Gastroesophageal reflux in children: the use of pH-impedance measurements and new insights in treatment
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Gastroesophageal reflux, esophageal function and gastric emptying in relation to dysphagia before and after anti-reflux surgery in children

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Submitted
ABSTRACT

In patients with severe gastroesophageal reflux (GER) disease not responding to medical treatment, fundoplication may be considered.

Objective: To assess GER, esophageal motility and gastric emptying in children before and after laparoscopic fundoplication and to identify functional parameters associated with postoperative dysphagia.

Methods: Combined impedance-manometry, 24hr pH-impedance and gastric emptying (GE) breath tests were performed before and after laparoscopic anterior partial fundoplication. Impedance-manometry studies were analyzed using conventional analysis methods and a novel automated impedance manometry (AIM) analysis.

Results: Twenty-five children were enrolled of whom ten (median age 6.4 (range 1.1–17.1) years), 7 male underwent fundoplication and were included. GER episodes reduced from 97 (69-172) to 66 (18-87) /24hrs, p=0.012. Peristaltic contractions were unaltered. Complete lower esophageal sphincter relaxations reduced after fundoplication (92 (76-100)% vs. 65 (29-91)%, p=0.038). Four (40%) patients developed post-operative dysphagia, of whom two transient. In those patients pre-operative GE was delayed compared to patients without postoperative dysphagia, 96 (71-104)min vs. 48 (26-68) min, p=0.032 and AIM analysis derived dysphagia risk index (DRI) was higher (56 (15-105) vs. 2 (2-6) p=0.016). Two patients underwent redo fundoplication.

Discussion: Fundoplication in children reduced GER without altering esophageal motility. Four patients who developed dysphagia demonstrated slower GE and higher DRI pre-operatively. AIM analysis may allow detection of subtle esophageal abnormalities potentially leading to postoperative dysphagia.
INTRODUCTION

Gastro-esophageal reflux (GER), the passage of gastric contents into the esophagus occurs in the majority of infants and children.\(^1\) It is referred to as GER disease when GER causes troublesome symptoms and/or complications.\(^1,2\) Current medical treatment is primarily based on suppression of gastric acid secretion by proton pump inhibitors (PPIs), although efficacy for reduction of symptoms of GER in children has not been proven.\(^3\) When patients continue to experience severe symptoms and/or esophagitis despite treatment with high doses of PPI, management is a major clinical challenge. In these patients anti reflux surgery may be considered, although the indications for this surgery are poorly defined in children\(^1,4,5\) and there is no uniformity between hospitals in the approach to infants and children with persisting GER disease despite medical treatment with PPI.\(^6\) Furthermore, objective methods to identify patients who are more likely to respond well to anti-reflux surgery have not been defined.\(^7,8\)

The primary goal of anti-reflux surgery is to reduce GER without inhibiting passage into the stomach of swallowed substances. Post operative dysphagia is the most frequently reported complication and may occur in 0-33% of children.\(^8,9\) Dysphagia is thought to be caused by the fact that fundoplication causes a higher pressure zone at the esophago-gastric junction. Different types of fundoplication have been developed (Nissen, Thal, Toupet) and dysphagia rates differ between the different techniques with the Thal fundoplication having the lowest incidence of post operative dysphagia.\(^9,10\)

Multichannel intraluminal impedance is a technique, which enables the assessment of the velocity and direction of flow of liquids and gasses through the esophagus.\(^11\) A combined manometry and impedance assembly enables determination of the relationship between esophageal pressures and esophageal bolus clearance. Until recently analyses of impedance and pressure had not yielded any variables predictive of post-operative complications and no markers to indicate patients with a higher risk for postoperative dysphagia in adults nor in children.\(^12-18\)

An automated impedance manometry (AIM) method for the objective, reliable and reproducible assessment of pharyngeal function in relation to ineffective pharyngeal swallowing and deglutitive aspiration has recently been described.\(^19,21\) This novel method has recently been used to assess new onset dysphagia after anti reflux surgery in adults by combining esophageal function parameters with dysphagia scores (personal communication J.C. Meyers).

The aim of this study is to assess GER, esophageal motility and gastric emptying in children before and after laparoscopic anterior partial fundoplication using both conventional methods of analysis and AIM, in order to identify functional parameters that are associated with the onset of postoperative complications such as dysphagia.
METHODS

Between 2007 and 2010 patients who were listed to undergo a fundoplication were studied prior to and after fundoplication. The study was conducted in the Wilhelmina Children’s Hospital/UMC Utrecht and Emma Children’s Hospital / AMC, Amsterdam. Prior to any study procedures parental informed consent was obtained. The study was approved by the ethical committees in both hospitals. Patients with severe GER disease, not responding to conservative or medical therapy, in whom a fundoplication was considered, were eligible to enrol in the study. Children who had undergone any previous esophageal or diaphragmatic surgery and those who had other structural abnormalities than an esophageal hiatal hernia were excluded.

Study and recording procedures

All medication known to affect gastric and esophageal motility and acid suppressants were stopped three days prior to the study. To assess esophageal motility and GER, a combined manometry and pH-impedance study was performed followed by 24 hr pH-impedance monitoring. Furthermore a gastric emptying breath test was performed and reflux questionnaires were completed.

Manometry and pH-impedance protocol

Subjects were fasted for at least four hours prior to the study. A stationary combined water perfused manometry and impedance assembly was positioned transnasally into the esophagus with the sleeve straddling the LES. A single use pH-impedance catheter (Unisensor pHTip ™disposable catheter) was used. The manometry and pH-impedance catheter were adjusted for age and height of the patients. After a ten minute adaptation period, patients received bolus challenges of 3-5ml in volume (3 ml in infants and five ml in older children) administered at intervals of >60 seconds. A total of five liquid (saline or fruit juice) and five semi-solid boluses (thickened formula in infants, and EFT-Viscous® (Sandhill Scientific) were administered in both the upright and supine position (total 20 boluses in each patient).

Manometric and impedance data were recorded during the study on the Stationary Solar Gastro System (Medical Measurement Systems, Enschede, The Netherlands). Manometry and impedance tracings were analyzed for esophageal motility following currently accepted standards22,23 in terms of the shape of the peristaltic contraction, peak amplitudes, LES relaxations, TLESRs, occurrence of GER and clearance of the swallow (reported as bolus transit time, based on a 50% drop and recovery in impedance). Furthermore, a novel, automated analysis based on impedance and manometry findings (automated impedance manometry – AIM analysis) was performed as described below.
Esophageal Automated Impedance Manometry (AIM) analysis

Raw manometric and impedance data for each bolus swallow were visualised over a 30 second window, exported from the recording system and analysed using MATLAB (version 7.9.0.529; The MathWorks Inc). Pressure and impedance data were smoothed by a cubic interpolation method which doubled the temporal data and increased the amount of spatial data by a factor of 10. The raw impedance data were standardised to the median impedance (presented therefore as median standardised units (msu) rather than ohms).

Derivation of Esophageal Pressure-Flow Variables

The spatial region of the esophageal pressure wave recorded across the pressure sensors and impedance segments array (Figure 1 A and B) was analysed in a separate pressure-impedance plot (Figure 1C). All esophageal pressures during swallowing were referenced to baseline pre-swallow esophageal pressures. The impedance nadir (NadImp) and peak

**Figure 1. AIM analysis (Printed in greyscale, also refer to full color figures, p. 201)**

A. Impedance-manometry assembly. B. Swallow on conventional impedance (top 6 channels) and manometry (bottom 8 channels) representation on screen. C. Combined impedance-manometry isocontour plot of a swallow. The solid black lines represent manometry values with the solid black line from top to bottom representing peak pressure throughout the swallow. The dotted black line represents nadir impedance value. The time between nadir impedance and peak pressure is calculated in panel D. The purple line represents mean impedance values, the black line mean pressure. The time between the point of nadir impedance and peak pressure (TnadImp-PeakP), the intra bolus pressure (IBP) and the intra bolus pressure slope (IBP-slope) are calculated.
pressure (PeakP) and the time interval from NadImp to peak pressure (TNadImp-PeakP) were automatically determined at all positions along the plot (Figure 1C). Guided by the timing of NadImp, the following variables were also determined at each position and averaged for the entire pressure impedance array (Figure 1D): the pressure at the time of NadImp (P-NadImp); the Intrabolus Pressure (IBP), estimated by calculating the median pressure recorded from NadImp to the mid time point of TNadImp-PeakP; the IBP slope, defined by the change in pressure over time from P-NadImp to the pressure at mid time point of TNadImp-PeakP.

In addition to evaluating individual AIM variables, a Dysphagia Risk Index (DRI) was constructed by combining AIM analysis variables so that abnormalities of function would be amplified (the DRI was based on adult data – results as yet unpublished, personal communication J.C. Meyers). Assuming that esophageal dysfunction predisposing to dysphagia would be associated with an increased IBP, increased IBP slope and a shorter TNadImp-PeakP, the DRI was defined based on the formula:

\[ \text{DRI} = \frac{\text{IBP} \times \text{IBP slope}}{\text{TNadImp-PeakP}} \]

24 hr pH-impedance

The pH-impedance catheter was left in place for 24 hour after the stationary combined manometry impedance protocol and positioned based on manometric detection of the LES. Data were recorded on an Omega ambulatory device (MMS, Enschede, The Netherlands). Patients were instructed to carefully record symptoms during the study in a written diary and by pressing the symptom recording button. Patients were encouraged to maintain daily routine as much as possible.

The 24 hr pH-impedance tracings were analyzed manually according to the accepted guidelines. We included liquid, mixed and gas GER for this analysis. Symptom association probability (SAP) was calculated. The SAP, a symptom association index, is a statistical means, based on the Fisher’s Exact test, to calculate the probability that GER and symptoms are unrelated. The SAP is calculated as \( (1 - P_{\text{Fisher’s Exact}}) \times 100\% \) and is considered positive when >95%. Impedance baseline values represent mucosal integrity and increase on PPI treatment in infants. To assess the impact of fundoplication on impedance baseline values we calculated the impedance baseline in an automated way as previously described (Chapter 3).

Gastric emptying breath test (GEBT)

A \(^{13}\text{C} \) Na-Octanoate (a stable isotope) breath test (GEBT) was performed to assess gastric emptying time. In patients >7 years of age or who were able to eat a pancake within 15 min, a solid gastric emptying test was performed (a 137 gram pancake with 100mg \(^{13}\text{C} \) labeled Na-Octanoate). For younger patients or who were unable to eat a pancake within 15 min, 100mg \(^{13}\text{C} \) labeled Na-Octanoate was added to a liquid study meal (infant formula or full cream milk). Breath samples were taken at 5-minute intervals during the first 30 minutes and at 15 minute intervals for the remaining 3.5 hr in the liquid GEBT protocol.
In the solid GEBT protocol test breath samples were taken every 15 minutes during four hours. The ratio between $^{12}\text{CO}_2$ and $^{13}\text{CO}_2$ content was analyzed using an isotope ratio mass spectrometer. $^{13}\text{CO}_2$ concentration was used to calculate gastric emptying half time (GE half time).

**Questionnaires**

Patients and/or their parents completed age appropriate GER questionnaires, although no validated GER questionnaires exist for children 1 – 12 years of age. For patients <1 year of age the validated I-GERQ was used. In older patients the Gastrointestinal Quality of Life Index (GIQLI), the GSRS, the Reflux Diagnostic Questionnaire (RDQ) and the GER Symptom Questionnaire GSQ were used.

**Surgical procedure**

All surgical procedures were performed at the Wilhelmina Children’s Hospital, Utrecht. Patients underwent a laparoscopic anterior, partial fundoplication (180-270 degrees). Dissection of the short gastric vessels was not necessary in any of the patients to create a floppy fundoplication. A posterior crus plasty was performed in all patients.

In two of ten patients, one with Down syndrome, the other with severe neurologic impairment, a gastrostomy was performed by laparoscopy after completion of the fundoplication. The gastrostomy was positioned between the corpus and the antrum of the stomach.

**Statistical analysis**

Parameters such as peak pressure and LES relaxation were derived from data from several swallows and are presented as the mean of the swallows. Similarly, the baseline impedance value was calculated in an automated fashion and is presented as the mean of all data points.

Data are not normally distributed and are therefore presented as median (IQR). Paired data (e.g. pre vs. post fundoplication) are compared using paired Wilcoxon signed rank test. Unpaired data are analyzed using the Mann-Whitney test. Dichotomous data are compared using a Chi-square or Fisher’s exact test (when one of the expected values is <5). Correlations are calculated using the Spearman correlation. A p-value <0.05 was considered statistically significant.

**RESULTS**

Twenty-five children in whom fundoplication was considered were enrolled in this study. The pediatric surgeons received conventional reports of manometry, pH-impedance and GEBT and decided whether or not to perform surgery based on these studies and their clinical impression. Reasons for not performing fundoplication were alternative diagnoses.
(gastroparesis, constipation, suspected malrotation and excessive saliva production) (N=10), clinical improvement (N=4) and one patient was unable to undergo laparoscopic fundoplication due to spastic tetraplegia with severe hip and knee contractures. Ten (40%) patients underwent fundoplication and were included for analysis. Patients had a median age of 6.4 years (Range 1.1 – 17.1 years) at time of the fundoplication, 7 (70%) were male, 4 (40%) patients had neurological impairment (NI). All patients underwent a laparoscopic anterior partial fundoplication. There were no complications during the surgical procedure. Median length of stay in hospital was 2 days. Based on clinical assessment and questionnaires, 4 patients developed post operative dysphagia. In two patients, the dysphagia resolved within four months after surgery. Two patients had persisting dysphagia, one with mild complaints not mandating treatment. The other patient with persisting postoperative dysphagia and recurrence of GER symptoms. This patient underwent redo fundoplication due to recurrent symptoms. In total two patients (20%) underwent redo fundoplication. The reason for redo fundoplication in the other patient (with NI) was continuous severe emesis.

**Effect of fundoplication on GER and esophageal motility**

The mean number of GER episodes, acid exposure and impedance baseline values based on 24 hr pH-impedance monitoring were significantly reduced after surgery (Table 1A). Conventional measures of esophageal motility and bolus clearance were not significantly

<table>
<thead>
<tr>
<th>A. 24 hr pH-MII</th>
<th>Pre surgery</th>
<th>Post surgery</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Total GER episodes</td>
<td>97 (69-172)</td>
<td>66 (18-87)</td>
<td>0.012</td>
</tr>
<tr>
<td>Acid GER episodes</td>
<td>37 (32-120)</td>
<td>10 (2-39)</td>
<td>0.013</td>
</tr>
<tr>
<td>Weakly acid GER episodes</td>
<td>18 (8-33)</td>
<td>20 (9-43)</td>
<td>NS</td>
</tr>
<tr>
<td>Acid exposure (%)</td>
<td>12,5 (8,0-22,7)</td>
<td>3,1 (1,0-6,1)</td>
<td>0.005</td>
</tr>
<tr>
<td>SAP (%)</td>
<td>86 (17-100)</td>
<td>45 (0-100)</td>
<td>NS</td>
</tr>
<tr>
<td>MII baseline dist hannel (Ohm)</td>
<td>874 (611-1415)</td>
<td>1001 (617-2452)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>B. Manometry MII</th>
<th>Pre surgery</th>
<th>Post surgery</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pressure (mmHg)</td>
<td>57 (49-72)</td>
<td>67 (47-71)</td>
<td>NS</td>
</tr>
<tr>
<td>Peristalic contractions (%)</td>
<td>73 (36-96)</td>
<td>64 (33-91)</td>
<td>NS</td>
</tr>
<tr>
<td>LES resting pressure (mmHg)</td>
<td>11 (7-21)</td>
<td>14 (9-27)</td>
<td>NS</td>
</tr>
<tr>
<td>Complete LES relaxation (%)</td>
<td>92 (76-100)</td>
<td>65 (29-91)</td>
<td>0.038</td>
</tr>
<tr>
<td>LES nadir pressure (mmHg)</td>
<td>1 (0-5)</td>
<td>3 (0-5)</td>
<td>NS</td>
</tr>
<tr>
<td>Bolus transit time (entrance – exit) sec</td>
<td>13,4 (10,3-21,5)</td>
<td>16,0 (9,9-23,4)</td>
<td>NS</td>
</tr>
<tr>
<td>TLESRs/hour</td>
<td>1,9 (0,7-4,4)</td>
<td>0,3 (0,0-2,4)</td>
<td>0.086</td>
</tr>
</tbody>
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<tr>
<th>C. GEBT</th>
<th>Pre surgery</th>
<th>Post surgery</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GE half time (min)</td>
<td>64 (45-96)</td>
<td>63 (48-78)</td>
<td>NS</td>
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</tbody>
</table>

Table 1. Comparison before and after fundoplication.
MII: impedance. SAP: symptoms association probability. P-values based on a paired Wilcoxon signed rank test.
altered (Table 1B). LES resting pressure increased slightly but not significantly after fundoplication. The percentage of complete LES relaxations was significantly lower after fundoplication, 95 (78-100)% vs. 65 (38-90)%, p=0.025. Although the protocol was not designed to measure change in TLESRs, we did see a trend in reduction of TLESRs per hour from 1.9 (0.7-4.4) to 0.3 (0.0-2.4), p=0.086. Gastric emptying was not altered by fundoplication in this group (Table 1C).

**Patients with and without postoperative dysphagia.**

None of the conventional GER and esophageal motility parameters before fundoplication were different between the group that developed dysphagia (N=4) and the group that did not (Table 2). Patients with postoperative dysphagia had significantly prolonged GE half time before fundoplication, 96 (71-104)min compared to patients without dysphagia, 48 (26-68)min, p=0.032 (Table 2).

Postoperative AIM assessment of dysphagia symptoms were available for nine children (the measurement of one patient without dysphagia could not be analyzed due to the absence of any peristalsis). Whilst individual variables were not significantly different, the dysphagia risk index (DRI) before surgery was significantly higher in patients with postoperative dysphagia compared to those without postoperative dysphagia (Table 2 and Figure 2).

<table>
<thead>
<tr>
<th></th>
<th>Dysphagia +</th>
<th>Dysphagia -</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>A. Conventional GER parameters</strong></td>
<td></td>
<td></td>
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<tr>
<td>Total GER episodes</td>
<td>125 (70-169)</td>
<td>96 (66-199)</td>
<td>NS</td>
</tr>
<tr>
<td>Acid exposure (%)</td>
<td>14.5 (2.7-24.1)</td>
<td>12.5 (8.9-22.8)</td>
<td>NS</td>
</tr>
<tr>
<td>SAP (%)</td>
<td>100 (69-100)</td>
<td>80 (0-96)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>B. Manometry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak pressure (mmHg)</td>
<td>64 (46-90)</td>
<td>57 (54-63)</td>
<td>NS</td>
</tr>
<tr>
<td>Peristalic contractions (%)</td>
<td>93 (75-99)</td>
<td>53 (19-81)</td>
<td>0.11</td>
</tr>
<tr>
<td>Complete LES relaxation (%)</td>
<td>94 (43-100)</td>
<td>92 (76-100)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>C. Gastric Emptying</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GE half time (min)</td>
<td>96 (71-104)</td>
<td>48 (26-68)</td>
<td>0.032</td>
</tr>
<tr>
<td><strong>D. AIM analysis</strong></td>
<td></td>
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</tr>
<tr>
<td>PeakP (mmHg)</td>
<td>48 (36-86)</td>
<td>39 (25-48)</td>
<td>NS</td>
</tr>
<tr>
<td>IBP (mmHg)</td>
<td>7.7 (5.1-11.3)</td>
<td>5.3 (4.3-5.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>IBP Slope (mmHg/sec)</td>
<td>6.0 (1.6-10.4)</td>
<td>2.3 (0.9-6.1)</td>
<td>NS</td>
</tr>
<tr>
<td>TnadImp-Peak (sec)</td>
<td>3.4 (3.1-3.6)</td>
<td>3.4 (3.0-4.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Dysphagia Risk Index</td>
<td>55.6 (14.9-105.0)</td>
<td>2.0 (1.7-5.9)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Table 2. Parameters before fundoplication in patients with compared to patients without postoperative dysphagia.

Patients who developed dysphagia after surgery had slower gastric emptying and a higher dysphagia risk index. SAP: symptom association probability. LES: Lower esophageal sphincter. GE: Gastric emptying. AIM: automated impedance manometry. PeakP: Peak pressure. IBP: Intra bolus pressure. IBP Slope: slope of intra bolus pressure. TnadImp-Peak: the time between the point of nadir impedance and the time of peak pressure.
Overall success

Patients were grouped based on whether they experienced any symptoms (including dysphagia, heartburn, vomiting, regurgitation, stomach aches) after 3 months (N=6, 60%), continued to need medication after 3 months (N=3, 30%), needed medication after 1 year (N=6, 60%), or needed a redo fundoplication (N=2, 20%). Patients who continued to receive medication at 3 months (N=3) had significantly lower numbers of TLESRs/hour (0.0 (0.0-0.9) vs 3.2 (1.1-4.8), p=0.017) and GER episodes (65 (54-70) vs 165 (85-175)/24 hr, p=0.017) before fundoplication, compared to patients without medication. Grouping the patients based on the use of medication after one year, experiencing symptoms at 3 months or redo fundoplication did not yield any differences in conventional GER and motility parameters, nor in the AIM analysis.

Neurological impairment

Patients with NI (N=4) were not more likely to experience complications after fundoplication, nor were they more likely to receive medication after the fundoplication. Preoperative GER, motility and AIM parameters were comparable between NI patients and normally developed patients before. The difference between pre and post fundoplication did not

Figure 2. AIM parameters compared between patients with and without post operative dysphagia. The dysphagia risk index (DRI) is clearly higher in patients who develop post operative dysphagia.
yield any other dissimilarity. Furthermore children with NI were not more likely to undergo redo fundoplication in this cohort.

**DISCUSSION**

This study showed that fundoplication in children effectively reduced the number of GER episodes and acid exposure, without significantly altering esophageal motility. Four patients developed postoperative dysphagia, of whom two patients had transient dysphagia. This was a cohort with severe complaints and highly selected based on preoperative manometry, impedance and astric emptying assessment. This strict selection may explain the higher rate of dysphagia than the incidence of 23% reported in a recent prospective trial on pediatric fundoplication. Patients who developed dysphagia demonstrated a significantly slower gastric emptying and higher dysphagia risk index (DRI) pre-operatively. This might suggest that these patients exhibit a degree of upper GI dysmotility before operation which may potentially lead to postoperative dysphagia following anti-reflux. AIM analysis and the derivation of the DRI, may allow detection of subtle esophageal abnormalities that are not detectable using conventional methods of impedance-manometry analysis. AIM analysis therefore has potential clinical utility for preoperative assessment of children being considered for anti-reflux surgery.

As previously observed in adults, the total number of GER episodes, including liquid, mixed and gas GER and acid exposure was significantly reduced after fundoplication. This is the first study to also observe an increase in impedance baseline values after fundoplication. Interestingly enough only acid GER was reduced, weakly acid GER was not reduced in this cohort, whereas one would expect all GER to be reduced regardless of acidity, due to the reinforced barrier function of the esophago-gastric junction (EGJ). In our study we observed the expected increase in EGJ barrier function in the reduced number of complete LES relaxations. The LES resting pressure and nadir LES pressure increased post fundoplication and TLESRs decreased. Although not reaching statistical significance these findings are consistent with expectations and the published literature. Conventional esophageal motility parameters were unaltered in this study. Esophageal motility has been previously observed to remain unaffected in children undergoing Nissen fundoplication. Fibbe et al showed in adults that oesophageal motility remained unchanged in 85% of patients and changed from pathological to normal in 20% and vice versa in 9% of the patients. They also found an association between increased failure of primary peristalsis and dysphagia symptoms. However, it does not appear that these changes are in any way linked to postoperative dysphagia. As is the case with the conventional GER and motility parameters measured in this study. Current assessments of esophageal motility by standard manometry are therefore not sensitive enough to predict postoperative dysphagia.
AIM analysis is an objective, reliable and reproducible tool to assess esophageal function. AIM analysis allows derivation of the dysphagia risk index (DRI) from new AIM variables that better describe the interaction between bolus movement and pressure generation within the esophageal lumen. This contrasts with the standard methods which analyse bolus movement and pressure generation separately. AIM analysis was initially developed for evaluation of pharyngeal swallowing, where it has greatly enhanced the clinical utility of impedance-manometry. Using pharyngeal AIM, deglutitive function can be assessed using the swallow risk index (SRI). The SRI is a global measure of swallow effectiveness and aspiration risk derived through the combination of AIM variables associated with the occurrence of deglutitive aspiration on videofluoroscopy. Using a similar iterative analysis approach, Myer’s et al. examined a range of esophageal AIM variables for potential associations with the occurrence of esophageal dysphagia in adults (personal communication). They identified IBP, IBP slope and TNadImp-PeakP as variables linked to dysphagia, combining these to derive the DRI which demonstrated a high degree of prognostic value for prediction of post operative new-onset dysphagia. Our findings in children undergoing fundoplication are similar to those described in adults and provide further proof of concept that the AIM analysis method may have clinical potential for assessment of esophageal function to assist decision making in relation to anti-reflux surgery.

A major strength of our approach is that AIM analysis is completely objective. Although the AIM analysis is more complex than standard methods, it is readily automated and simple to apply. Furthermore, in practice we experienced a large number of swallows that were very difficult to analyse manually, due to multiple swallowing or movement artefacts. These problems are common to studies in young children who often do not swallow on command and, if they do, often swallow multiple times. We found that such swallows were much more easily analysed using the AIM algorithmic method. Therefore AIM analysis was more time efficient and also yielded a greater number of analysable swallows from the database.

We observed that the four patients who developed postoperative dysphagia had a longer GE half time compared to the patients that did not develop dysphagia. The role of gastric emptying in GER disease remains poorly understood. Delayed gastric emptying has been associated with GER disease, nevertheless promotility agents do not reduce GER. It seems fairly well established in adult patients that fundoplication increases GE rate. However, the relation between delayed gastric emptying and postoperative complications remains controversial. Delayed gastric emptying has been reported to adversely influence outcome of surgery by some authors. Other studies, including one large prospective trial, observed no relationship between gastric emptying and outcome of surgery. Unlike our esophageal findings, it is not immediately apparent how a longer GE halftime pre-operatively may contribute to the symptom of dysphagia. The literature is inconsistent on this issue and, with limited data, we are unable to speculate further on this finding.
Despite low numbers of patients that ultimately received anti-reflux surgery in our study, our primary results are in accordance with larger studies in both adults and pediatric patients. This includes both the failure of conventional manometric analysis to show differences in relation to dysphagia, and the observation of elevated DRI in relation to dysphagia (Myers). Findings of this pilot study are very encouraging, but will need to be explored further by way of larger prospective cohort study that ideally utilises the state-of-the-art method of high resolution solid-state pressure-impedance recording and allows for the establishments of diagnostic criteria. Obvious from our pilot study is the fact that the incidence of postoperative dysphagia was high in this highly selected cohort. This suggests that current attempts to select patients based on clinical history, standard impedance-manometry and modification of operative technique, whilst appearing logical, have not been successful and a new approach is needed.

In conclusion, laparoscopic anterior partial fundoplication is effective in reducing GER, however complications such as postoperative dysphagia remain a problem in this selected patient population. The novel AIM analysis showed that developing postoperative dysphagia may be related to pre-existing sub clinical impairment of esophageal function, leading to dysphagia only when EGJ resistance is increased by surgery. Furthermore, by combining variables to derive a Dysphagia Risk Index, we show that AIM analysis may allow for patient screening to quantify the risk of developing post fundoplication dysphagia. AIM is a highly promising, objective and reproducible new analysis that is superior to conventional GER and motility parameters in indicating patients who are more likely to develop postoperative dysphagia.

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REFERENCE LIST


