High- resolution manometry combined with impedance measurements discriminates the cause of dysphagia in children.

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Abbreviations

AIM	Automated Impedance Manometry
EGJ	Esophago-Gastric Junction
EPT	Esophageal Pressure Topography
GERD	Gastro-Esophageal Reflux Disease
HRM	High Resolution Manometry
HRMI	High Resolution Manometry Impedance
IBP	Intrabolus pressure
IBP-slope	Intrabolus Pressure slope
ICD	Iso Contour Defect
IRP	Integrated Relaxation Pressure
NS	Not Significant
PFI	Pressure Flow Index
PNI	Pressure at Nadir Impedance
PP	Peak Pressure
TNIPP	Time from Nadir Impedance to Peak Pressure

What is already known about this subject:

- Pressure-flow analysis (PFA) can detect abnormalities in esophageal motility using integrated analysis of bolus propulsion and bolus flow during swallowing.
- AIM analysis has recently been reported to be useful in identifying subtle pre-operative esophageal dysfunction in adult patients who developed post-fundoplication dysphagia as well as in patients with non-obstructive dysphagia.

What are the new findings:

- Pressure flow parameters can distinguish the cause of dysphagia in pediatric patients
- Combined high resolution manometry and impedance measurements with pressure-flow analysis can differentiate pediatric patients with dysphagia symptoms in relation to either weak peristalsis (poor bolus clearance) or over-pressurization (abnormal bolus flow resistance).

How might it impact on clinical practice in the future?

- This study supports the use of a novel objective analysis method on recordings that are readily used in pediatric clinical practise.
- The pressure flow approach allows discriminating esophageal dysfunction in relation to dysphagia symptoms in children. This has not been achieved in children with current analysis methods.
- The new findings of this study allow a dichotomous categorization of esophageal function, which may help to guide the selection of the most optimal treatment such as pharmacological or endoscopic therapy.

ABSTRACT

Pressure-flow analysis allows assessing esophageal bolus transport in relation to esophageal pressures. This study aimed to characterize pressure-flow metrics in relation to dysphagia in pediatric patients. We analysed esophageal pressure impedance recordings of 5ml liquid and viscous swallows from 35 children (17M, mean 10.5±0.8 yrs). Primary indication for referral was GERD (9), post-fundoplication dysphagia (5), idiopathic dysphagia (16), trachea-esophageal fistula (2) and other (3). Peristaltic function was assessed using the 20mmHg iso-contour defect and the timing between bolus pressure and flow was assessed using the Pressure Flow Index, a metric elevated in relation to dysphagia. Patients were stratified in relation to dysphagia and to peristaltic defect size. Dysphagia was characterized by a weaker peristalsis for liquids and higher Pressure Flow Index for viscous. When patients were stratified based on weak or normal peristalsis, dysphagia with weak peristalsis related to a larger iso-contour defect size and dysphagia with normal peristalsis related to higher Pressure Flow Index

Conclusion: Pressure-flow analysis enables differentiation of patients with dysphagia due to weak peristalsis (poor bolus clearance) from abnormal bolus flow resistance (esophageal outflow-obstruction). This new dichotomous categorization of esophageal function may help guide the selection of optimal treatment such as pharmacological or endoscopic therapy.

KEYWORDS

Esophageal motility; high resolution manometry; impedance measurement; dysphagia

INTRODUCTION

Early satiety, perception of food getting stuck in the esophagus, gagging, pain, food refusal and vomiting are common clinical symptoms of esophageal dysphagia in children. These symptoms may be indicative of an underlying esophageal motility disorder potentially caused by impaired esophageal propulsion or increased resistance to bolus flow at the esophago-gastric junction (EGJ). Currently, high resolution manometry (HRM) is becoming the standard investigation for diagnosis of esophageal dysmotility [5]. HRM recordings with esophageal pressure topography (EPT) enables features of peristalsis, such as the pattern and integrity of the contraction, as well as the extent of EGJ relaxation to be more easily determined via objective metrics [20,10,4]. The clinical interpretation of EPT metrics for the diagnosis of esophageal motility disorders is currently guided by the Chicago Classification [2]. However the applicability of the Chicago Classification to the pediatric population remains problematic as certain important metrics such as integrated relaxation pressure and distal latency, are age and size dependent, and therefore, require adjustment in order to improve diagnostic accuracy in children [23]. Furthermore, pediatric EPT data are limited due to clinical challenges [22] and normative values are lacking due to ethical restrictions.

Despite the fact that the HRM technique allows identification of esophageal motility disorders, the relationship between esophageal contractile patterns and bolus transport disruption, leading to bolus hold up perception and symptoms, is far from clear, even in adults. Symptoms of dysphagia poorly correlate with conventional manometric findings [6] and the underlying cause of these symptoms still remains unclear in a large proportion of dysphagia patients [6, 7, 9, 18].

The evidence that HRM based metrics are improving the predictability of bolus transit failure is inconsistent [1], suggesting that manometry as a standalone technique may not be sensitive

enough to elucidate esophageal motility events underlying ineffective esophageal bolus clearance and/or dysphagia. Therefore combining esophageal pressure patterns with bolus flow measured by intraluminal impedance was proposed to assess bolus transport throughout the esophageal lumen and across the EGJ [12, 13, 14]. Unfortunately, the combined manometry-impedance measurements yielded little in terms of further diagnostic insights in patients presenting with dysphagia [13, 14].

A novel analysis method combining pressure and impedance has been recently developed [16]. Pressure-flow analysis (PFA) has been shown to detect pharyngeal bolus residue and aspiration during deglutition [16] as well as esophageal bolus hold up in relation to dysphagia in both adults [3, 11, 15, 17, 21] and to a limited extend in pediatric populations [8].

We hypothesize that PFA may be an adequate tool to differentiate the underlying motility disorders causing esophageal dysphagia in a heterogeneous cohort of children presented with dysphagia symptoms. Therefore, the purpose of this study was to characterize pressure-flow metrics in relation to dysphagia symptoms in pediatric patients.

METHODS

Subjects

High resolution manometry impedance recordings from 35 children (17M, 18F, mean 10.5±0.8yrs SD) (Table 1) were retrospectively included. All studies were conducted at the Centre for Motility and Functional Gastrointestinal Disorders at Boston Children's Hospital, USA. The primary reasons for referral included gastroesophageal reflux disease (GERD; n=9), post-fundoplication dysphagia (n=5), dysphagia of unknown etiology (idiopathic;

n=16), tracheo-esophageal fistula (n=2) and other (dysphagia after resection of hemangioendothelioma; n=1, behavioral issues; n=1, chest pain; n=1). Patients with achalasia were excluded from the present study. Access to patient files was approved by the Research Ethics Committee, Boston Children's Hospital, USA (P00001287).

Study Protocol

Manometry-impedance data were acquired using a 3.2mm diameter solid state catheter incorporating 36, 1cm spaced pressure sensors and 12 adjoining impedance segments spaced at 2cm (Unisensor USA Inc, Portsmouth, NH).

Subjects were intubated after topical anaesthesia (2% lidocaine) was applied to the nose, and the catheter was positioned with sensors straddling the upper esophageal sphincter (UES), entire esophageal body and EGJ with at least 2 manometric sensors positioned in the stomach. Pressure and impedance data were acquired at 20Hz (Solar GI, MMS, Netherlands) with the patient sitting semi-supine. A maximum of 10 boluses of 5ml saline (0.9% NaCl) and 5ml viscous bolus (Sandhill Scientific Inc) were administered orally via a syringe after a minimum 5-min accommodation period.

Dysphagia assessment

Patient clinical notes were reviewed to collect data on underlying conditions, dysphagia symptoms and past therapies. Patients were classified as positive for dysphagia if perception of bolus hold up during deglutition of a solid bolus was reported by the patient or parent/caregiver during the pre-consultation leading to the manometric assessment.

Data analysis

Pressure flow analysis metrics were objectively derived from the raw pressure-impedance data using using AIMplot, a purpose designed analysis software (Copyright T Omari,

MATLAB version 2009b, The MathWorks Inc, Natick, MA, USA). Analysis was performed blinded to final diagnosis. The AIM analysis method is illustrated in Figure 1. AIMplot derived parameters have been described previously (17-22). The following pressure-flow variables were derived:

a) Peak Pressure (PP, mmHg): marker for esophageal contractile strength.
b) Pressure at Nadir Impedance (PNI, mmHg): intrabolus distension pressure during bolus transport.
a) Intrabolus Pressure (IBP, mmHg): marker for obstruction.
b) IBP slope (IBP slope, mmHg/sec): marker for the degree of pressurisation needed to propel the bolus onward.
c) Time from Nadir Impedance to Peak Pressure (TNIPP, sec): time interval between nadir impedance (identifying the centre of bolus) and peak esophageal pressure: marker marker of how far ahead of the peristaltic wave the bolus moving.
d) Pressure Flow Index (PFI) reflects the relationship between intrabolus pressure and bolus flow timing in the esophagus. The PFI is calculated using the formula PFI = (IBP * IBP slope)/(TNIPP) and is a predictive measure elevated in relation to dysphagia (17-18). PFI serves as global measure of pressure-flow.

Pressure-flow metrics were derived for the whole length of the esophagus as well as the most distal part of the esophagus (from transition zone to EGJ). The peristaltic integrity was also assessed on the HRM plot using the 20mmHg iso-contour defect (ICD) (5).

This PFA analysis was performed in a heterogenouos group of 30 children presenting with esophageal dysphagia without underlying anatomic and congenital malformations. Pressure-flow metrics derived from 25 healthy controls aged 20-50yrs with no dysphagia (7M; mean age 36.1± 2.2yrs) was used as a control reference range (10^{th} -90^{th} percentile; collated at the

Gastroenterology Unit, WCH, North Adelaide, Australia and the Intestinal Procedures Unit, RGH, Daw Park, Australia).

Statistical analysis

All statistical analyses were performed using SigmaPlot 11.0 (Systat Software Inc., Chicago,IL, USA). Patients were stratified with or without dysphagia depending on the presence of symptoms of dysphagia on solids as obtained from the clinical notes. Furthermore, patients were stratified as having weak or normal peristalsis depending on the peristaltic defect size on HRM (weak peristalsis = ICD >2 cm) [24]. AIM parameters were averaged for all liquid and viscous swallows prior to all analysis. Data are expressed as mean ± SEM or Median [IQR]. Grouped data comparisons were done using One Way Analysis of Variance (Bonferroni *post-hoc*) or one Way Analysis of Variance on the Ranks (Dunn's *post-hoc*).

RESULTS

1. Pressure-flow metrics relation to reported symptoms of dysphagia on solids.

In 35 patients, a total of 658 swallows were analysed comprising 343 liquid and 315 semisolid boluses (Table 2).

Out of 25 patients reporting dysphagia (Table 1), all had reported dysphagia to solids. Although, pressure-flow metrics for the whole oesophagus did not discriminate children reporting dysphagia, PFI in the distal esophagus was significantly increased for viscous boluses. Furthermore, a larger ICD for liquid boluses was also found in patients reporting dysphagia to solids. Data are shown in Table 2.

2. Pressure-flow metrics according to underlying pathology

This analysis was performed in the 30 children without underlying anatomic and congenital malformations. All patients were clinically presented with symptoms of dysphagia: 9 had GERD, 5 were investigated post fundoplication and16 presented with idiopathic dysphagia. Table 3 summarises the ICD and pressure-flow metrics for liquid and viscous boluses between these three diagnostic groups. For liquid boluses, the TNIPP in post-fundoplication patients was significantly shorter compared to the GERD patients who had not undergone anti-reflux surgery. For viscous boluses, an overall trend for higher PNI was seen within the post-fundoplication group, although statistical significance was not reached (p=0.06).

3. The relationship between peristaltic integrity and oesophageal bolus pressurisation

Patients were further stratified based on the presence of normal or weak peristalsis as indicated by the ICD size (12). Patients with a history of dysphagia to solids displayed significantly larger peristaltic breaks for both liquids and viscous boluses (Figure 2). Bolus pressurisation, as indicated by PFI, was increased in patients with dysphagia to solids (Table 2), however, when stratified on peristaltic capacity (normal vs. weak) no differences were found (Figure 3). This finding is illustrated by a clinical case of a post fundoplication patient in Figure 4. In a two year old girl with post- fundoplication dysphagia, standard EPT metrics yielded normal findings for esophageal peristaltic integrity (ICD <2cm) and EGJ pressure (IRP4s = 3mmHg). However, pressure-flow analysis metrics demonstrated that the patient exhibited a highly elevated PFI suggesting high flow resistance during swallowing (liquid PFI = 344 and viscous PFI = 1447). Careful review of the manometric tracing, revealed frequent episodes where the initiation of a pharyngeal swallow failed to inhibit the progression of esophageal primary peristaltic wave and thus, suggesting an impaired deglutitive inhibition in this patient._

4. Esophageal motility profile of pediatric patients with history of dysphagia to solids

Pediatric patients were stratified into using a dichotomous motility matrix based on PFI and ICD (Figure 5). Patients without a history of dysphagia were situated within the range of young adult healthy controls (10^{th} – 90^{th} percentile) whereas patients with a history of dysphagia were located outside the range.

DISCUSSION

Dysphagia in children is still a very poorly understood clinical phenomenon. Symptoms of vomiting, perception of food being stuck in the esophagus, early satiety and food refusal suggest a link to failed esophageal bolus transport, however in a significant group of these children no clear abnormal motility patterns can be seen either by standard or HRM manometry. Esophageal motility disorders are typically assessed with intraluminal manometry which does not provide any direct information about esophageal bolus transit. In adults, the benefit of combined pressure-impedance recordings has shown to be limited [13, 14] but this may be due to the fact that in these studies pressure and impedance measurements were analysed separately [19]. To date, no pediatric studies are available studying the diagnostic yield of combining HRM and impedance measurements. The current study used a new automated method to analyse HRM-impedance recordings in a combined fashion to fully characterize pressure-flow patterns in the esophageal body of pediatric patients with

dysphagia. Pressure-flow analysis has been previously used to describe the interactions between esophageal bolus movement and pressure patterns during liquid and semisolid boluses in adults with dysphagia [17-21)] [3, 11, 15, 17, 21] and it has been shown that PFA can give insights into the potential pathophysiology of dysphagia.

Overall we found that esophageal bolus pressurisation (as indicated by the PFI) differentiates children with and without a history of dysphagia irrespective of their peristaltic function. The combination of HRM and pressure-flow analysis allows the differentiation of patients in relation to weak esophageal peristalsis (large ICD) and/or abnormal bolus flow resistance (high PFI). Moreover, in post-fundoplication patients the timing of esophageal motor response and bolus movement differ.

According to the Chicago Classification (CC) criteria, the current gold standard for the diagnostic interpretation of high resolution manometry recordings in adults, poor esophageal contractility is defined based on the length of the peristaltic defect break size. Break size is calculated as the largest continuous break in the 20mmHg isobaric contour [2]. In our patients the break size was larger in children with dysphagia compared to patients without dysphagia when swallowing liquids suggesting that this reduced segmental contractility of the esophagus would lead to inadequate bolus transport and thus symptoms of dysphagia. However, the optimal ICD length criteria used to predict bolus transport failure and to explain symptoms of dysphagia in pediatric patents is still under discussion [1]. Due to the lack of age appropriate normative criteria, complementary additional information may be needed to support a CC motility disorder diagnosis [23]. Pressure-flow analysis may provide such evidence. For example, the PFI is a global measure of esophageal function, which takes into account the level of bolus pressurisation and pattern of flow. In the current study, the PFI differentiated children with and without dysphagia irrespective of their peristaltic integrity. Hence, when a primary motor disorder pattern is determined through application of the CC algorithm, the PFI

may determine if these findings may be driving symptom perception and therefore are of clinical relevance.

The variety of underlying medical pathologies that present with dysphagia is vast. In our pediatric population underlying primary diagnoses were also heterogeneous; yet three major underlying diagnostic groups could be identified i.e. GERD, post fundoplication patients and a group of patients with undefined aetiology excluding the previous two categories. The data (Table 2) show that the timing of esophageal motor responses to bolus movement is different in pediatric post fundoplication patients compared to the other diagnostic subgroups of patients with dysphagia. In post fundoplication patients, a shorter time was observed between the point when the oesophagus is most distended (nadir impedance) and the bolus peak pressure, indicating a more pressurised bolus travelling through the oesophagus in closer proximity to the peristaltic wave front. This may be EGJ outflow related rather than being the consequence of poor esophageal contractility.

To further explore the relationship between peristaltic integrity (size of the segmental defect expressing bolus clearance) and esophageal luminal resistance to bolus flow (PFI), we dichotomously stratified the current pediatric patient cohort. Our data show that the combination of EPT and pressure-flow analysis can also differentiate pediatric patients with dysphagia with symptoms in relation to either weak peristalsis (poor bolus clearance) or to abnormal bolus flow resistance (high intra-bolus pressure relative to flow). This is an important finding, which may guide the need for pharmacological or endoscopic therapies.

This study has limitations. We studied children with heterogeneous causes of dysphagia retrospectively based on the clinical reporting of symptoms of dysphagia on solids and used young adults as controls, as currently no paediatric normal values exist. Future prospective studies assessing perception of bolus hold up in pediatric patients are needed to rule out whether the proposed parameters also link with detection of bolus hold up and symptom

generation during swallowing. The fact that subtle bolus flow differences are detected by pressure-flow metrics in this heterogeneous group of pediatric patients is in our view promising, especially in relation to the post fundoplication patients. Our measurements are also more objective, and not subject to individual interpretability, making our findings more robust. We recognise that the cause of symptoms may differ with specific entities of dysphagia pathology such as, for example, non-obstructive dysphagia. Studies investigating more specific subgroups of children with dysphagia are ongoing.

In conclusion, we combined high resolution manometry impedance recordings to objectively derive pressure-flow variables which reveal subtle abnormalities of esophageal function that link with the dysphagia symptoms of pediatric patients. Pediatric dysphagia patients have an increased PFI in the distal esophagus. Dichotomous categorization of dysphagia patients based on either esophageal peristaltic integrity or PFI may help guide the selection of optimal therapy being either treatment of weak peristalsis (hypocontractile esophagus) or treatment of the EGJ obstruction. Pressure-flow analysis is a promising tool for the clinical interpretation of esophageal motility and further optimization of medical interventions.

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FIGURE LEGENDS

Figure 1

A. An esophageal pressure topography plot showing pressures associated with a 5ml viscous bolus swallow. Five space-time landmarks define the region of interest (ROI) for calculations (i. the time of onset of swallow; ii. the time of proximal peak pressure; iii. the proximal margin of the esophageal pressure wave sequence; iv. the position of the transition zone; v. distal margin of the esophageal pressure wave sequence).

B. Derivation of the AIM analysis pressure flow metrics in an impedance–manometry line plot. Guided by the timing of landmarks Nadir Impedance (NI) and Peak pressure (PP), the AIM metrics are measured along the pressure-impedance array using an automated software algorithm**.**

Figure 2

Isocontour defect data stratified in relation to either normal or weak peristalsis. Weak peristalsis is defined by the presence of an isocontour 20mmHg defect size larger than 2cm on the pressure topography plot. Data of dysphagic patients are presented in black, non dysphagic patient data in grey. Data were analysed using ANOVA, p-values from significant post-hoc tests (Dunn's method corrected for multiple comparisons) are presented, *$p<0.05$.

Figure 3

Pressure flow index data stratified in relation to either normal or weak peristalsis. Weak peristalsis is defined by the presence of an isocontour 20mmHg defect size larger than 2cm on the pressure topography plot. Data of dysphagic patients are presented in black, non

dysphagic patient data in grey. Data were analysed using ANOVA, p-values from significant post-hoc tests (Dunn's method corrected for multiple comparisons) are presented, *$p<0.05$.

Figure 4

Recordings in a two year old girl who developed dysphagia to solids follow fundoplication for GERD. A. shows example swallows in standard esophageal pressure topography (EFT) format and B-C show AIM pressure-flow metrics. The panels show **A.** Four consecutive bolus swallows demonstrating repeated failure of secondary swallows to inhibit peristalsis. **B.** An esophageal pressure topography plot showing pressures associated with a 5ml viscous bolus swallow. Five space-time landmarks define the region of interest (ROI) for calculations (i. the time of onset of swallow; ii. the time of proximal peak pressure; iii. the proximal margin of the esophageal pressure wave sequence; iv. the position of the transition zone; v. distal margin of the esophageal pressure wave sequence). **C.** Bolus trajectory pathway defined using TNIPP. This identifies bolus passage (NI) relative to the esophageal pressure wave (PP).

Figure 5

Dichotomous presentation of the relation between oesophageal integrity (ICD) and oesophageal luminal resistance (PFI) in 35 children with and without dysphagia. The figure presents a categorisation of esophageal pressure-flow profiles in 35 pediatric patients with dysphagia based upon pressure flow index (PFI) and isocontour defect (ICD). This categorisation enables a separation of patients who have predominantly abnormal bolus clearance (large ICD) and/or those with abnormal flow resistance (high PFI). Mean data for viscous boluses from patients with and without dysphagia are presented.

TABLE LEGENDS

Table 1

Patient characteristics. Data are expressed as percentage or as Mean±Standard Deviation (SD) or Median with interquartile ranges (IQR).

Table 2

Pressure-flow metrics (AIM parameters) in relation to the presence of dysphagia to solids in 25 pediatric patients for liquid boluses (n=35) and viscous boluses (n=31). Data presented as mean±SEM or median [IQR] and are compared using a One Way ANOVA, *$p<0.05$.

Table 3

Pressure flow metrics (AIM parameters) for liquid and viscous boluses in relation to underlying pathology. Data are presented as mean±SEM or median [IQR] and compared using a One Way ANOVA (*$p<0.05$ using a Bonferroni *post-hoc*).

464 TABLE 1

Table 1. Patient characteristics (N= 35)

Age	Mean±SD (years)	10.5 ± 0.8,
	Median IQR	10.54 [1.96-19.64]
Male		17 (49%)
Weight	Mean±SD (kg)	54.7 ± 23.1
Height	Mean±SD (cm)	155.37 ± 20.9
Reason for referral		
Idiopathic dysphagia (unknown aetiology)		16 (40%)
Gastroesophageal reflux disease		9 (27%)
Patient post-resection of hemangio-endothelioma		1 (3%)
Patient with Behavioural issues		1 (3%)
Chest pain		1 (3%)
Investigations for dysphagia performed post-surgery		7 (24%)
• Tracheoesophageal fistula		2
• Post-Nissen fundoplication		5

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466 TABLE 2

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		5ml Liquid Bolus		5ml Viscous Bolus	
		No Dysphagia N= 10	**Dysphagia N= 25**	**No Dysphagia N= 9**	**Dysphagia N= 23**
Whole Esophagus					
PP	mmHg	58±6	49±4	59±9	54±5
PNI	mmHg	4±1	2±0	5±1	6±1
IBP	mmHg	6±1	5±1	9 [4-11]	8 [6-11]
IBP slope	mmHg/s	6 [2-9]	7 [5-11]	10 [8-11]	9 [7-14]
TNIPP	sec	3.3±0.2	3.4±0.1	2.7±0.2	2.6±0.2
PFI		50 [9-102]	59 [25-125]	100 [63- 169]	67 [49-160]
ICD	cm	2 [1-3]	4 [2-8]*	2 [0-3]	3 [1-9]
Distal Esophagus					
PP	mmHg	62±7	50±5	60±10	55±6
PNI	mmHg	4±1	3±0	6 [2-10]	6 [4 -8]
IBP	mmHg	5 [3-7]	5 [3-6]	7±2	9±1
IBP slope	mmHg/s	4 [2-8]	4 [3-7]	5 [4-7]	6 [4-13]
TNIPP	sec	3.8±0.2	3.8±0.2	2.9±0.2	2.9±0.2
PFI		43 [16-99]	26 [9-126]	32 [13-67]	61 [25-139]*

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TABLE 3

LIQUID SWALLOWS		GERD N = 9	Post Fundo Dysphagia N = 5	Idiopathic Dysphagia N = 16	ANOVA
Whole Esophagus					
ICD	cm	4±1	2±1	5±1	0.217
PP	mmHg	47 [36, 71]	54 [45, 83]	43 [36, 63]	0.372
PNI	mmHg	2±1	3±1	3±1	0.947
IBP	mmHg	5±1	5±2	5±1	0.886
IBP slope	mmHg/s	5 [3, 7]	10 [4, 20]	7 [5, 9]	0.317
TNIPP	sec	3.7±0.2	2.8±0.3*	3.3±0.2	0.039*
PFI		60 [23, 71]	102 [14, 238]	55 [23, 140]	0.917
Distal Esophagus					
PP	mmHg	45 [39, 76]	55 [47, 90]	42 [31, 67]	0.362
PNI	mmHg	3±0	4±1	3±1	0.431
IBP	mmHg	4±1	6±2	5±1	0.625
IBP slope	mmHg/s	4 [2, 6]	7 [1, 20]	4 [3, 5]	0.656
TNIPP	sec	4.2±0.2	2.4±0.2	3.8±0.2	0.054
PFI		55 [4, 74]	129 [14, 250]	22 [9, 66]	0.435

*p<0.05 versus GERD as tested by ANOVA (Bonferroni *post-hoc*)

VISCOUS SWALLOWS		GERD N = 8	Post Fundo Dysphagia N = 5	Idiopathic Dysphagia N = 15	ANOVA
Whole Esophagus					
ICD	cm	3±1	1±0	5±1	0.112
PP	mmHg	62±11	68±8	51±6	0.386
PNI	mmHg	4±1	8±2	7±4	0.139
IBP	mmHg	7±1	12±3	10±2	0.094
IBP slope	mmHg/s	10 [8, 14]	10 [6, 33]	10 [7, 14]	0.771
TNIPP	sec	2.9±0.3	2.5±0.4	2.6±0.2	0.639
PFI		102 [69, 151]	65 [44, 787]	67 [50, 232]	0.947
Distal Esophagus					
PP	mmHg	64±12	71±8	52±6	0.331
PNI	mmHg	4±1	10±2	6±1	0.065
IBP	mmHg	7 [2, 11]	14 [4, 20]	8 [5, 10]	0.347
IBP slope	mmHg/s	5 [4, 12]	4 [3, 30]	6 [4, 10]	0.956
TNIPP	sec	3.1±1.0	2.8±1.2	2.9±0.8	0.731
PFI		32 [15, 97]	38 [16, 779]	61 [25, 117]	0.418

List of individual contributions

Nathalie Rommel Roles: study concept and design, analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript; statistical analysis; study supervision.

Taher I. Omari Roles: study concept and design; analysis and interpretation of data; drafting of the manuscript; critical revision; study supervision.

Margot Selleslagh Roles: analysis of data, critical revision of the manuscript.

Stamatiki Kritas Roles: analysis of data, critical revision of the manuscript.

Charles Cock Roles: critical revision of the manuscript.

Rachel Rosan Roles: Data acquisition and critical revision of the manuscript.

Leonel Rodriguez Roles: Data acquisition and critical revision of the manuscript.

Samuel Nurko Roles: study concept and design; acquisition, analysis and interpretation of data; critical revision; study supervision.

Conflict of Interest

T Omari and N Rommel have AIM technology patent to disclose. None of the other authors have any conflict of interest to disclose.