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Pressure-flow characteristics of normal and disordered esophageal motor patterns: A pediatric study

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Background: The Chicago Classification allows disordered esophageal motor dysfunction to be characterized into four main categories based on esophageal pressure topography (EPT) metrics. As an adjunct to EPT, pressure flow analysis relates impedance-detected bolus movement to pressure-detected bolus propulsion. The aim of this study was to perform pressure-flow analysis in a cohort of Chicago Classified pediatric patients. We hypothesized that patients within the different Chicago Classification categories would exhibit a different pressure-flow signature.

Methods: Combined high-resolution impedance-and solid state pressure recordings were performed in 76 pediatric patients referred for diagnostic manometric investigation (32M; 9.1 ± 0.7 years) and 25 healthy adult controls (7M; 36.1 ± 2.2 years) using the Solar GI acquisition system (MMS, The Netherlands). Standardized saline and viscous boluses were tested. EPT metrics were calculated and an age-adjusted Chicago-Classification determined for each patient using MMS analysis software (version 8.23). Pressure-flow analysis of swallows was performed using purpose designed MATLAB-based software (AIMplot, T. Omari) which calculated the pressure-flow index (PFI), a composite measure of bolus pressurization relative to flow and the impedance ratio (IR) a measure of the extent of bolus clearance failure.

Results: Based on EPT metrics, patients were mostly classified as Normal (38, 50%) or with a Category 4 disorder, usually weak peristalsis (28, 31.5%). Three (3.9%) had a Category 3 disorder, five (6.6%) had a Category 2 disorder (EGJ outflow obstruction) and two (2.6%) a Category 1 disorder (Achalasia Type II). Pressure-flow analysis of healthy control studies defined the reference ranges (90^{th} Percentile) for PFI and IR as ≤ 142 and ≤ 0.49 respectively. Pediatric patients who had pressure-flow characteristics within these limits were mostly classified with Normal esophageal motility according to the Chicago Classification (62%). The majority of patients with pressure-flow characteristics outside these limits also had an abnormal Chicago Classification (61%). Patients with a high PFI and a disordered motor pattern all had EJG outflow obstruction. Patients with high IR and a disordered motor pattern were either achalasia, weak peristalsis or absent peristalsis (Figure 1).

Conclusions: Disordered esophageal motor patterns were associated with an altered pressure-flow signature. By defining the degree of over-pressurization and/or extent of clearance failure, pressure-flow analysis may be a useful adjunct to EPT-based classification of primary esophageal motor disorders. These additional insights have clinical relevance by potentially defining the optimal treatment strategy for individual dysphagia patients.

Key words: children – AIM-analysis – Chicago classification – high resolution manometry

Abbreviations

AIM analysis	Automated impedance manometry analysis
CDP	Contractile deceleration point
CFV	Contractile front velocity
DCI	Distal Contractile Integral
DL	Distal Latency
HRM	High resolution manometry
IRP	Integrated relaxation pressure
LES	Lower esophageal sphincter
MII	Multichannel intraluminal impdedance
NadImp	Nadir impedance
PeakP	Peak pressure
PFI	Pressure flow index
P-NadImp	Pressure at the time of NadImp
UES	Upper esophageal sphincter

Background

The Chicago Classification (CC) establishes normative values and guidelines for the diagnostic evaluation of esophageal motility by high-resolution manometry (HRM). The CC groups esophageal motor dysfunction into four main categories based on esophageal pressure topography (EPT) metrics. In order of severity, these disorder categories are achalasia (Category 1), EGJ outflow obstruction (Category 2), disorders never observed in healthy individuals (Category 3; absent peristalsis, diffuse esophageal spasm or hypercontractile esophagus), and motor patterns outside the normal range (Category 4; weak peristalsis, frequent failed peristalsis, hypertensive peristalsis or rapid contraction). With available technologies, esophageal motility evaluations are now relatively easy to perform in children. However important metrics, particularly IRP4s and distal latency, are altered in relation to patient age and size. This is problematic for translation of the CC to pediatric settings and may lead to overdiagnosis of disorders such as EGJ outflow obstruction and DES (Singendonk, 2014).

Intraluminal impedance can be measured in conjunction with pressure to provide additional information regarding bolus flow (i.e. High Resolution Impedance-Manometry, HRIM). The standard approach to the analysis of impedance waveforms has been to use a categorical classification system based on determining the proportion of swallows that completely clear bolus residues (Tatuian, 2005). Using this approach, impedance is analyzed in isolation to dichotomously define complete or incomplete bolus transport. The diagnostic value of intraluminal impedance recording has been potentially enhanced by Pressure-Flow Analysis (PFA). This approach directly integrates impedance measurements, defining bolus flow, with pressure measurements, defining the forces that drive flow. PFA is readily automated making it simple to perform and has been shown to be reproducible in the hands of experienced and inexperienced users alike (Rohof, 2014).

In dysphagia patients, PFA has identified two predominant patterns of abnormality. Firstly, excessive flow resistance during bolus propulsion and secondly, extreme degrees of bolus retention when bolus transport is incomplete (Chen et al., 2013; Loots, 2013; Myers, 2012; Nguyen, 2013, Omari 2013, Rommel 2014). Additionally, PFA metrics have been found to correlate with symptom intensity (Chet al., 2013, Omari UEG Journal 2013, Rommel et al., NMO 2014). Therefore, PFA may complement routine diagnosis based on the CC, as it offers the possibility of quantifying degrees of pressure-flow dysfunction amongst individuals who have an equivocal CC diagnosis. Alternatively, PFA could provide corroborative evidence of flow resistance which could further support a diagnosis of EGJOO and, theoretically, guide the need for interventions such as DGJ dilatation.

The aim of this study was therefore to assess the added value of applying pressure-flow analysis to pediatric HRIM recordings. The first step was to perform pressure-flow analysis in a cohort of pediatric patients studied using HRIM, secondly to assess the relationship between EPT metrics and PFA metrics and thirdly, to correlate both EPT and PFA metrics with the intensity of dysphagia symptoms. We hypothesized that patients within the different CC categories would exhibit different pressure-flow signatures and that greater pressure-flow abnormalities would be associated with more severe symptoms.

Methods

Subjects

High-resolution impedance manometry recordings of liquid and viscous swallows of pediatric patients <18 years were extracted from a database of studies conducted at the Gastroenterology Unit of the Women's and Children's Hospital, Adelaide, Australia between May 2010 and September 2013. The primary basis for referral of patients was feeding/eating difficulty (dysphagia), gastro-esophageal reflux disease (GERD) and investigation prior to laparoscopic gastric band surgery (LAGB). Studies from 25 healthy adult subjects aged 20-50 years and free from gastrointestinal symptoms were also evaluated for comparison (7 M; mean age 36.1 ± 2.2 years). Access to study files of patients undergoing esophageal manometry investigation was approved by the Women's and Children's Hospital Human Research Ethics Committee.

Dysphagia symptoms

The severity of dysphagia symptoms was assessed using Dakkak's validated composite dysphagia score (scale 0-45, 0=none) (Dakkak, 1992). A Dakkak score between 1 and 10 indicates the presence of dysphagia symptoms with liquids and some semisolids and a score greater than 10 indicates the presence of symptoms with solids.

Manometric Protocol

The esophageal motor function of all subjects was assessed using a 3.2mm diameter solid state manometric and impedance catheter incorporating 25 1cm-spaced pressure sensors and 12 adjoining impedance segments, each of 2 cm (Unisensor USA Inc, Portsmouth, NH). Pressure and impedance data were acquired at 20Hz (Solar GI acquisition system, MMS, The Netherlands). Patients were intubated after application of topical anesthesia (lignocaine spray or gel) and studied sitting or held by a parent in the upright posture. Adult controls were studied in a sitting posture, using the same catheter and methods. If the pressure-impedance sensor array was not large enough to accommodate the entire region from UES to EGJ, the catheter was positioned with sensors straddling the distal esophagus from transition zone to stomach. Ten liquid and ten viscous test boluses were administered orally via syringe. Bolus volume ranged from 3ml-10ml depending on patient size and bolus tolerance. Controls were given 5x5ml and 5x10ml boluses.

Data analysis

Measurements based on Esophageal Pressure Topography

Standard EPT metrics necessary for the utilization of the CC algorithm (Bredenoord, 2012) were determined using automated analysis software following manual placement/adjustment of landmarks to define gastric position, EGJ proximal and distal margin, transition zone, swallow onset and contractile deceleration point for each individual liquid swallow (MMS version 9.1, Enschede, The Netherlands). The standard EPT metrics derived were (i) Integrated Relaxation Pressure (IRP4s), (ii) Contractile Front Velocity (CFV, cm/sec), (iii) Distal Contractile Integral (DCI, mmHg/cm/sec), (iv) Distal Latency (DL, sec) and (v) peristaltic 20mmHg isocontour break size (BS, cm) (Bredenoord, 2012). The established CC algorithm was applied to the cohort using age-adjusted cut-off values for age-dependent EPT metrics as previously described (Singendonk et al., 2014).

Esophageal Pressure-flow analysis

To perform PFA, raw pressure-impedance data for all swallows were visualized over a 30-s window and exported from the recording system in ASCII text format. Data was then uploaded and analyzed using purposed designed software (AIM*plot* copyright T Omari, MATLAB version 2012a, the MathWorks Inc, Natick, MA, USA). As previously reported (Myers, 2012; Loots, 2013; Nguyen, 2013; Chen 2013; Omari 2013; Rohof 2013), seven pressure-flow variables were derived from the automated analyses: (i) pressure at nadir impedance (PNadImp, mmHg), (ii) peak pressure (PeakP, mmHg), (iii) median intrabolus pressure (IBP, mmHg), (iv) time interval between nadir esophageal impedance and peak esophageal pressure (TNadImp-PP, sec), (v) IBP slope (IBP slope, mmHg s^{-1}), (vi) the impedance ratio (NadImp/ImpPeakP Ratio) and (vii) Pressure Flow Index (PFI). The impedance ratio has been identified as a potential marker of incomplete bolus transit (Chen 2013; Omari 2013; Rohof 2013). The pressure flow index (PFI) is based on an empirical formula, which was designed to amplify differences in key AIM analysis metrics seen in relation to symptoms of dysphagia (Myers 2012; Loots, 2013; Nguyen, 2013; Chen, 2013). The PFI has been shown to be higher in circumstances of pressure-flow abnormality.

All pressure-flow metrics were derived for the distal esophagus from EGJ to transition zone for both liquid and viscous boluses. A control range for stratification of patient data was defined by data derived from young healthy controls.

Statistical analysis

Data for all liquid and viscous bolus swallows captured during each manometric study were averaged and compared in relation the EPT diagnosis and between patients and controls. Parametric data are expressed as mean ± standard error and non-parametric data are expressed as median [interquartile range]. Grouped data were compared using One Way Analysis of Variance or Kruskal-Wallis One Way Analysis of Variance on Ranks. Pearson correlation coefficients were calculated to explore bivariate correlations between EPT and AIM parameters. Proportionate differences were tested with chi-square test. The association between EPT and AIM parameters on one hand and dysphagia symptom perception scores on the other hand were tested using Spearman correlations. A *p* value <0.05 was considered statistically significant. Statistical tests were performed using IBM SPSS Statistics 20 (SPSS Inc, Chicago, IL) and Sigmaplot 11.0 (Systat Software, San Jose, CA).

Results

A total of 106 manometric studies were extracted from our database. Of these studies, 26 were not considered evaluable due to technical or protocol violation reasons (pressure or impedance channel failure, position not adequate to resolve EGJ pressures or inadequate capture of liquid swallows for CC diagnosis). 36 patients were referred for manometric investigation for clinically relevant dysphagia (n=21 considered oropharyngeal dysphagia on clinical grounds, n = 15 considered esophageal dysphagia on clinical grounds) and 27 patients were referred due to GERD symptoms. Eleven studies were performed in adolescent morbidly obese patients, before undergoing a laparoscopic placement of a gastric band. 16 studies were performed post-surgery (n=7 tracheoesophageal fistula or esophageal atresia repair, n=5 post-Nissen fundoplication, n=4 achalasia intervention). The four studies that were performed post-achalasia intervention (i.e. myotomy or dilatation) were excluded from analysis. 76 studies from 68 patients (32 M; mean age at study 8.9 ± 0.7 years) were analyzed. The database included six individuals who underwent two (n=4) or three (n=2) repeated studies due to persistent symptoms. The mean distance from nares to LES upper border margin was 32.0 ± 7.7cm in patients <18 years and 43.0 ± 0.6cm in adult controls.

Measurements based on Esophageal Pressure Topography

The established Chicago Classification algorithm was applied to the cohort using age-adjusted cut-off values as previously described (Singendonk, 2014). Esophageal motor disorders were characterized in 50% of pediatric patients (mostly Category 4 disorders), and 52% of controls (all Category 4 disorders).

Pressure flow analysis in relation to normal and disordered motility

PFA of liquid bolus swallows was performed on 74 studies of which 69 also had sufficient viscous bolus swallows for analysis. Figure 1 compares data for pressure-flow variables for liquid and viscous boluses amongst studies grouped by esophageal motor disorder Category. Those studies classified into the most severe categories of motor disorder, namely Category 1 (Achalasia) and Category 2 (EGJ outflow obstruction) were characterized by having the highest PFI. Patients of Category 1 had significantly higher IR when compared to patients with normal motility and patients with Category 4 disorders. Patients classified with a Category 3 disorder (DES and Absent Peristalsis) showed lower PeakP when compared to patients with normal motility. Overall, pressure-flow metrics that were derived based on viscous swallows appeared more discriminatory and demonstrated greater statistical confidence for most comparisons when compared to liquid swallows.

Characterization of patients based upon viscous bolus pressure flow index and impedance ratio

PFA of healthy control studies defined the reference ranges (90^{th} Percentile) for PFI and IR based on viscous boluses as ≤ 142 and ≤ 0.49 respectively. Applying these ranges as normative criteria, six patient studies recorded an abnormal PFI and 22 studies recorded an abnormal IR. This enabled a two-way differentiation of patients based on pressure-flow characteristics. Namely, those with normal bolus pressurization and clearance (Group 1) and those with abnormal clearance and/or abnormal pressurization (Group 2). Figure 2A shows a dichotomous stratification of patients' studies using PFI and IR in combination. Studies within the control range of PFI and IR (Figure 2B) mostly had normal motility based on EPT (62%). Patients with abnormal IR and/or PFI (Figure 2C) were in contrast mostly abnormal based on EPT analysis (61%). There was a significant difference between the proportion of different EPT diagnoses amongst the group of patients with normal and abnormal PF characteristics (x^2, $p < 0.001$). Pediatric patients who had pressure-flow characteristics within these limits were mostly classified with Normal esophageal motility according to the Chicago Classification (62%). The majority of patients with pressure-flow characteristics outside these limits also had an abnormal Chicago Classification (61%). Patients with a high PFI and a disordered motor pattern all had EJG outflow obstruction. Patients with high IR and a disordered motor pattern were either achalasia, weak peristalsis or absent peristalsis (Figure 2).

Correlations between EPT and AIM metrics

Correlations amongst EPT metrics and pressure-flow metrics are shown in Table 1. PeakP as calculated by AIM analysis correlated significantly with DCI and inversely with the 20mmHg segmental defect on HRM, independent of bolus type. A higher IR correlated with higher IRP4, as well as with lower DCI for both bolus types and a shorter DL for viscous boluses. Higher IRP4 values were also found to correlate with higher PFI, smaller IBP slope and shorter TNadImp-PeakP.

Dysphagia symptom severity and clinical reason for manometry

Dakkak scores prior to manometric investigation were assessed for 34 of the 76 studies. Fourteen patients reported no dysphagia symptoms (Dakkak=0), 6 patients reported dysphagia symptoms with liquid and viscous boluses ($0 < \text{Dakkak} \leq 10$) and 13 patients reported dysphagia symptoms with solids (Dakkak > 10). Based on Kruskall-Wallis analysis, Dakkak scores were significantly higher in the group of patients that were referred for manometric investigation due to dysphagia symptoms or GERD when compared to the patients that underwent a manometry pre-LAGB (mean Dakkak = 14.8 ± 11.2 vs mean Dakkak = 0.1 ± 0.2, $p < 0.001$)). Dakkak scores were numerically higher in patients referred for dysphagia compared to GERD, however this did not reach statistical significance (mean Dakkak = 16.2 ± 11.3 vs mean Dakkak = 10.9 ± 11.5, p = 0.41). Difficulty with eating solids (Dakkak > 10) was reported in none of pre-LAGB patients, 42% of GERD patients and 62% of patients referred for dysphagia (Fig 3). Amongst dysphagia patients only, there was no difference in Dakkak score between those considered to have an oropharyngeal or esophageal aetiology.

Dysphagia severity and EPT metrics and diagnosis

An abnormal CC classification diagnosis was found in the majority (56%) of patients that were referred for manometry with dysphagia symptoms, covering the whole spectrum of broad CC categories (Fig 3). GERD and pre-LAGB patients were mostly classified with normal esophageal motility or a Category 4 disorder (GERD 48% normal, LABG 73% normal). We found significant correlations between dysphagia symptom severity based on Dakkak scores and the EPT metrics IRP4, DL and BS (table 3). Although this same trend was observed in the cohort of patients with clinical dysphagia symptoms, the correlation between BS and Dakkak score was the only that remained in significance.

Dysphagia severity and pressure-flow characteristics

The majority of patients with clinically evident dysphagia also exhibited abnormal pressure-flow characteristics (58%). Within this patient group, significant correlations were found between Dakkak score and the pressure-flow metrics PNadImp and IBP in the distal esophagus (table 2), but not in the proximal esophagus ($r = 0.39$, $p = 0.22$ and $r = 0.40$, $p = 0.20$ respectively). The majority of GERD and pre-LAGB patients exhibited normal pressure-flow characteristics (65% and 73% respectively). Within these patient groups we did not identify correlations between dysphagia symptom severity based on Dakkak score and PF metrics.

Discussion

Based on HRIM recordings, this study describes the interaction between esophageal bolus flow and pressurization patterns in pediatric patients. In this study, we show that disordered esophageal motor patterns are associated with altered pressure-flow characteristics. In addition, we found patients with dysphagia symptoms to more likely have disordered motility based on both EPT and PFA. By using the PFI and IR in a dichotomous fashion, we observed a two-way stratification of pediatric patients within the four broad CC Categories. That is, abnormality based upon bolus flow-resistance characteristics and/or bolus clearance failure. A similar dichotomous distribution has been previously reported in a cohort of adult non-obstructive dysphagia patients who were stratified for a normal or ineffective esophageal motility pattern. In our cohort, patients with a normal pressure-flow signature mostly had normal motility based on EPT, whereas patients with the most severe categories of motor disorder, namely Category 1 (achalasia) and Category 2 (EGJ outflow obstruction) also exhibited altered pressure-flow characteristics.

Although PFA is more complex than conventional methods, its automation and objectivity in the derivation of additional functional measures of bolus movement in relation to esophageal pressurization may complement a purely isometric pressure-derived diagnosis of disordered and normal esophageal motility. Corroboratory evidence in support of a CC diagnosis is important in children in particular, because of the lack of established age-appropriate reference ranges for the EPT metrics which drive the CC. Hence, in Category 1 Achalasia patients, the Impedance Ratio may define the degree and extent of bolus retention over multiple swallows. In Category 2 patients with a diagnosis of EJG outflow obstruction, findings of an abnormal PFI may provide a useful adjunct measure to corroborate flow resistance across the EGJ. In Category 3, 4 patients, abnormal pressure-flow findings may elevate to clinically relevant, motor patterns of otherwise unclear significance. Finally, in patients with Normal motility based on CC, pressure-flow findings may help distinguish patients with hypersensitivity from those with a real motor disorder. Of all the CC disorder Categories, we have shown that EGJ outflow obstruction in particular will tend to be over-diagnosed in children when the standard adult criterion (i.e. IRP4s>15mmHg) is applied (Singendonk et al., 2014). Whilst age and size adjustment may improve diagnosis, there remains a need to otherwise confirm a manometric diagnosis of EGJOO before taking further therapeutic measures.

Our study also assessed the relationship between standard EPT metrics and pressure-flow metrics. Consistent with earlier findings (Rommel et al, 2014), higher PeakP correlated significantly with a higher DCI and smaller peristaltic break size. A higher IR correlated with a higher IRP4 , lower DCI and large break size. This is consistent with incomplete EGJ relaxation and/or poor contractile vigor of the esophageal body being associated with less effective bolus clearance.

As the pathophysiology of dysphagia is thought to be multifactorial, depending on muscle contraction and luminal compliance/resistance, we also assessed whether PFA allowed differentiation of symptomatic dysphagia patients from patients without dysphagia symptoms. The majority of patients referred with clinical evident symptoms of dysphagia exhibited abnormal IR and/or PFI. By quantifying the cumulative effects of three key pressure-flow metrics, the PFI attempts to embody the multifactorial causes of dysphagia in a single predictor of bolus flow resistance. In adult studies, the PFI has been shown to correlate with perception of bolus transit in both patients with non-obstructive dysphagia and healthy controls (Chen et al, 2013; Omari et al, 2013; Rommel et al, 2014). As the IR is a measure of the degree and extent of bolus clearance failure, elevated IR in dysphagic patients suggests that bolus residue build up may be one of the contributing factors of the perception of dysphagia. Similar findings are reported by Rommel et al., who found significantly lower impedance at peak pressure in dysphagic patients, suggesting residual bolus presence during occlusion (Rommel, 2014). When we assessed symptom severity in our cohort of dysphagic patients, we also identified a strong correlation of Dakkak scores with IBP and PNadImp in the distal esophagus. This observation is most likely consistent with compartmentalized pressure build-up in the distal esophagus which may be a direct result of EGJ obstruction.

Patients referred with GERD symptoms mostly exhibited normal pressurization and clearance patterns. However, dysphagia perception scores were still higher in this group when compared to the pre-LAGB patients. An explanation for this finding might be that these patients experience dysphagia symptoms due to esophageal hypersensitivity, possibly secondary to reflux-esophagitis. We also observed Category 4 disorders to be the predominant motor disorders in GERD patients. An earlier study in a cohort of adult dysphagic patients without major motility disorders (i.e. no Category 1, 2 or 3 CC disorder), found that small and large breaks occurred more frequently in dysphagic patients when compared to healthy controls (Roman, 2010). As hypotensive or disordered peristalsis have been shown in association with incomplete bolus transit, earlier studies suggested that this may explain the manifestation of dysphagia (Kahrilas, 1988; Roman, 2010; Tutuian, 2004). In our study, we did not specifically observe poor contractile vigor in the GERD group, or a relation between break size and symptoms in GERD. However, larger peristaltic breaks were observed in relation to higher Dakkak scores overall.

This study had some limitations. Firstly, reference ranges for the PFI and IR were based on adult controls. This was unavoidable due to ethical considerations which prohibit us from performing invasive procedures in healthy children. We also acknowledge the heterogeneity of our cohort and that many patients with dysphagia were considered on clinical grounds to have an oropharyngeal aetiology. However we note the high prevalence of esophageal motor disorders in these patients and symptoms based on a Dakkak score which was designed to elucidate esophageal symptoms. Lastly, there are some factors regarding the manometric procedure that might have influenced our findings. In particular our patients received boluses of variable volumes depending on bolus tolerance and patient size and this may have influenced intrabolus pressures and IRP4s in particular (Ren, 1993; Omari, 2013).

In conclusion, we found disordered esophageal motor patterns to be associated with altered pressure-flow characteristics. By defining the degree of over-pressurization and/or extent of clearance failure, pressure-flow analysis may be a useful adjunct to EPT-based classification of primary esophageal motor disorders. The possibility of a more simplified categorization of esophageal dysfunction using PFI and IR may have additional clinical value by determining optimal treatment strategies which may target either abnormal motor function or hypersensitivity.

Figure 1. Comparison of pressure-flow metrics determined for patients with a normal or disordered Chicago Classification motor patterns.

Parametric data expressed as median ± SE, non-parametric data (P Nadir Impedance, IBP and PFI for viscous boluses) expressed as mean ± SE. P-values for Kruskal-Wallis One Way Analysis of Variance on Ranks and One Way ANOVA Analsysis are shown for liquid (L) and viscous (V) boluses.

* indicates pairwise statistical significance vs. Category 3 for both L and V boluses ($*_V$ significance only for V boluses), # indicates pairwise statistical significance vs Category 1 for both L and V boluses ($\#_V$ significance only for V boluses).

Figure 2. **Patient Stratification based on average distal esophagus. Pressure Flow Index and Impedance Ratio measured for viscous boluses**.

A. A scatter plot of PFI vs. IR for individual patients with colours indicating the category of Chicago Classification determined for each. The green square demarcates the control range for PFI/IR based on 90^{th} percentile of values determined from asymptomatic young adults. Pressure-flow values outside this box were considered to be of disordered HRM pattern. Graphs B and C show the proportion of patients with findings of normal or disordered esophageal motility within and outside the range pressure-flow values of healthy controls. **B.** Patients who had pressure-flow characteristics within control limits were mostly classified as having normal motility. **C.** Patients with abnormal clearance (high IR) and/or abnormal pressurisuation (high PFI) were mostly classified with disordered motility, usually of Category 4 subtypes. The relative distribution of specific motor pattern categories amongst the two pressure-flow groups was significantly different (Chi squared $p<0.001$).

Figure 3. Dysphagia symptom severity, CC and PFA based diagnosis in relationship with clinical reason for manometric investigation.

Dysphagia symptom severity (Dakkak score), CC based diagnosis and PFA based diagnosis for the three main groups of reasons of referral for manometric investigation. The majority of patients referred for dysphagia had Dakkak scores > 10 (n=8, 62%), an altered CC based diagnosis (n=20, 56%) and abnormal PF characteristics (n=19, 58%). Almost all patients pre-LAGB surgery had Dakkak scores of zero (n=8, 89%), a normal CC based diagnosis (n=8, 73%) and normal PF characteristics (n=9, 82%). Most patients referred for GERD had Dakkak scores < 10 (n=7, 58%) and normal PFA characteristics (n=15, 65%)

[*]Data on dysphagia symptom severity available for n=34 patients, [#]data on PFA based diagnosis available for n=67 patients.

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