Peer Review File

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Reviewer comments

Comment 1: Please reference current published consensus guidelines on key minimum measures for pharyngeal manometry reporting.

> Reply 1: We have referenced the current published guidelines (reference 21) and have made the minimum measures – known 'core outcome set' clearer in the Table 1.
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> Changes in the text: Recently, an international working group recommended a standardised testing protocol and defined set of pressure and impedance measures ('core outcome set') for application in both clinical and research settings, to address the variability of testing protocols (number of swallows assessed and bolus medium) and reported metrics (Table 1) (21).

Comment 2: I would also suggest some discussion of normative values, and ambiguity regarding their definition

> Reply 2: We acknowledge that pharyngeal manometry is an evolving field and have discussed the initial issues with collecting normative values for P-HRM-I, however, we believe that these issues have been addressed by the P-HRM-I international working group standardised protocol.
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> Changes in the text: Recently, an international working group recommended a standardised testing protocol and defined set of pressure and impedance measures ('core outcome set') for application in both clinical and research settings, to address the variability of testing protocols (number of swallows assessed and bolus medium) and reported metrics (Table 1) (21). Since that time, normative data of asymptomatic healthy adult controls (18-79 years old) of a moderate cohort size (n=50) reported the mean and standard deviation of core and additional outcome measures (metrics not included in the core outcome set such as BPT and SRI) (34). More recently, the normative data set of a large asymptomatic cohort (n=120) reported core UOS outcome measures (22). Furthermore, access to an online analysis platform like www.swallowgateway.com allows the clinician to compare quantified results of an

individual patient against these healthy ranges. It is acknowledged that ongoing normative data collection will allow the refinement of diagnostic thresholds.

Comment 3: May I suggest a little more discussion of the relevant evidence to support/refute the use of pharyngeal manometry in the management of these conditions, and the clinical implications. It is adequate for example in Case 3 & 4 but less so in Case 2

Reply 3: We have expanded the discussion for Case 2 (Globus) and highlighted that in a small number of cases, P-HRM-I can be beneficial to exclude potential UOS dysfunction and provide patients with biofeedback of healthy swallowing.

Changes in the text: In the absence of significant self-reported swallowing issues, most patients would be reassured by the Otolaryngology examination findings and discharged (38). In a small number of cases, a P-HRM-I assessment can be beneficial to exclude potential UOS dysfunction or hypertonicity contributing to globus sensation, and provides the patients with biofeedback of healthy swallowing. The P-HRM-I biofeedback is particularly helpful in those patients presenting with minor/inconsistent swallowing difficulty and globus for confirmation of a swallow within the normal range of P-HRM-I.

For a typical patient, the P-HRM-I output should demonstrate an appropriately coordinated swallow comparable to the spatio-temporal plot shown in the healthy example (Figure 1a). Furthermore, pharyngeal and UOS pressure and impedance measures should be within normal limits. An additional advantage of P-HRM-I is that the catheter can be placed to extend across the oesophagus to assess for contributory oesophageal motility disorders such as achalasia or oesophageal spasm (18).

This globus case highlights the benefit of using P-HRM-I to assess pharyngeal swallowing without the use radiation (VFSS). Additionally, P-HRM-I offers an immediate assessment of UOS dysfunction with the potential application of biofeedback for the patient (42). The clinician can review the pharyngeal topography plots of the individual swallows for features of UOS dysfunction using the recently proposed classification scheme describing UOS disorder types (22)

Comment 4: I don't think this is a cogent statement as a Barium swallow is a surrogate mucosal / anatomical evaluation in the context of globus, and is not utilised to assess

pharyngeal swallowing - They can also be complimentary investigations, so it's not an either/or situation necessarily. Perhaps a VFSS may be a better comparison, and perhaps temper the word 'un-necessary', as some may argue that even a manometric study is 'un-necessary' in the context of globus, without dysphagia and alarm features, and normal endoscopy.

> Reply 4: Thank you for your feedback. We have amended the statement highlight the potential benefit of P-HRM-I without the need for radiation (VFSS); this has been further addressed in the previous reply and changes.
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> Changes in the text: This globus case highlights the benefit of using P-HRM-I to assess pharyngeal swallowing without the use radiation (VFSS).

Comment 5: replace 'inferring' with 'implying'

> Reply 5: This has been changed in the text.
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> Changes in the text: Biomechanical pressures, timing and impedance metrics at the UOS demonstrated abnormal values, implying UOS dysfunction

Comment 6: The argument that altered pressures/metrics directly represents dysfunction may be true, but you should take care to distinguish this from diagnosing 'dysphagia', as swallow metrics may be altered or elevated, and yet, this doesn't necessarily result in a dysfunctional swallow. So again, I would temper this statement.

> Reply 6: We have amended this statement to highlight that pharyngeal contractile integrals highlight generated pressures within the pharynx, as opposed to VFSS/FEES, where this would be inferred. We have also acknowledged that an abnormal P-HRM-I metric in isolation may not be clinically significant or relevant and that it should be considered in the context of the patients reported symptoms and available imaging assessments (although multiple abnormal manometric findings, correlate to worsening swallow function visualised on VFSS).
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> Changes in the text: The pharyngeal contractile integral metrics provide direct measure of generated pressures within the pharyngeal lumen (21), in contrast to inferred dysfunction from imaging assessments. Furthermore, P-HRM-I at the UOS is considered advantageous when compared with imaging assessments (55). It is important to recognise that an abnormal P-HRM-I metric in isolation may not be

clinically significant and should be considered in conjunction with patient reported symptoms and any available imaging assessments.

Comment 7: Fig. 3b 650 replace 'infer' with 'imply'

Reply 7: This has been changed

Changes in the text: These data imply UOS dysfunction associated with the cricopharyngeal bar, indicating this patient may benefit from UOS dilatation or surgical intervention.

Editorial Comments

Comment 1: We suggest the authors cite relevant literature to demonstrate the correlation between the P-HRM-I and the VFSS in assessing swallowing function. It would be better to understand why the focus of this paper is on the P-HRM-I rather than the gold standard VFSS based on this and the quantitative shortcomings of the VFSS. For the authors' reference:

- Park D, Oh Y, Ryu JS. Findings of Abnormal Videofluoroscopic Swallowing Study Identified by High-Resolution Manometry Parameters. Arch Phys Med Rehabil. 2016 Mar;97(3):421-8.

- Lan Y, Xu G, Dou Z, Lin T, Yu F, Jiang L. The correlation between manometric and videofluoroscopic measurements of the swallowing function in brainstem stroke patients with Dysphagia. J Clin Gastroenterol. 2015 Jan;49(1):24-30.

Reply 1: Thank you for your feedback, the correlation of VFSS and P-HRM-I has been included into the third paragraph of the introduction. These references have also been added. We have highlighted that VFSS and FEES provide a visual information of bolus transfer (aspiration and penetration), however, unlike P-HRM-I, these assessments are unable to provide insight into the biomechanics of the swallow breakdown.

Changes in the text: A videofluoroscopic swallowing study (VFSS) or a flexible endoscopic evaluation of swallowing (FEES) are widely used instrumental assessments, but they provide limited insight into the biomechanical breakdown (5). Despite advancements in quantitative reporting tools (6, 7) for visual instrumental assessments, there remains no globally accepted measures, leaving clinical interpretation of the swallow beyond identifying penetration and aspiration, predominantly dependent on clinician experience (8, 9)….. It can identify and

localise alterations in the swallowing mechanism and determine the underlying pathophysiological breakdown leading to dysphagia. P-HRM-I metrics have been demonstrated to correlate with and be a predictor of aspiration on concurrent videofluoroscopic studies (10, 11, 12, 13).

Comment 2: Which hospital did the case examples in clinical research databases come from? Please add the detailed information instead of using vague descriptions “clinical research databases”.

Reply 2: We have specified which hospitals these cases have been extracted from in the text.

Changes in the text: Case examples have been extracted from studies from two centres: Flinders Medical Centre (Adelaide, Australia) and St George Hospital (Sydney, Australia) (approved by Southern Adelaide Clinical Human Research Ethics Committee and St Vincent’s Hospital Human Research Ethics Committee).

Comment 3: We suggest the authors give more content about the complications of P-HRM-I and the relevant complications rates for the readers’ convenience.

Reply 3: Specific percentages of the reported complications have been included in the review

Changes in the text: P-HRM-I has been demonstrated to have high patient tolerability, with similarly low rates of complications (gagging 14%, vomiting 2% and epistaxis <1%) (22) as those reported for other trans-nasal procedures, such as nasoendoscopy. In our experience, complication rates are far lower and only occur during placement of the catheter and will resolve once the catheter is appropriately placed.

Comment 4: The review provides an informative summary of the application of P-HRM-I based on the case examples. Despite growing enthusiasm for P-HRM-I as a diagnostic modality, there are still some unsolved problems. We prefer the authors ever add your thoughts regarding those unsolved question based on the clinical experience in this clinical review. For example, when is an P-HRM-I -only procedure appropriate? What are the

circumstances under which adjunct radiology should be considered essential? We believe the readers would benefit from the content.

> Reply 4: Thank you for your feedback. The utility of P-HRM-I as a stand-alone or adjunct imaging swallowing assessment (based on our clinical experience) has been added to the third paragraph of the discussion.
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> Changes in the text: This paper illustrates the potential for P-HRM-I assessments in extending the interpretation of imaging swallowing assessments. These findings may facilitate the continued clinical adoption of this novel technology by Otolaryngologists. P-HRM-I can be utilised either as a stand-alone assessment or as an adjunct to fluoroscopy (VFSS). In our centre, we utilise stand-alone P-HRM-I mainly in patients with an anticipated low aspiration risk, patients who have had VFSS recently performed (10, 25) or in those where VFSS is difficult to perform due to patient or location factors (intensive care unit patients). A concurrent VFSS and P-HRM-I will be conducted in patients with known severe dysphagia.

Comment 5: Besides, as the reference 21 stated, the ability of P-HRM-I to predict outcomes, determine therapeutic effects, monitor disease recovery or progression or enable biofeedback training is currently unknown. According to the P-HRM-I swallowing study, different treatments were suggested to the case examples in the paper. Whether the therapeutic outcomes was available of case 3a, 3b, 4a and 4b (i.e., did the case 3a gain good outcome after management of swallowing exercises and dietary modifications)? If available, provide add the information which might further highlight the added value of a P-HRM-I assessment.

> Reply 5: Repeat data (standardised patient outcomes or HRM data) was not available. This review was aiming to highlight how P-HRM-I can be applied in ENT practice for a typical caseload. The P-HRM-I interpretations have been supported through case examples from our gastroenterology colleagues. Further studies are required to assess the therapeutic outcomes for ENT procedures and interventions prospectively.

Comment 6: We are also eager to hear the authors' views about the future direction of P-HRM-I. Should P-HRM-I be preserved as a comprehensive, stand alone, pharyngeal examination to diagnose a pharyngeal dysfunction? Which aspects should we focused on for P-HRM-I in the future ENT practice?

Reply 6: We have included and discussed the future direction of P-HRM-I in the fourth paragraph of the discussion.

Changes in the text: To improve translation into the clinical setting, a classification scheme has recently been proposed, categorising the biomechanical breakdown at the pharynx and UOS (25). Additionally, quantitative P-HRM-I metrics allow for longitudinal assessments of dysphagia or to evaluate and guide the true effect of an intervention (dietary modifications, targeted swallowing exercises, UOS dilatation, cricopharyngeal myotomy or Botox) on swallowing outcomes, (17, 18, 19, 20, 64). These quantitative measures enable demonstration of treatment efficacy…… We anticipate that continued and increased uptake of P-HRM-I across multiple centres may facilitate the collection of normative data, improving the generalisability of this translational swallowing assessment technology.