fundoplication.[92]

Further studies have used combined multi-channel intraluminal oesophageal impedance with manometry to address this question and reported that LOS pressure and relaxation, peristalsis and bolus transit had no bearing on postoperative dysphagia.[93]

Preoperative manometry does prevent antireflux surgery being performed in the rare patient who presents with clinical features suggestive of gastro-oesophageal reflux disease but has a primary motility disorder such as achalasia or diffuse oesophageal spasm and allows accurate pH probe placement. It should be undertaken for these purposes, but not to change the type of antireflux surgery proposed.

Symptomatic patients after antireflux surgery

1.10 HRM can provide useful diagnostic information not obtainable by standard manometry among patients with dysphagia after antireflux surgery.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Dysphagia after antireflux surgery is not predicted by abnormal preoperative manometry[91 92 94] or by impedance measurement of oesophageal transit of a liquid or viscous bolus preoperatively or postoperatively[93 95] but rather by the degree of wrap.[92] Endoscopy and barium radiology detect abnormalities in a minority of patients, usually related to an anatomic or structural defect (such as a slipped or migrated wrap, or a gastric volvulus) occurring after surgery.[96 97]

SM is of no value in evaluating postoperative dysphagia[91 94] although recent careful studies with a Dent sleeve have shown a correlation between postoperative dysphagia and higher LOS residual pressure, raised intrabolus pressure IBP ahead of the peristaltic wave and lower peak peristaltic wave pressure.[95]

Most postoperative dysphagia is due not to oesophageal body motility disorders but due to gastro-oesophageal outlet obstruction, which is most commonly identified using HRM rather than during barium radiology.[98]Multiple water swallows and a solid test meal demonstrate outlet obstruction more frequently than single water swallows in post-fundoplication dysphagia.[44] Outflow obstruction with solid swallows is most predictive of a response to dilatation, with 58% of patients having symptom relief from subsequent balloon dilatation (the remaining non-responders required revisional surgery). The solid test meal mimics 'physiological' activity, and abnormalities can be related to the occurrence of symptoms of dysphagia during HRM.

A new HRM derived measurement of gastro-oesophageal barrier function termed the 'oesophagogastric junction contractile integral' is calculated in a similar fashion to the DCI for oesophageal body motility. This is altered to a different extent by different degrees of fundoplication wrap, compared with the preoperative reflux patient and healthy controls. However, it not yet clear if this measurement will predict postoperative dysphagia.[99]

Patients with suspected rumination

1.11 Rumination syndrome usually can be confidently diagnosed clinically on the basis of a typical history but if the diagnosis is unclear, the patient needs convincing of the diagnosis or objective evidence is required prior to therapy, HRM with impedance after a test meal can be utilised to identify diagnostic features. Simultaneous impedance provides additional confirmatory and diagnostic information.

GRADE evidence: Moderate

Strength recommendation: Strong

Rumination is an underreported syndrome characterised by near effortless postprandial regurgitation. It was thought to be confined to childhood and to those with developmental disabilities but it is now recognised to occur at all ages. To diagnose the condition, the history is key with (according to the Rome III diagnostic criteria): at least 3 months of regurgitation without preceding nausea or retching only during and up to 2 hours after meals, never at night; and the regurgitated food tastes 'pleasant' (not acidic) so the food can be chewed and re-swallowed.[100] A variety of other symptoms may be present (including heartburn, nausea, abdominal pain and weight loss) so confident diagnosis by history alone may not always be possible.

The cardinal event during or immediately preceding rumination is voluntary (although subconscious) abdominal wall contraction. This is associated with low pressure at the gastro-oesophageal junction which is easily overcome by the sudden rise in intragastric pressure.[100] These events, combined with retrograde passage of gastric contents, are best appreciated after a test meal with combined HRM and impedance/pH monitoring, the latter confirming that the regurgitated material is non-acidic and not gas.[101–103] Typical features are easily recognised: a pressure rise in the abdomen (>30 mm Hg) and in the oesophagus extending to the proximal oesophagus, together with an open LOS and UOS are characteristic.[104 105] The addition of impedance/pH monitoring confirms fluid regurgitation and helps differentiate 'variants' associated with belching (gastric or supragastric) and triggering by true acid reflux episodes.[104 105]

2. CATHETER BASED OESOPHAGEAL REFLUX MONITORING, INCLUDING pH AND IMPEDANCE MONITORING

Equipment

pH and pH/impedance catheters

pH catheters consist of one, usually antimony, pH electrode but can include a second electrode for simultaneous gastric and oesophageal pH, or proximal and distal oesophageal pH monitoring.

pH/impedance catheters consist of a minimum of pH electrode and six impedance rings spaced longitudinally from the tip of the catheter. pH/impedance monitoring detects retrograde flow of liquid or gas in the oesophagus and any corresponding drop in pH. This allows reflux episodes to be measured irrespective of their acidity or contents.

Patient preparation

Patients should undergo endoscopy after at least 2 weeks off proton pump inhibitors and, if appropriate, mucosal biopsies, prior to referral for oesophageal reflux monitoring for symptoms of heartburn, acid regurgitation or chest pain, to rule out mucosal causes for their symptoms. Patients referred for reflux monitoring for cough or throat symptoms, who do not have heartburn, acid regurgitation, chest pain or dysphagia, do not require endoscopy, as the incidence of oesophageal mucosal disease appears to be very low.

If pH or pH/impedance monitoring is to be conducted off medication, proton pump inhibitors should be stopped for 7 days and histamine H2 antagonists for 3 days before the study.[106] Antacids should not be consumed on the day of the study. Patients should fast for 6 hours prior to the test. Informed consent should be obtained.

There is likely to be an increased risk of bleeding from the nose during oesophageal reflux monitoring in patients taking antiplatelet agents, such as clopidogrel, and anticoagulants such as warfarin or direct acting oral anticoagulants. In the absence of guidelines or data on this risk, we cannot make a categorical recommendation that these agents are discontinued for oesophageal reflux monitoring but suggest that patients should be warned about the small increased risk, and in patients taking warfarin it is ensured that their international normalised ratio is within the therapeutic range (and not above) prior to testing. Individual practitioners may, however, wish to consider the individual risk of nosebleed balanced against the risk of discontinuing the anticoagulant/antiplatelet agent in each case.

Performing the test

Calibration should be undertaken in line with the manufacturer's instructions. The probe should be placed 5 cm above the upper border of the LOS as previously determined by oesophageal manometry. This prevents the electrode temporarily entering the stomach during oesophageal shortening associated with swallowing.[86]

Any staff member performing the procedure should be either fully trained and accredited by the AGIP in this procedure or supervised by a fully trained and accredited practitioner

Restrictions during ambulatory oesophageal reflux monitoring

During the recording period, patients should be encouraged to partake in their usual daily activities. Restrictions on diet, smoking, alcohol and exercise should be minimal to increase the chance of correlating symptoms and oesophageal acid exposure.

Meal periods should be removed from the pH or pH/impedance recording analysis to improve the separation of normal and abnormal oesophageal acid exposure.[107] To help determine this and improve recording of analysis of symptoms, patients should complete a diary during reflux monitoring to document the timing of meals, symptoms and supine periods.

Duration of ambulatory oesophageal pH or pH/impedance monitoring

Patients should ideally undergo a minimum of 24 hours of reflux monitoring. International consensus has suggested that a minimum of 16 hours of monitoring is needed to obtain clinically useful data.[108]

Analysis of pH and pH/impedance monitoring

Criteria for acid reflux event

A fall below pH 4 in oesophageal pH is taken to indicate acid reflux.

Oesophageal pH monitoring variables

A number of variables are used to differentiate patients with gastro-oesophageal reflux disease and asymptomatic controls. These include: percentage total time oesophageal pH <4; percentage time upright oesophageal pH <4; percentage time supine oesophageal pH <4; number of episodes oesophageal pH <4; number of episodes oesophageal pH <4 for more than 5 min; and the longest single episode oesophageal pH <4. A composite score was developed to express them.[109] However, the composite score has no advantage over the simpler percentage total time oesophageal pH <4.[1]

The previous guidelines suggested that, in the absence of locally determined ranges for physiological acid reflux, the following should be utilised: percentage total time oesophageal pH <4 <5%; percentage upright time oesophageal pH <4 <8%; percentage supine time oesophageal pH <4 <3%; and number of episodes pH <4 for >5 min <3.[1] However, it is now recommended that rather than a single cut-off value for percentage total time oesophageal pH <4, based on one 24 hour reflux monitoring period, that there should be two absolute values with total time <4% considered normal and total time >6% considered definitively abnormal, with values between 4% and 6% inconclusive.[110]

Analysis of symptoms

Different scoring systems have been suggested to provide information as to whether the patient's symptoms (restricted

to heartburn, acid regurgitation or chest pain) are related to episodes of reflux.

Symptom index

The symptom index (SI) is the number of symptom events associated with reflux as a percentage of the total number of symptom events.[111] A SI of at least 50% is the optimal threshold.[112] The SI is limited by the number of symptoms recorded during the monitoring period, as few recorded symptoms and numerous reflux episodes can produce false positive results.

Symptom association probability

The symptom association probability (SAP) is a statistical calculation used to determine the association of symptoms with reflux. It is calculated by dividing the data into 2 min sections and determining whether reflux and/or symptoms occurred in each section.[113] An SAP probability of >95% is considered positive as it implies a <5% chance that the association between symptoms and reflux has occurred by chance. The SAP score should therefore be examined first and if it is >95%, it is only then worth examining the other available symptom association measure to see if the SI also suggests an association.

Recommendations for pH and pH/impedance monitoring reporting

General information

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

Oesophageal acid exposure and symptom analysis

The following parameters should be included for acid exposure: percentage total time pH <4; percentage upright time pH <4; percentage supine time pH <4; and number of episodes pH <4 for >5 min.

The SI and SAP for the patient's symptoms for acid reflux episodes and all reflux episodes during impedance monitoring and the number of symptomatic events during the study should be included.

Technical aspects of reflux monitoring

2.1 Automatic analysis of oesophageal pH recordings and symptom association with acid reflux episodes is adequate for pH monitoring in patients, provided the recording is checked for artefacts and major technical issues, and that times of meals and symptoms have been accurately recorded.

GRADE evidence: Low

Strength recommendation: Strong

A comparison of manually editing pH recordings in healthy volunteers and patients to remove episodes of apparent acid reflux caused by ingestion of food or drink with simply excluding the meal period from the analysis found a close agreement in all pH parameters for distal oesophageal pH recordings.[114] Therefore, provided the recording is checked manually for artefacts and major technical issues with the recording, and that meal periods and symptom events are recorded accurately by the patient, and the former excluded from the analysis, automated analysis of oesophageal pH parameters and symptom association is adequate for clinical purposes.

2.2 Analysis of oesophageal pH/impedance recordings requires manual editing of reflux episodes and symptoms, to obtain accurate reflux quantification and reflux symptom association assessment.

GRADE evidence: Moderate

Strength recommendation: Strong

Analysis of impedance recordings is subject to marked variability between clinicians and automated computer analysis.[115 116] Automatic analysis overestimates the number of weakly acidic reflux episodes and inaccurately reports symptom association with non-acid reflux episodes. There is a need for manual editing of tracings and this can be confined to the 2 min window preceding symptoms, as this yields symptom association scores concordant with a full manual analysis with excellent interobserver agreement.[117] After editing, computer analysis can still be a helpful tool to quantify reflux and assess the relationship between reflux episodes and symptoms.[117]

2.3 To enhance the chance of establishing a diagnosis of gastro-oesophageal reflux disease and a symptom association with acid reflux, patients undergoing pH monitoring should not take acid suppression.

GRADE evidence: Moderate

Strength recommendation: Strong

A retrospective case series of patients undergoing pH monitoring suggests that very few patients (<4%) have persistent abnormal acid exposure when taking twice daily proton pump inhibitors but 30% when taking once daily proton pump inhibitors.[118] Furthermore, the key combination for confidently diagnosing gastro-oesophageal reflux disease of excess acid exposure and a significant association between acid reflux and the patient's symptoms is much less common in studies carried out on acid suppression (3.4%), compared with studies off acid suppression (30.4%).[119]Patients should therefore undergo pH monitoring off all acid suppression to maximise the chance of diagnosing excess acid reflux and a significant symptom association with acid reflux.

2.4. In patients with heartburn or acid regurgitation symptoms not responding to a proton pump inhibitor twice daily, if pH/impedance monitoring is required it should be undertaken on proton pump inhibitors if the patient has previous pathological endoscopic or pH monitoring findings, and the study should be performed off proton pump inhibitors if they have no previous such demonstration of pathological gastro-oesophageal reflux disease.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Patients undergoing pH/impedance monitoring in the context of heartburn or acid regurgitation not responsive to twice daily proton pump inhibitors, who have a high probability of gastro-oesophageal reflux disease (from previous endoscopic or oesophageal pH monitoring findings), should undergo the study on twice daily proton pump inhibitors, as this allows the establishment of whether the proton pump inhibitor dose is sufficient and the assessment of the association between persistent acid or non-acid reflux and symptoms.[120–122] Quantitative analysis of pH/impedance (acid exposure and number of reflux episodes) added to symptom/reflux association allows better phenotyping between refractory non-erosive reflux disease and functional heartburn.[123]

In order to demonstrate or exclude gastro-oesophageal reflux disease in patients without previous positive endoscopic or pH monitoring findings, pH/impedance monitoring should be performed off proton pump inhibitor therapy to quantify reflux and maximise the chance of diagnosing a significant symptom/reflux association.[124]

2.5 In patients with heartburn, acid regurgitation or chest pain, symptom association with reflux episodes is best assessed with both the SAP and SI.

GRADE evidence: Low

Strength recommendation: Conditional/weak

In a study involving two pH/impedance studies 1–4 weeks apart in the same subjects, the number of reflux episodes and the number of reflux episodes associated with heartburn, acid regurgitation or chest pain symptoms were highly reproducible.[125] In contrast, the number of symptom events reported was less reproducible, with a reduction in number between the two studies. Consequently, the SAP correlated well between the two pH/impedance tests but the SI was less reproducible. When acid reflux episodes alone were examined, only the SAP had very good reproducibility. Both symptom association measures (SAP and SI) were found to be reproducible but the SAP performed more consistently. In a study utilising pH monitoring alone, SAP was also found to be more reproducible than SI and it was recommended that SI not be used by itself given its limitations, particularly when symptoms were either infrequent (two or less episodes) or very frequent (>12 episodes).[126]

Two studies have reported significant underreporting of cough episodes based on contemporaneous audio recordings.[127 128] Symptom indices should therefore not be utilised for symptoms other than heartburn, acid regurgitation or chest pain, if based on patient reporting of symptomatic episodes.

2.6 In patients with throat or respiratory symptoms, dual probe distal oesophageal and proximal oesophageal or pharyngeal pH monitoring has no advantage over single probe distal oesophageal pH monitoring.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Case series of patients undergoing distal and proximal oesophageal or pharyngeal pH monitoring have shown a good correlation between distal and proximal oesophageal acid exposure.[129 130] However, the correlation between distal oesophageal and pharyngeal acid exposure was very poor.[129] In studies of healthy volunteers using impedance to define swallowing and reflux episodes, only 13% of pharyngeal pH drops were found to be due to reflux from the stomach and the rest were due to swallowing artefacts.[131] This explains the poor correlation between pharyngeal and distal oesophageal pH monitoring, and since proximal and distal oesophageal pH correlate well, there is no value in using more than one pH probe, which should be placed in the distal oesophagus.

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease

2.7 Patients with symptoms suspected to be due to gastro-oesophageal reflux disease should undergo a therapeutic trial of a proton pump inhibitor as the initial diagnostic approach.

GRADE evidence: Moderate

Strength recommendation: Strong

In the absence of evidence of erosive oesophagitis at endoscopy or when endoscopy has not been undertaken, patients with symptoms suspected to be due to gastro-oesophageal reflux should undergo a therapeutic trial of a proton pump inhibitor, rather than reflux monitoring.[132] A therapeutic trial of a proton pump inhibitor is cheaper, less invasive and more widely available than reflux monitoring.[133] High dose, twice daily proton pump inhibitor trials are more sensitive compared with pH monitoring.[134] A reduction of at least 75% in symptom frequency provided the highest sensitivity for a diagnosis of gastro-oesopahgeal reflux disease based on pH monitoring.[133]

A therapeutic trial of a proton pump inhibitor in patients with symptoms suspected to be due to gastro-oesophageal reflux disease should therefore consist of a twice daily full dose proton pump inhibitor for 4 weeks and be regarded as positive if there is at least a 75% reduction in symptom frequency.

If patients with symptoms suspected to be due to gastro-oesophageal reflux fail to respond to such a trial of a proton pump inhibitor, the proton pump inhibitor should be withdrawn, the diagnosis reconsidered and if gastro-oesophageal reflux is still considered a likely diagnosis, the potential value of further investigation by endoscopy and/or reflux monitoring discussed with the patient.

In patients with symptoms suspected to be due to gastro-oesophageal reflux disease with a positive response to a therapeutic trial of a proton pump inhibitor, we recommend, in view of its relatively low specificity for gastro-oesophageal reflux disease, discontinuing therapy and observing the patient's progress. If their symptoms return, they should be treated with the lowest dose of acid suppression sufficient to control their symptoms.[132]

2.8 Reflux monitoring with pH or pH/impedance is not recommended in patients with gastro-oesophageal reflux disease symptoms responsive to proton pump inhibitor therapy in who antireflux surgery is not planned.

GRADE evidence: Moderate

Strength recommendation: Strong

In patients with typical gastro-oesophageal reflux disease symptoms and a good response to proton pump inhibitor therapy, the correct diagnosis of gastro-oesophageal reflux disease can be made on clinical grounds and has a high sensitivity but relatively low specificity.[135] Performing reflux monitoring with pH or pH/impedance in these patients does not increase significantly the diagnostic yield. In patients with non-cardiac chest pain or other extra oesophageal symptoms, an initial therapeutic trial with a proton pump inhibitor is cost-effective compared with initial reflux monitoring tests.[136] Increased acid reflux is the most frequent reason for chest pain of oesophageal origin. If patients have a positive response to a proton pump inhibitor, further functional tests are not recommended.[137 138] However, if patients with typical gastro-oesophageal reflux disease symptoms (heartburn or acid regurgitation) wish to undergo antireflux surgery, preoperative reflux monitoring off proton pump inhibitors is indicated. If patients with atypical symptoms (chest pain, throat and respiratory symptoms) choose to continue their treatment with antireflux surgery, they should undergo reflux monitoring to confirm the relationship between their atypical symptoms and reflux.

2.9 In patients with heartburn or regurgitation not responding to twice daily proton pump inhibitors, reflux monitoring should be performed with pH/impedance monitoring, rather than pH monitoring alone. This technique allows diagnosis of increased acid exposure, association between symptoms and acid or non-acid reflux, and identification of phenotypes—ie, non-erosive reflux disease, hypersensitive oesophagus and functional heartburn.

GRADE evidence: Moderate

Strength recommendation: Strong

Case series of patients undergoing oesophageal pH monitoring for persistent gastro-oesophageal reflux disease symptoms despite proton pump inhibitor therapy reveal that persistent excess acid exposure despite taking a once daily proton pump inhibitor is seen in 30% of patients.[118] In patients studied while

taking twice daily proton pump inhibitors, persistent acid exposure is very uncommon, affecting around 7% of patients with heartburn or acid regurgitation and 1% of patients with chest pain, throat or respiratory symptoms. It is therefore logical to suggest in the first instance that in patients with persistent symptoms despite a once daily dose of proton pump inhibitor that the dose is increased to twice daily.

A cost analysis based on a case series of patients undergoing pH monitoring suggests that oesophageal pH monitoring is of value in refuting a diagnosis of gastro-oesophageal reflux disease in patients who fail to respond to proton pump inhibitors, through saving the cost of unnecessary proton pump inhibitor therapy.[139]

However, pH/impedance monitoring has highlighted the fact that pH monitoring does not detect all gastro-oesophageal reflux episodes when little or no acid is present in the refluxate, whereas impedance identifies the relation of reflux of all types to persistent symptoms and the importance of non-acid reflux in patients taking proton pump inhibitors.[120 140] pH/impedance monitoring reduces false negative studies compared with when pH monitoring alone is undertaken. In patients with endoscopic reflux oesophagitis and therefore established gastro-oesophageal reflux disease but normal total acid exposure on reflux monitoring, 89% had a positive symptom association for acid and/or non-acid reflux on impedance monitoring.[141] Furthermore, in a study of two separate pH/impedance studies in the same subjects, the number of reflux episodes and the number of reflux episodes associated with gastro-oesophageal reflux symptoms were highly reproducible, unlike the number of acid reflux episodes.[125] Approximately 60% of non-erosive reflux disease patients, who are refractory to proton pump inhibitors, have a positive reflux/symptom association, primarily due to non-acid reflux.[142 143] Classifying patients with symptomatic non-acid reflux as having a hypersensitive oesophagus reduces the number of patients classified as having functional heartburn and guides therapy. Finally, pH/impedance monitoring off proton pump inhibitor therapy best predicts response to antireflux therapy. Key parameters with predictive value include increased total acid exposure time and the correlation between symptoms and all reflux episodes (acid and non-acid) detected by impedance.[144]

2.10 In patients with chest pain, throat or respiratory symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors, we recommend performing reflux monitoring with pH/impedance, as this enables the diagnosis of pathological gastro-oesophageal reflux disease and/or an association between symptoms and acid or non-acid reflux.

GRADE evidence: Low

Strength recommendation: Strong

In patients with chest pain, throat or respiratory symptoms not responding to twice daily proton pump inhibitors, we recommend performing reflux monitoring.[145] pH/impedance monitoring enables the diagnosis or exclusion of both pathological acid gastro-oesophageal reflux and/or an association between symptoms and acid or non-acid reflux.[146]Patients with increased acid exposure and associated symptoms are the most likely to respond to proton pump inhibitor treatment. pH/impedance monitoring allows recognition of patients with hypersensitivity to non-acid reflux and oesophageal distension.[127 147] These patients may have chest pain or respiratory symptoms that do not respond to proton pump inhibitor therapy. Furthermore, impedance allows detection of reflux episodes with high proximal extent that in some respiratory disorders can favour microaspiration.[146]

In patients with symptoms of chest pain, throat or respiratory symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to a proton pump inhibitor twice daily, if pH/impedance monitoring is required it should be undertaken on proton pump inhibitors if the patient has previous pathological endoscopic or pH monitoring findings, and the study should be performed off proton pump inhibitors if, as is much more common, they have no previous such demonstration of pathological gastro-oesophageal reflux disease.

Patients with idiopathic pulmonary fibrosis, cystic fibrosis and lung transplantation with suspected gastro-oesophageal reflux disease

2.11 Patients with idiopathic pulmonary fibrosis, cystic fibrosis or other pulmonary disorders that might require lung transplantation, should have reflux monitoring with pH/impedance to detect pathological acid or non-acid gastro-oesophageal reflux prior to intensive proton pump inhibitor treatment or antireflux surgery.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Patients with idiopathic or scleroderma related pulmonary fibrosis, cystic fibrosis or other pulmonary disorders that might require lung transplantation, should have reflux monitoring with pH/impedance to detect pathological acid or non-acid gastro-oesophageal reflux prior to intensive proton pump inhibitor treatment or antireflux surgery.[148–150] In these patients, a diagnosis of gastro-oesophageal reflux based on symptoms is not sensitive enough. In patients with idiopathic pulmonary fibrosis, reflux is associated with a hypotensive LOS and abnormal oesophageal peristalsis, and often extends into the proximal oesophagus.[151 152] In cystic fibrosis and in patients post lung transplant, acid gastro-oesophageal reflux is common, but non-acid gastro-oesophageal reflux may also occur and be the origin of microaspiration and further pulmonary complications.[153]

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease and antireflux surgery planned

2.12 Patients with symptoms suspected to be due to gastro-oesophageal reflux disease responsive to a proton pump inhibitor should undergo oesophageal pH monitoring, rather than pH/impedance, before antireflux surgery to confirm excess oesophageal acid exposure and/or an association between symptoms and acid reflux episodes.

GRADE evidence: Moderate

Strength recommendation: Strong

In patients undergoing laparoscopic antireflux surgery for gastro-oesophageal reflux disease symptoms,[154 155] those with abnormal acid exposure on pH monitoring preoperatively had better long term patient satisfaction and less gastro-oesophageal reflux or dysphagic symptoms post-surgery. Similarly, in a randomised controlled trial of laparoscopic antireflux surgery versus proton pump inhibitors, excellent long term results were achieved with 85% in remission at 5 years following surgery of a carefully selected study group with endoscopic oesophagitis or abnormal acid exposure on pH monitoring and a symptomatic response to proton pump inhibitors.[156]Patients with gastro-oesophageal reflux disease symptoms responsive to proton pump inhibitor treatment that wish to undergo antireflux surgery should therefore have preoperative pH monitoring to confirm excess oesophageal acid exposure and/or an association between symptoms and acid reflux episodes.

Even in patients whose symptoms are responsive to proton pup inhibitor therapy, it has been suggested that preoperative

evaluation with pH/impedance monitoring can identify those with normal acid exposure but increased non-acid reflux episodes and/or an association between non-acid reflux and symptoms, potentially increasing the number of patients suitable for antireflux surgery.[157 158] However, in patients responsive to proton pump inhibitors, acid reflux is the cause of their symptoms and, therefore, evaluation of non-acid reflux with impedance is not relevant or necessary.

2.13 Patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responsive to a proton pump inhibitor should undergo oesophageal pH/impedance monitoring, rather than pH monitoring alone, before antireflux surgery to confirm excess oesophageal acid exposure and/or an association between symptoms and acid or non-acid reflux episodes.

GRADE evidence: Low

Strength recommendation: Strong

Case series of patients undergoing antireflux surgery suggest that responding to a proton pump inhibitor is associated with better long term symptomatic outcomes following surgery.[159] Case series utilising pH/impedance monitoring, rather than pH monitoring alone, preoperatively suggest that this increases the chance of finding a positive symptom association with any reflux event.[157 158] Although abnormal oesophageal acid exposure best predicts response to antireflux surgery over an average of 3 years, a positive SAP score for any impedance detected reflux was also independently associated with symptom response to antireflux surgery.[144] As refractoriness to acid suppression is associated with worse long term outcomes following antireflux surgery, careful selection of patients for antireflux surgery is essential, and we would recommend evidence of excess acid reflux and a positive symptom association on both the SAP and SI with reflux episodes as selection criteria for antireflux surgery.

In patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to a proton pump inhibitor twice daily, before undergoing antireflux surgery, they should undergo pH/impedance monitoring off proton pump inhibitors to confirm excess oesophageal acid exposure and/or an association between symptoms and acid or non-acid reflux episodes.

Patients with recurrent or persistent gastro-oesophageal reflux symptoms following antireflux surgery

2.14 Patients with recurrent or persistent gastro-oesophageal reflux symptoms following antireflux surgery should undergo reflux monitoring by pH/impedance, rather than pH monitoring alone, as this can objectively confirm or reject persistent gastro-oesophageal reflux and exclude other causes for symptoms, such as supra-gastric belching.

GRADE evidence: Low

Strength recommendation: Conditional/weak

Most patients respond well to antireflux surgery. However, there is a proportion of patients who are persistently symptomatic. There is a poor correlation between postoperative reflux symptoms and actual gastro-oesophageal reflux: 68% of patients who were taking acid reducing medications postoperatively had normal reflux monitoring.[160 161] Reflux monitoring should be performed early in the evaluation of patients with recurrent or persistent symptoms after fundoplication to avoid potentially unnecessary acid suppression therapy. Patients with recurrent or persistent symptoms following antireflux surgery should undergo reflux monitoring by pH/impedance, rather than pH monitoring alone. pH/impedance monitoring can objectively confirm or reject persistent gastro-oesophageal reflux and exclude other causes for symptoms, such as non-acid reflux or supra-gastric belching.[162 163] Fundoplication controls acid and non-acid reflux, but gas reflux is reduced to a lesser extent. In a subgroup of patients, persistent reflux symptoms after antireflux surgery are neither caused by acid nor by non-acid reflux, including gas. Fundoplication alters the belching pattern by reducing gastric belching (air venting from the stomach) and increasing supragastric belching (swallowed air vented without reaching the stomach).[163] This explains the increase in belching experienced by some patients after fundoplication, despite the reduction in gastric belching. It can be hypothesised that the reduction in gastric belching after fundoplication incites patients to increase supra-gastric belching in a futile attempt to vent air from the stomach.

3. WIRELESS OESOPHAGEAL PH MONITORING

Equipment and patient preparation

Wireless pH monitoring consists of a radio telemetry pH capsule attached to a delivery system and an external receiver.

In patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to a proton pump inhibitor twice daily, who require wireless pH monitoring, we recommend the study should always be performed off proton pump inhibitors.

Prior to wireless pH monitoring the capsule is activated and the wireless receiver is checked to be receiving the signal from the capsule. It is calibrated according to the manufacturer's instructions. The vacuum suction should be tested prior to the procedure. Patient preparation prior to the test is as described under catheter based reflux monitoring. Patients should fast for 6 hours prior to the test.

There may be an increased risk of oesophageal bleeding during or following wireless pH monitoring in patients taking antiplatelet agents, such as clopidogrel, and anticoagulants such as warfarin or direct acting oral anticoagulants. In the absence of guidelines or data on this risk, we cannot make a categorical recommendation that these agents are discontinued for wireless pH monitoring but suggest that patients should be warned about the small increased risk, and in patients taking warfarin it is ensured that their international normalised ratio is within the therapeutic range (and not above) prior to testing. Individual practitioners may, however, wish to consider the individual risk of oesophageal bleeding balanced against the risk of discontinuing the anticoagulant/antiplatelet agent in each case. We recommend following the BSG guidelines on antiplatelets and anticoagulants, if antiplatelets or anticoagulants are to be discontinued before wireless pH monitoring.[164]

Procedure

Patients undergoing wireless monitoring typically have an endoscopy prior to placement of the capsule. The wireless capsule is inserted via the mouth and placed 6 cm above the endoscopically determined squamocolumnar junction. Suction is then applied at a minimum of 550 mm Hg and for a minimum of 30 s to ensure the oesophageal mucosa has filled the suction chamber of the capsule. The delivery mechanism is then activated as per the manufacturer's instructions to release the capsule from the delivery device. Once the capsule is released, the suction is released and the delivery device removed. The clinician can then confirm capsule attachment by reinserting the endoscope.

The capsule usually sloughs off after a few days and rarely requires endoscopic removal. Early detachment of the capsule is described in 4–15% of wireless pH monitoring tests[165 166] and complications including significant chest pain have been reported in up to 9% of patients, requiring endoscopic removal in 1.5–4%.[167 168] Perforation has been reported very rarely.[169] If endoscopic removal is required, for example for severe chest pain, this can be performed using a snare to detach the capsule. Patients should not undergo an MRI examination within 30 days of wireless pH monitoring. A screening x-ray should be undertaken to ensure the capsule has passed if an urgent MRI examination is required.

Wireless pH monitoring variables and symptom analysis

Studies in healthy volunteers have suggested that the upper limit of normal for total time oesophageal pH <4 is slightly higher for wireless pH monitoring at 5.3%, compared with 5% for catheter based reflux monitoring.[167]

Symptom analysis is as described under catheter based reflux monitoring.

Recommendations for wireless pH monitoring reporting

As described under catheter based reflux monitoring.

Technical aspects of wireless pH monitoring

3.1 Wireless pH monitoring should be undertaken for at least 48 hours, as this increases the number of patients found to have excess acid exposure and the number of symptoms available for symptom association analysis.

GRADE evidence: High

Strength recommendation: Strong

Wireless pH monitoring is better tolerated than catheter based monitoring, producing less interference with daily activities, eating, sleeping and work.[170] Prolonged studies (>24 hours) are therefore feasible and acceptable to patients. It is also recognised that there can be considerable day to day variability in oesophageal acid exposure and symptom reporting, and a more prolonged period of pH monitoring can potentially produce a higher diagnostic yield. Analysis of the second 24 hour period of a 48 hour wireless pH study confirms this, increasing the proportion of patients with a pathological acid exposure time by 12.4% and doubling the symptoms reported, leading to a change in symptom association in 20% of patients.[171] Similar analyses found that the proportion of patients with a pathological acid exposure time increased by 22%, and 12.5% with the addition of a second 24 hours to the monitoring period.[172 173] A 20% rate of pathological acid exposure during the second 24 hours of a wireless pH study was also reported in a group of patients with proton pump inhibitor refractory reflux symptoms, a normal upper gastrointestinal endoscopy and normal acid exposure and symptom index for the first 24 hours.[174]

There may also be an enhanced symptom correlation with a 48 hour versus a 24 hour study, perhaps due to a decreased effect of sedation during endoscopy with a longer study. Significantly increased SAP scores for reflux symptoms have been reported during the second 24 hours compared with the first 24 hours.[175] Wireless pH monitoring should therefore be undertaken for at least 48 hours.

3.2 Wireless pH monitoring can be undertaken for up to 96 hours, if the capsule has not detached and the results at 48 hours are indeterminate, but both 'worst day' and 'average' analyses should be undertaken to determine a diagnosis of gastro-oesophageal reflux disease.

GRADE evidence: Moderate

Strength recommendation: Conditional/weak

Given that a more prolonged period of oesophageal pH recording provides more information for analysis, it would seem logical that, if the results at the end of a standard 48 hour recording period are indeterminate, a further recording period is undertaken. Extending the recording period for wireless pH monitoring up to 96 hours has been shown to increase diagnostic yield, both in terms of abnormal oesophageal acid exposure and symptom association.

A significantly higher diagnostic yield from a 96 hour than a 48 hour wireless pH test has been reported, mainly by allowing the SAP to be determined in more patients.[176] Others have reported similar small increases in diagnostic yields with studies that were prolonged from 48 to 96 hours.[174 177 178] However, in most patients with a pathological diagnosis from a prolonged (48–96 hours) wireless pH study, following a normal catheter based study, the diagnosis could be made in the first 24–48 hours of the prolonged wireless study.[178]

Prolonged wireless pH monitoring improves the diagnostic yield but this is dependent on the analysis methodology. The single 'worst day' for acid exposure results is often reported in published studies.[167 179] An alternative analysis is the 'average' of all days recorded.[167 177 180] Results based on 'worst day' analysis are associated with a steady increase in yield with longer monitoring, as results can only go in one direction, such that prolonged monitoring increases, and never decreases, the number of patients considered to have gastro-oesophageal reflux disease. Alternatively, 'average' measurements are stable and statistically robust over the time period measured with a high specificity for a gastro-oesophageal reflux disease diagnosis, as borderline cases 'dilute' over time.[177 178] This is the consequence of the high day to day variation in reflux episodes and symptom events. Specificity was reportedly increased from 84.5% with 'worst day' analysis to 94.8% when the first 2 days were averaged.[167] At 96 hours, 47% of patients had pathological oesophageal acid exposure using 'worst day' analysis, compared with 37% using the 'average' analysis, as borderline cases normalised.[178]

While 'worst day' analysis might be more appropriate in patients with intermittent symptoms, specificity decreases and the risk of a false positive diagnosis increases due to brief or isolated alterations in acid exposure.[177 178 181] Therefore, 'average' analysis is a more conservative assessment of pathological acid exposure and a positive result is more likely to be true, as it reduces variability.

The most logical approach in clinical practice appears to be to decide at 48 hours whether to prolong the wireless pH monitoring study further. If the first 2 days provide consistent results (ie, both are clearly positive or both are clearly negative) then it is unlikely that the subsequent 2 days will alter the diagnosis and further prolongation is likely to be unnecessary. Conversely, if the results of the first 2 days are discordant, markedly variable or borderline, prolonging the study duration would provide more data on which to base a definitive diagnosis. However, the latest wireless pH recorders are capable of recording for 96 hours and if such a recorder is utilised, the patient should simply be asked to bring their recorder back in 96 hours, so that the patient does not need to make an extra visit at 48 hours.

Patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors

3.3. Wireless pH monitoring should be undertaken in patients with symptoms suspected to be due to gastro-oesophageal reflux disease but not responding to twice daily proton pump inhibitors who require pH monitoring but who have been intolerant of catheter based monitoring, leading to inconclusive results, or who would be very likely to be poorly tolerant.

GRADE evidence: Moderate

Strength recommendation: Strong

Standard naso-oesophageal pH catheters can be uncomfortable and socially embarrassing, and limit normal physical activities, sleeping and dietary intake. It has been found that 5–10% of patients are intolerant of naso-oesophageal intubation, have anatomical abnormalities such as nasal septal defect or fail to complete 24 hours of ambulatory catheter based pH monitoring.[182 183] Patients with negative reflux monitoring results but ongoing gastro-oesophageal reflux disease symptoms are considered to have a 'functional' oesophageal disorder (ie, functional heartburn). However, one in three patients will have a different diagnosis, if the pH study is repeated on two separate days, with reproducibility ranging from 77% to 83%,[182 184–186] so the reliability of such a diagnosis can be limited. The diminished clinical value and diagnostic yield of 24 hour catheter based monitoring is likely to be related to the high physiological day to day variability in acid exposure and symptom reporting; limitations that are more pronounced when reflux episodes are infrequent and symptoms are intermittent (eg, less than six per day).[170 177 184 187] As a consequence, patients with false negative results may be denied appropriate therapy.

Studies have shown that wireless pH monitoring is better tolerated than catheter based monitoring, producing less interference with daily activities, eating, sleeping and work.[170 183] This suggests a role for wireless pH monitoring not only in patients who cannot tolerate the catheter but also in the group whose catheter based study gives inconclusive results, as the wireless monitoring may provide definitive diagnostic information and allow discontinuation of inappropriate drug therapy or determine the appropriateness of undertaking antireflux surgery.

Although there are potential advantages of wireless pH monitoring over standard nasal catheter based testing, these must be balanced against the significantly increased expense of wireless pH monitoring, including the cost of endoscopy to assist insertion. Positioning the wireless pH capsule per orally with topical local anaesthesia based on the manometrically determined position of the LOS, rather than with endoscopic guidance, is feasible and well tolerated in the majority of patients, and could potentially reduce the cost of a wireless pH study.[188] However, this is rarely undertaken in clinical practice and will not be possible in those who were intolerant of catheter insertion.

In summary, despite the higher associated costs, wireless pH monitoring should be undertaken in patients with gastro-oesophageal reflux symptoms refractory to twice daily proton pump inhibitors, who have been intolerant of catheter based monitoring causing inconclusive results or who would be very likely to be poorly tolerant (eg, due to anatomical abnormalities), in whom wireless pH monitoring is likely to change management.

AUDIT

Items that could be subject to audit to establish high standards of oesophageal manometry and reflux monitoring include:

1. Any staff member performing manometry or reflux monitoring should either be fully trained and accredited by the AGIP in this procedure or supervised by a fully trained and accredited practitioner.
2. All patients undergoing manometry for the investigation of dysphagia should undergo at least one form of adjunctive testing (eg, larger volumes of water, solid/viscous swallows or a test meal).
3. All patients undergoing going manometry to investigate dysphagia should have previously undergone endoscopy (and mucosal biopsy).
4. All patients undergoing reflux monitoring should have manometry to guide probe placement.
5. All patients undergoing antireflux surgery should have manometry to exclude major oesophageal motility disorders.
6. All impedance recordings should be manually edited to ensure accurate reflux symptom association.
7. All patients should have at least two methods of symptom association assessed (eg, SAP and SI).
8. All patients should undergo reflux monitoring prior to antireflux surgery.

FUTURE RESEARCH

High resolution manometry

1. How can HRM and novel HRM parameters (eg, OGJ contractile integral) be used to predict the presence of gastro-oesophageal reflux disease?
2. Can we use HRM parameters to prognosticate who might respond well or less well to antireflux surgery?
3. Is OGJ outflow obstruction with no other cause another form of achalasia or is it a separate clinical entity?
4. What is the role of endoflip in assessing oesophageal function and can this help prognosticate who might benefit from intervention (eg, either with obstruction or reflux)?

Reflux monitoring

1. Further data on pH/impedance monitoring in healthy asymptomatic subjects is required to clarify normal impedance monitoring values.
2. To assess the reproducibility and validity of the new impedance parameters (mean nocturnal baseline impedance and post reflux swallow induced peristaltic wave index) and confirm their clinical value in discriminating patients with different reflux phenotypes.

Wireless pH monitoring

1. The feasibility of non-endoscopic placement of a wireless pH capsule to try to reduce the costs involved.
2. Research into methods to reduce the early detachment rate for wireless pH monitoring.

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