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Upper Gastrointestinal Function in Morbidly Obese Adolescents before and Six Months after Gastric Banding

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Abstract

Background: The effects of laparoscopic gastric band (LAGB) placement on upper gastrointestinal tract function in obese adolescents are unknown. Therefore, our aim was to determine the short-term effects of LAGB on esophageal motility, gastroesophageal reflux, gastric emptying, appetite-regulatory hormones and perceptions of postprandial hunger and fullness.

Methods: This study was part of a prospective cohort study (March 2009-December 2015) in one tertiary referral hospital. The study included obese adolescents (14-18 years) with a body mass index (BMI) >40 (or ≥ 35 with comorbidities). Gastric emptying was assessed by ^{13}C -octanoic acid breath test, pharyngeal and esophageal motor function by high-resolution manometry with impedance (HRIM), and appetite and other perceptions using 100-mm visual analogue scales. Dysphagia symptoms were scored using a Dakkak questionnaire. Data were compared pre- and post-LAGB placement and at the six-month follow-up.

Results: Based upon analysis of 15 adolescents, at six months follow-up, LAGB placement: i) led to a significant reduction in weight and BMI; ii) increased fullness and decreased hunger post-meal; iii) increased symptoms of dysphagia after solid food; and, despite these effects, iv) caused little or no changes to appetite hormones, while (v) effects on gastric emptying, esophageal motility, esophageal bolus transport and esophageal emptying were not significant.

Conclusion: In adolescents, LAGB improved BMI and altered the sensitivity to nutrients without significant effects on upper gastrointestinal tract physiology at six months follow-up.

Introduction

Childhood obesity is increasing, with 7% of Australian 2-18 year olds now obese (body mass index; BMI > 30) (1, 2) and at increased risk of developing obesity-related morbidity.(3-5)

The obesity problem is best addressed through a comprehensive multidisciplinary approach encompassing both prevention and long-term treatment. However, even aggressive adolescent-targeted non-surgical weight-loss programmes (i.e. dietary restrictions and/or increase in exercise) have high drop-out and failure rates.(6, 7) In these cases, bariatric surgery may be considered as a management option.

Laparoscopic Adjustable Gastric Band (LAGB) surgery involves the placement of an adjustable band around the most proximal part of the stomach.(8) By compartmentalising the stomach, LAGB limits total gastric volumes. In addition, the flow restriction induced by LAGB placement impedes the process of normal emptying of esophageal luminal content causing localised distention in the region of the esophago-gastric junction (EGJ) and gastric cardia. It has been proposed that this localised distension may directly stimulate vagal afferent pathways leading to increased fullness and reduced hunger via central mechanisms.(9, 10)

Morbid obesity is associated with increased prevalence of disordered esophageal motility, dysphagia, gastroesophageal reflux disease (GERD) and esophageal erosions, and it is hoped that surgically-induced weight loss may improve these symptoms.(11-13) However, a recent study, using both barium swallow and manometry in morbidly obese adults, found gastric banding to be associated with a higher prevalence of esophageal motility abnormalities, specifically impaired relaxation of the lower esophageal sphincter (LES), and impaired esophageal bolus transit.(11) Additionally, 'pseudo-achalasia', as a consequence of chronic esophageal outflow obstruction, has been reported.(14)

The available evidence in adolescents to date suggests that LAGB can be very effective for reducing food intake leading to successful BMI lowering in the short- and longer term.(8, 15-19) Therefore, the potential advantages of adjustability and reversibility have been used as reasons to consider LAGB in adolescent patients, thus, “buying time” for behavioral modifications to be achieved as the patient enters adulthood.

Whilst this data supports clinical efficacy of LAGB use in adolescents, the effects of LAGB surgery on esophago-gastric motility and meal related gut perceptions are not well characterised in adolescent patients. Therefore, we conducted a study in obese adolescents referred for bariatric surgery to characterise the *short-term* physiological changes in upper gastrointestinal tract function induced following LAGB placement. Our aim was to determine the effects of LAGB on esophageal motility, gastroesophageal reflux, gastric emptying, appetite hormones, as well as perceptions of postprandial fullness and hunger. We hypothesised that LAGB placement would cause a measureable increase in flow resistance at the EGJ, delay gastric emptying, alter the release of appetite-related hormones, and reduce hunger and increase fullness in response to a meal.

Methods

Patients

This study was carried out as part of a prospective single-centre observational study (March 2009 – December 2015) to determine the efficacy and safety of LAGB in adolescents. The study was approved by the Human Ethics Committee of the Women’s and Children’s Hospital Adelaide (HREC 2168/5/15). Twenty-one adolescent obese patients (9 male: 12 female) under the management of the Department of Surgery, Women’s and Children’s Hospital and referred for bariatric surgery by LAGB were prospectively enrolled. All patients were 15 – 18 years old (median age 17.3 years) and considered for bariatric surgery because

they had a BMI > 40 kg/m² (or BMI > 35 kg/m² with at least one obesity-related comorbidity; including pre-diabetes ($n = 2$), high ALT ($n = 10$), abnormal lipid profile ($n = 10$), use of atorvastatin ($n = 1$), use of continuous positive airway pressure for obstructive sleep apnoea ($n = 1$) and hypertension on antihypertensive medication ($n = 1$). The median BMI was 47.1 (IQR 39.9 – 52.5). All patients had failed a diet and lifestyle modification program.

The full study clinical management protocol has been published previously.(20) In this paper, we report on 15 patients who underwent additional investigations of motility, appetite perceptions and gut hormones.

Controls

Control data was available for the pharyngo-esophageal function testing component of this study (details below). The data from eight young healthy adults free from gastrointestinal symptoms and with a normal BMI (2 male, age 24.1 ± 2.7 years, range 20.7-27.5 years, BMI 24.4 ± 5.2 kg/m²) were used as the comparator.

Time Points

The study protocol involved repeat physiological and symptomatic assessments, which were performed at three study time points designed to run in tandem with routine clinical management and pre/post-operative workup as below:

1. Pre-operative baseline (PreOp-BI), at three months before surgery and before commencement of a very-low calorie diet (Optifast® VLCD™ as clinically prescribed).
2. Pre-operative on Optifast diet (PreOp-OD), immediately prior to surgery.
3. Post-operative follow-up (Post-Op) six months post-surgery.

Solid Gastric Emptying

Gastric emptying was assessed with the ^{13}C -octanoic acid breath test. On the morning of the measurement day, fasting breath samples were collected, followed by consumption of the test meal of a pancake containing 100 μL ^{13}C -octanoic acid (99% enrichment; Cambridge Isotope Laboratories). All subjects ate the meal within 20 minutes. After consumption of the meal, breath samples were collected as previously described (21) then subjects were permitted a small low-fat lunch. The ^{13}C -labeled carbon dioxide content of breath samples was analysed to calculate the parameters applicable to gastric emptying: gastric half emptying time ($t_{1/2}$), time of maximum emptying rate (t_{max}) and the gastric emptying coefficient (GEC).(21)

Appetite Perceptions

Hunger, fullness and nausea were assessed using 100-mm visual analogue scales and based on an established method validated for appetite perception in healthy subjects.(22, 23) The scales were administered during performance of the ^{13}C gastric emptying breath test, immediately prior to each breath sample being taken. Subjects were familiarized with these scales prior to the commencement of the study. Subjects were requested to make a vertical mark along each 100-mm line that best matched the strength of their perception at the time. Each score was determined by measuring the distance from the left side of the line to the mark.

Blood Analysis of Gut Hormones

Venous blood samples were collected in EDTA-containing collection tubes at baseline and then 90 min following consumption of the pancake meal. The blood samples were then spun for 10 min at 1000xg and plasma removed. Plasma was aliquoted into smaller volumes and frozen until analysed as described below.

Simultaneous quantification of the human metabolic analytes, ghrelin (pg/mL), total glucagon-like peptide-1 (GLP-1; pg/mL), peptide tyrosin tyrosin (PYY; pg/mL), leptin (pg/mL), was performed on plasma aliquots using a customised Millipore MILLIPLEX MAP Human Metabolic Magnetic Bead Panel (MPHMHEMAG34K07). All plates were incubated overnight (16-18hrs) at 4°C. Incubation with biotinylated antibodies and subsequent addition of streptavidin-phycoerythrin was performed following washing of beads to complete the assay before the Median Fluorescent Intensity was acquired using a MAGPIX Luminex analyser. Data was exported from Luminex xPONENT acquisition software and analysed using MILLIPLEX Analyst software.

Pharyngeal and Esophageal Function Testing

Pharyngeal and esophageal motor function of all patients and controls was assessed by high resolution manometry with impedance (HRIM). A 3.2-mm diameter solid state HRIM catheter, incorporating 25 1-cm-spaced pressure sensors and 12 adjoining impedance segments, each of 2 cm (Unisensor USA Inc, Portsmouth, NH), was used. Pressure and impedance signals were acquired at 20Hz (Solar GI acquisition system, MMS, The Netherlands).

Subjects were intubated after application of topical anesthesia (2% lignocaine spray or gel) and studied sitting in the upright posture. The catheter was positioned with sensors straddling the region from the proximal margin of the velopharynx to the EGJ. Patients were given 5 x 5ml and 5 x 10ml test boluses of liquid (0.9% normal saline) orally via syringe. The interval between consecutively administered swallows was >20sec.

- Esophageal Pressure Topography Plot (EPT) Analysis

To obtain a manometric diagnosis, esophageal pressure topography plots (EPT) of the HRIM studies were analysed using automated analysis software (MMS, version 9.3). Standard EPT metrics for the application of the Chicago Classification (CC) algorithm derived were i) integrated relaxation pressure (IRP4s, mmHg), ii) contractile front velocity (CFV, cm/s), iii) distal contractile integral (DCI, mmHg cm/s), iv) distal latency (DL, s) and peristaltic 20mmHg isocontour defect size (ICD, cm).(24) A baseline CC diagnosis was based on ten liquid swallows following the hierarchical algorithm. To gain insight into pharyngeal and esophageal function pre-and post-LAGB placement, Pressure Flow Analysis (PFA) was performed on the recorded liquid swallows.

- Pharyngeal and Esophageal Pressure Flow Analysis (PFA)

Pharyngeal PFA was performed by using *Swallow Gateway*TM, an interactive online analysis platform (swallowgateway.com developed by T Omari). The methods for derivation of these variables by PFA have been described in detail in several previous publications (25-27) and have been recently reviewed.(28) For this study we report the Swallow Risk Index (SRI), a composite score indicative of global swallowing function (26) and three swallow function variables. These were the upper esophageal sphincter (UES) admittance (or inverse impedance), which correlates with UES opening,(29) the peak pressure generated by the pharynx, and the post-deglutitive UES peak pressure.

- Esophageal Pressure Flow Analysis (PFA)

Automated analysis (Figure 1) was applied to each swallow using purpose built software (*Esophageal AIMplot*, copyright T Omari) programmed in MatLab (The MathWorks Inc, Natick, MA, USA). Data based on *AIMplot* software algorithms have been previously published.(30-34)

The three classes of pressure-flow variables that are then algorithmically derived are described in Figure 1. *Bolus Flow Latencies* 2. *Intra-Bolus Distension Pressure* during bolus transport and 3 *Intra-Bolus Ramp Pressurisation* was measured over time. Effectiveness of *Bolus Clearance* was determined based on the Impedance Ratio A higher ratio indicates *less* effective bolus clearance (Figure 1E).

In addition to the above, we included the measurement of trans-EGJ *Bolus Flow* based on the method of Lin.(35, 36) Using the impedance signals, the duration of bolus presence (called *Bolus Presence Time*, BPT) was determined. Using the manometry signals, the flow-permissive pressure gradient periods (i.e. esophageal pressure > crural and gastric pressure) within the overall period of bolus presence were identified. Bolus Flow Time (BFT) was defined by the sum of the flow-permissive pressure gradient periods. A shorter BFT is indicative of a reduced esophageal emptying.(32, 33)

Assessment of Dysphagia Symptoms

Patients completed a symptom assessment questionnaire, including a validated dysphagia questionnaire modelled on the composite dysphagia score of Dakkak and Bennett.(37) This assessed dysphagia for 9 different food types with increasing viscosity (water to meat; scale 0-45; no dysphagia = 0) and has been previously used in the context of pediatric dysphagia.(33)

Gastroesophageal Reflux Testing

Reflux episodes were recorded using a ComforTec MII/pH probe which was used in combination with a Sleuth system recording device (Sandhill Scientific, Highlands Ranch, CO, USA). Studies were analysed for the occurrence of liquid GER episodes and acid exposure time (reflux index, RI % time pH <4 in both upright and supine position, excluding

meal times) using automated software (*Autoscan* and *GERD Check*; Sandhill Scientific). RI was considered abnormal if >5%.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics 23 (IBM Corporation, USA). Continuous data were summarized as mean \pm SD or median (interquartile range [IQR]) according to normality. All within-group comparisons were performed using repeated measures ANOVA (General Linear Model with repeated measures and post-hoc analysis with Bonferroni correction for multiple comparisons). Between-group comparisons were performed using the paired-samples Student's *t* test or Mann-Whitney U test. A p-value <0.05 was considered to represent statistical significance.

Results

All enrolled patients received LAGB placement surgery. Of the 15 patients, gastric emptying data were complete for 13 across the three visits. Pharyngeal and esophageal function data were complete for 10 and 7 patients pre- and post-LAGB placement, respectively; the remaining patients either declined to undergo the full pharyngeal and esophageal swallow protocol at one of the time-points. Table 1 provides an overview of the patients included in the data analysis.

Weight and BMI

There was a significant main effect of time point for both body weight ($F = 39.795$, $p < 0.001$) and BMI ($F = 37.160$, $p < 0.001$). Compared to baseline both the low-calorie diet and the LAGB placement showed a significant pairwise reduction in BMI ($43.9 \pm 7.1 \text{ kg/m}^2$ vs

41.8±6.8kg/m² (p =0.001) vs 36.3±7.5kg/m² (p<0.001) and weight (126.5±25.6kgvs 120.4±24.2kg(p=0.001) vs 105.0±25.5kg, p<0.001).

Solid Gastric Emptying

There was a significant main effect of time point for GE t_{1/2} and GE t_{max} (Figure 2), but not GEC (F = 1.824, p = 0.207). Compared to baseline, the low-calorie diet was associated with a slowing of gastric emptying (pairwise significance for GE t_{max} only), however, gastric emptying time post LAGB placement was not different from baseline (Figure 2).

Appetite Perceptions

Hunger perception typically increased over time after the consumption of the pancake meal, conversely fullness decreased over time (Figure 3 A and C). Average hunger perception overall showed patients were significantly less hungry following the very low calorie diet and post-operatively (Figure 3 B). Average fullness perception overall showed that the patients were significantly fuller following LAGB placement (Figure 3 D). Nausea was infrequently reported and not significantly changed at different study time points (VAS PreOp-BL 0.14 ± 0.06, PreOp-OD 0.56±0.46 and PostOp 0.26±0.14, F 0.569, p = 0.479).

Gut Hormones

Full repeat blood measurements were available for 8 patients. Plasma leptin concentration was the only hormone showing a significant main effect of study time point. At 0 and 90min respectively leptin levels were 34055 ± 5912 and 34367 ± 5966 pg/ml during visit 1, 27626 ± 6172 and 28405 ± 6160 pg/ml during visit 2 and 21730 ± 8250 and 21842 ± 8401 pg/ml post operatively (Overall F = 7.230, p = .007 (Visit 1 vs Visit 3, p=0.055); at 0min F = 7.607, p = .006 (Visit 1 vs Visit 3 p=0.049); at 90min F = 6.820, p = .009 (Visit 1 vs Visit 3 p = 0.063)).

There were no main effects of time point in relation to other hormones tested (Ghrelin, $F = 1.945$, $p = .180$; GLP-1, $F = .037$, $p = .964$; PYY, $F = .604$, $p = .561$).

Pharyngeal and Esophageal Function Testing

- Pharyngeal Function

Complete results from pharyngeal liquid bolus swallows before and after LAGB placement were available for 10 patients. There was no correlation between weight or BMI at baseline and pharyngeal function. Global swallow function (Swallow Risk Index) and individual parameters of UES opening (maximum admittance) and pharyngeal contractile vigor were not significantly altered following the very low calorie diet or LAGB placement. There were also no differences in pharyngeal parameters between patients (pre- and post-LAGB) and controls (Figure 4).

- Esophageal Function

Thirteen patients underwent HRIM measurement post-LAGB placement, however only seven patients also underwent HRIM prior to band placement. Comparisons of EPT and PFA parameters pre- and post-LAGB are, therefore, based solely on the seven patients that completed HRIM at both time-points. For evaluation of the relationship between post-operative Dakkak scores and post-LAGB weight loss and HRIM variables, the thirteen patients with available HRIM data post-LAGB were evaluated.

Typically, the presence of the LAGB was not obviously visible to the naked eye on the manometric tracing. In all cases the EGJ region was readily identifiable via the pressures generated by the tonically contracted LES and transient contraction of the extrinsic crural diaphragm during inspiration. We anticipated that placement of the LAGB would create a

compartmentalised pressure region immediately below the EGJ. In reality, this was only clearly observed in one of the thirteen patients (see example Figure 5).

At baseline, one LAGB patient was diagnosed with Ineffective Esophageal Motility (IEM) according to the CC V3.0; IEM is considered a variant of motility with unclear clinical significance. The other six patients had normal esophageal motility. Of the control subjects, three had IEM and five had normal esophageal motility. There was no correlation between weight or BMI at baseline and any of the EPT parameters. There was a trend towards slower contractile front velocity (CFV) and longer distal latency (DL) in patients pre- and post-LAGB when compared to the controls (CFV post-LAGB vs control; $p=0.001$; DL pre-LAGB and post-LAGB vs control; $p = 0.043$ and $p = 0.006$ respectively, other p -values NS). This indicated a slower rate of propagation of the esophageal peristaltic contraction after LAGB placement (Figure 6).

There was no correlation between weight or BMI at baseline and any of the Pressure Flow Analysis parameters. None of the PFA parameters differed significantly in patients pre- and post-LAGB. When compared to the healthy controls, obese patients post-LAGB had a significantly longer distension-contraction latency ($p = 0.040$). There was no difference in either the period of bolus presence above the EGJ or the predicted period of trans-EGJ bolus flow time (Figure 7).

Dysphagia Symptoms

Post-LAGB Dakkak scores were available for 14 patients (mean Dakkak = 12.5 ± 8.8 , range 0-25). Of these patients, 12 had post-LAGB manometry data (mean Dakkak = 11.5 ± 9.8 , range 0-25). Amongst these patients, there was no correlation between Dakkak score and weight loss post-LAGB (Spearman's $r = 0.236$, $p = 0.484$). The only parameter that correlated significantly with higher Dakkak score was a shorter bolus flow time (Spearman's $r = -$

0.711, $p = 0.010$; from $n=12$ patients). Data of the seven patients that successfully underwent HRIM analysis pre-and post-LAGB placement were analysed separately. None of these patients reported swallowing difficulties pre-LAGB placement (all Dakkak = 0) and scores were significantly different post-treatment (Dakkak = 10.4 ± 3.307 , range 0 – 20; RM-ANOVA - $F = 9,947$, $p = 0.020$). In this subgroup, no significant correlation between Dakkak score and weight loss post-LAGB could be identified (Spearman's $r = 0.234$, $p = 0.613$). Assessing esophageal PFA variables in relation to dysphagia symptoms, we found that a higher post-operative Dakkak score correlated with a shorter bolus flow time ($r = -0.955$, $p = 0.001$).

Gastroesophageal Reflux

Results of pH-metry were complete before and after LAGB placement in six of 21 patients. Only two of these patients had repeat combined pH-MII measurement. Reflux index (RI) was significantly higher pre-LAGB placement compared to post-LAGB placement (RI= 10.6 ± 8.5 vs RI= 1.7 ± 1.7 ; RM-ANOVA - $F = 8.476$, $p = 0.033$). Three patients (50%) had abnormal reflux index (i.e. >5%) pre-LAGB placement; reflux index remained abnormal in one of these patients post-LAGB.

Discussion

This study evaluated the short-term physiological effects of LAGB in an adolescent cohort. Consistent with previous studies performed in adults undergoing LAGB(10, 38-41), our main findings were that LAGB: i) leads to a significant reduction of weight and BMI; ii) increases perception of post-meal fullness and somewhat reduces hunger; iii) increases symptoms of dysphagia to solids; and, despite these effects, iv) causes little or no change to plasma concentrations of appetite-regulatory hormones. In addition, our study applied state of the art

methods to assess the short-term effects of LAGB on upper GI motor function. This revealed only inconsistent and/or subtle effects on gastric emptying, esophageal motility, esophageal bolus transport and esophageal emptying.

Several studies in adults using barium swallow and/or esophageal manometry have shown that LAGB placement is associated with multiple esophageal motility changes, which are primarily related to proximal migration of the inflatable band. Migration of the band has been shown to result in increased LES pressure, impaired LES relaxation(42, 43) and increased esophageal dilatation(44, 45) mimicking achalasia. Based upon Dakkak scores, we identified a significant increase in dysphagia symptoms, particularly in relation to solids. The subtle, but statistically significant, effects on motility that we did see, namely slower peristaltic propagation (slower contractile front velocity and longer distal latency), can be considered physiologically consistent with increased esophageal flow-resistance following LAGB placement; although we note that distension pressure, the most direct measure of flow resistance, was not changed.

It is likely that the biomechanical effects observed may be more pronounced in response to more viscous or solid boluses, which warrants evaluation. Indeed, the patient-reported Dakkak scores clearly identify a significant increase in bolus hold-up symptoms, particularly in relation to solids. Higher post-operative Dakkak scores were correlated with a shorter bolus flow time, this finding links bolus hold up symptoms to altered biomechanics, specifically reduced esophageal emptying. Similar findings have also been reported in relation to symptom severity in patients with non-obstructive dysphagia and achalasia.(46) While dysphagia symptoms and reduced esophageal emptying appeared linked, neither correlated with efficacy as defined by weight loss, hence, there may be other determinants of the efficacy of the LAGB procedure.

The relationship between LAGB and GERD appears complex, with studies showing both an improvement or worsening in GERD symptoms.(39, 47-51) We did not assess the occurrence of GERD symptoms in the current study, however, our data indicate significantly reduced esophageal acid exposure post-LAGB. This may be a direct result of LAGB placement and/or weight loss in our cohort. A reduction in acid GER after LAGB placement has been previously described(52). A recent study also compared LAGB patients with and without symptomatic GERD and found that GERD symptoms were specifically associated with elevated esophageal acid exposure manifesting from an increase in the number and duration of reflux events.(53) On face value these data suggest that the LAGB may, in some instances, be acting as a physical barrier impeding retrograde flow of liquid gastric contents from the stomach, whilst exacerbating GER in other cases. We did also consider the possibility that the localised distension of the LAGB pouch, thought to activate the putative vagal mechanism of appetite regulation by LAGB, would also directly stimulate reflux via transient lower esophageal sphincter relaxation triggering.(9, 10, 54). Recent advice that an appropriately adjusted LAGB should *reduce*, rather than increase, GER therefore seems mechanistically counterintuitive; the known mechanism of reflux and the putative mechanism of weight loss involve stimulation of vagal pathways that appear to be co-localised within the same region of the gut.(53)

Gastrointestinal functions, particularly gastric emptying and gut hormones, have been established to play important roles for the regulation of appetite and food intake.(55)

However, our study appears to demonstrate therapeutic efficacy for weight loss and changes in appetite sensations without marked changes in these functions other than a reduction in plasma leptin hormone whose secretion is known to reduce with loss of body fat mass. This raises for us questions regarding the mode of efficacy of this procedure. Distension of the small segment of stomach above the band has been proposed to be relevant, however our

results show that LAGB affected esophageal bolus transport only subtly, suggest that a biomechanically relevant flow restriction is not necessary for the procedure to be efficacious. A more prevalent view is that the effect is occurring within the gastric fundus that is immediately distal to the band. Data derived from animal models suggest that LAGB may alter appetite-regulatory hormones(56) (57) (58), however, LAGB also elevates the neural activation of vagal afferent signalling to the nucleus of the solitary tract.(9) Other potential indirect modes of efficacy, including the role of extrinsic compression causing interference with appetite regulation mechanisms via vagal and splanchnic pathways to the CNS are as yet unexplored.

The strengths of the current study include the prospective single-centre enrolment with a single pediatric bariatric surgeon. Although a sample size of 15 patients may be regarded as small, it should be noted that one of the largest prospective bariatric surgery studies in the USA (Teens LAB consortium) only included data of 11 adolescents post LAGB.(59) We do, however, acknowledge that the current study has a relatively high level of missing data because of partial lack of patient tolerance and compliance with the study interventions. We have chosen to only report data on those patients that completed measurements over all investigated time-points to provide the most reliable overview of effects of the very low calorie diet and LAGB placement.

In conclusion, we report weight loss and altered appetite perceptions in adolescents undergoing LAGB placement, however, did not identify major changes in gut hormones or upper gut motility that plausibly explain these effects of the procedure. Dysphagia was apparent and was associated with reduced esophageal emptying. Dysphagia may become a more pronounced complication over time. Future studies are, therefore, warranted to investigate the role of the described methods for motility assessment as future tools to monitor and potentially manage patients' post-LAGB placement.

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Figure Legends

Figure 1 – Esophageal pressure flow analysis. Example 5ml liquid swallow from a post-LAGB study.

Automated analysis was applied to each swallow within a region of interest (see ROI inset lower right; EB, esophageal body). **A.** A pressure topography iso-contour plot with superimposed lines showing the position of the Nadir Impedance (thick purple line; indicating peak distension) and Contractile Peak (thick red line; indicating peak pressure) over time. The analyst fine-tuned landmarks paying particular attention to the Transition Zone (TZ), the Contractile Deceleration Point (CDP; yellow dot) and Crural Diaphragm (CD). **B.** *Bolus Flow Latencies* were determined based on the pressure and impedance recording at the CDP level. These were the Swallow to Distension Latency (SDL) from swallow to Nadir Impedance (NI) and Distension to Contraction Latency (DCL) from NI to Contractile Front (CF). **C.** *Intra-Bolus Distension Pressure* during bolus transport was determined as the Pressure at Nadir Impedance which was determined along the esophagus based on the average Distension Pressure (DP) within three anatomical regions approximating the different phases of bolus transport. These were DP during bolus accommodation (DPA, pressures UES to TZ), DP during compartmentalized transport (DPCT, pressures TZ to CDP) and DP during esophageal emptying (DPE, pressures from CDP to CD). **D.** *Intra-Bolus Ramp Pressurization* was measured over time from NI to CF within the distal esophagus (25% of TZ to CDP length; see points 0 (at CDP), +1 and +2 cm in Panel A). The Ramp Pressurization (RP) was determined by the mean gradient of pressure change over time. **E.** Effectiveness of *Bolus Clearance* was determined from TZ to CDP based on the Impedance Ratio ($IR = NI/Impedance \text{ at Contractile Peak}$). A higher IR indicates *less* effective bolus clearance.

Figure 2. Solid gastric emptying of a pancake meal recorded preoperatively at enrolment baseline (PreOp-BL), following 4 weeks Optifast diet (PreOp-OD) and post LAGB placement (PostOp). Data are only presented for patients who completed all sets of repeated measures over the three study periods (n=13). Graphs show the estimated marginal mean (with standard error bars). Repeated Measures ANOVA descriptive parameters (F, p-value and partial eta squared) are shown for each overall estimated marginal mean comparison. Pairwise significance is based on post-hoc test following Bonferroni correction.

Figure 3. Perception of hunger and fullness in response to pancake meal at enrolment baseline (PreOp-BL), following 4 weeks Optifast diet (PreOp-OD) and post LAGB placement (PostOp). Data are only presented for patients who completed all sets of repeated measures over the three study periods (n=13). Graphs show the estimated marginal mean (with standard error bars). Repeated Measures ANOVA descriptive parameters (F, p-value and partial eta squared) are shown for each overall estimated marginal mean comparison. Pairwise significance is based on post-hoc test following Bonferroni correction.

Figure 4. Measures of pharyngeal function recorded preoperatively at enrolment baseline (PreOp-BL) and post LAGB placement (PostOp). Data are only presented for patients who completed HRIM measurement pre- and post-LAGB placement (n=10). Data from 8 young healthy adults are also included. Graphs show the (estimated marginal) mean values. Students *t*-test and Repeated Measures ANOVA parameters are only shown if significant.

Figure 5. Esophageal HRIM of two patients post-LAGB. **A.** Panel represents HRIM image typically seen in the patient cohort post-LAGB – i.e. no evidence of HRIM of the LAGB in situ (Patient 13 in Table 1). **B.** Panel represents HRIM image of the one patient with a typical image of compartmentalized pressurization just below the EGJ. The upper high-pressure zone

coincided with the PIP (*). The lower high-pressure zone results from constriction of the stomach by the LAGB (Patient 1 in Table 1). Dakkak scores (20.5 vs 21 respectively) and percentage weight loss (-28.3% for both patients) post-LAGB were similar for these two patients.

Figure 6. Measures of Esophageal Pressure Topography (EPT) analysis recorded preoperatively at enrolment baseline (PreOp-BL) and post LAGB placement (PostOp). Data are only presented for patients who completed HRIM measurement pre- and post-LAGB placement (n=7). Data from 8 young healthy adults are also included. Graphs show the (estimated marginal) mean values. Students *t*-test and Repeated Measures ANOVA parameters are only shown if significant. Pairwise significance is based on post-hoc test following Bonferroni correction.

Figure 7. Measures of Pressure Flow analysis (PFA) recorded preoperatively at enrolment baseline (PreOp-BL) and post LAGB placement (PostOp). Data are only presented for patients who completed HRIM measurement pre- and post LAGB placement (n=7). Data from 8 young healthy adults are also included. Graphs show the (estimated marginal) mean values. Students *t*-test and Repeated Measures ANOVA parameters are only shown if significant. Pairwise significance is based on post-hoc test following Bonferroni correction.

A. Intra-Bolus Distension pressures and Intra-Bolus Ramp Pressurization. **B.** Flow latencies. **C.** Measure of esophageal clearance. **D.** Measures of esophageal emptying.

Table 1 – Overview of patient’s clinical characteristics

Patient number	Gender	Baseline Visit 1 (PreOp-BI)			Visit 2 (PreOp-OD)	Visit 3 (postOp)	
		Age (yrs)	BMI (kg/m ²)	Chicago Classification	BMI (kg/m ² ; % loss)	BMI (kg/m ² ; % loss)	Dakkak
1#,\$	M	18.7	44.1	NA	38.7 (-12.2%)	31.6 (-28.3%)	21
2#,\$	F	16.1	38.4	NA	38.3 (-0.0%)	34.0 (-12.6%)	19
4#,\$	M	17.6	38.7	NA	37.5 (-3.1%)	34.6 (-10.7%)	NA
6#,\$	F	17.5	51.2	NA	50.2 (-2.0%)	47.6 (-7.0%)	23
7\$	M	17.5	49.3	NA	48.5 (-1.5%)	43.4 (-11.8%)	8
8\$	F	14.0	35.1	NA	34.0 (-3.1%)	30.9 (-12.1%)	3.5
10	F	17.2	43.4	Normal	39.9 (-8.0%)	38.7 (-10.7%)	0
11#	F	15.7	37.9	Ineffective Motility	34.7 (-8.5%)	34.7 (-27.2%)	20.5
13	F	18.0	34.0	Normal	34.1 (+0.2%)	24.3 (-28.3%)	20

14 ^{#,§}	F	15.8	51.1	NA	46.8 (-9.0%)	37.9 (-26.8%)	1.5
15	F	16.5	52.9	Normal	50.5 (-4.0%)	52.0 (-2.0%)	12
16	M	18.1	55.2	Normal	52.4 (-5.0%)	43.5 (-21.2%)	16
17*	M	16.9	37.2	Normal	35.0 (-6.1%)	29.8 (-20.1%)	0.5
18	F	18.0	45.9	Ineffective Motility	44.9 (-2.0%)	32.6 (-29.1%)	4.5
20 ^{*,§}	F	17.4	NA	NA	59.7 (NA)	48.9 (-18.1%)	25

#No pharyngeal HRIM data available for these patients; §No esophageal HRIM data available for these patients; *No gastric emptying data available for these patients.