Mo1933

DUODENAL LAYER MORPHOMETRY TO GUIDE DUODENAL MUCOSAL RESURFACING IN PATIENTS WITH AND WITHOUT TYPE 2 DIABETES MELLITUS: RESULTS OF A SINGLE-CENTER INTRALUMINAL IMAGING PILOT STUDY

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Background: Endoscopic metabolic therapies, such as duodenal mucosal resurfacing (DMR) aimed at improving glycemic control in patients with Type 2 diabetes mellitus (T2DM) target the duodenal mucosa. It is unknown whether baseline differences in duodenal layer thickness exist among subjects with and without T2DM and how this may affect DMR. Aim: To assess potential duodenal morphometric differences between patients with and without T2DM using volumetric laser endomicroscopy (VLE) and radial endoscopic ultrasound (rEUS) imaging modalities. Methods: Single-center, observational, *in vivo* pilot study of subjects who underwent VLE and rEUS of the upper gastrointestinal tract during endoscopy. Measurements of the duodenal mucosal layer were recorded using both imaging modalities for all subjects to correspond with the 4th, 3rd and 2nd portion of the duodenum. All images were analyzed by a single investigator who was blinded to patient's condition. Results: Between March and July 2016, 20 subjects were enrolled, 55% male, average age 64 years (range: 36-92 years) and 50% with a diagnosis of T2DM. No differences in mucosal thickness measurements were observed along the entire length of the duodenum. Mean duodenal mucosal layer thickness among patients with and without T2DM was 0.49 mm and 0.53, respectively, with a significant difference observed in duodenal mucosal layer thickness between these two groups (Table) (P=0.033). A limitation to these analyses was compression of the VLE catheter against the duodenal wall, which appeared to influence measurements of mucosal wall thickness. This was addressed by assigning a qualitative compression score to each measurement location based on the mucosal image features (compression score ranged from 0 for fully observable villi, to 3 for no villi observable). For each increment in compression score, measured mucosal thickness decreased by 0.16 mm (P=0.0015). In a secondary multivariate analysis, the impact of the compression score appeared to be greater than T2DM on mucosal thickness (Table). For the rEUS measurements, mean duodenal mucosal layer thickness was similar but more variable among subjects with and without T2DM (1.09 mm versus 1.48 mm, respectively) with no significant difference in duodenal mucosal layer thickness observed between the two groups (P=0.106). Conclusions: VLE and, to a lesser extent, rEUS, allow reliable estimation of duodenal mucosal thickness which may facilitate DMR. Duodenal mucosal layer thickness did not appear to vary according to the presence of T2DM nor the location along the duodenum. The effects of compression of the VLE catheter created a significant effect on duodenal mucosal thickness, findings that need further exploration. Additional studies are warranted to enhance imaging and histological evaluation of the duodenal surface to further refine endoscopic metabolic therapies.

Univariate and multivariate analysis of duodenal mucosal thickness

Univariate Analysis: Effect of Type 2 Diabetes Mellitus (T2DM) on Duodenal Mucosal Thickness (mm)				
Imaging Modality	With T2 DM	Without T2DM	Difference	p-value
	Mean (Range)	Mean (Range)	Mean (95% CI)	
VLE	0.49 (0.43-0.53)	0.53 (0.46-0.61)	-0.05 (-0.09 to -0.00)	0.033
rEUS	1.09 (0.68-2.14)	1.48 (0.51-2.26)	-0.39 (-0.88 to 0.09)	0.106
Multivariate Analysis Linear Model: Effects of T2DM and Compression Score on Duodenal Mucosal Thickness (mm) with VLE				
Variable	Coefficient	95% CI	p-value	
T2DM	-0.029	-0.061 to 0.004	0.104	
Compression Score	-0.139	-0.224 to 0.054	0.0053	

VLE= volumetric laser endomicroscopy; rEUS= radial endoscopic ultrasound; T2DM= Type 2 Diabetes Mellitus; CI= confidence interval

Mo1934

SINGLE CATHETER FOR DUODENAL MUCOSAL RESURFACING DEMONSTRATES SIMILAR SAFETY PROFILE WITH IMPROVED PROCEDURE TIME WHEN COMPARED TO ORIGINAL DUAL CATHETER: MULTICENTER STUDY OF SUBJECTS WITH TYPE 2 DIABETES

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Introduction: Abnormalities in duodenal mucosa, nutrient absorption, and entero-endocrine cell population in patients with type 2 diabetes (T2D) are thought to play pathophysiological roles in the insulin resistance signal as observed through duodenal-exclusion bariatric surgery. Duodenal Mucosal Resurfacing (DMR) is an endoscopic procedure that resurfaces the duodenal mucosa via hydrothermal ablation exerting metabolic benefit by likely modifying nutrient-mucosa signalling. DMR is being investigated as a treatment for metabolic diseases including T2D. The safety and efficacy of the original DMR dual-catheter system have been previously described, and an integrated single-catheter system has since been developed. We compared DMR procedural performance and safety between the two catheter systems in patients with uncontrolled T2D. **Methods:** Data on the dual- and single-catheter systems were extracted from the single arm, multicentre REVITA-1a (R1a) trial, and the second cohort of the first-in-human (FIH) and REVITA-1b (R1b) trials, respectively. Primary safety endpoints included device/procedure-related serious adverse events (SAEs), unanticipated adverse device effects (UADEs), and hypoglycemic events. Based on significant glycemic efficacy in the FIH study (first cohort), procedure success was defined as 3 and 5 ablations per patient with the dual- and single-catheters. **Results:** In dual (n=28; age 55.4±9 years, BMI 32.3±4.3 kg/m^2, HbA1c 8.5±1.0%) and single-catheter groups (n=23; age 58.1±6.8 years, BMI 30.8±4.3 kg/m^2, HbA1c 8.3±1.1%, baseline mean±SD), procedure success was similar (80/84 [95%] and 111/115 (97%) of intended ablation completed). The median procedure time with single-catheter was less (52 [Interquartile range (IQR), 45] min) than with dual-catheter (79 [IQR, 53] min). Overall adverse events (AEs) and procedure related AEs occurred at numerically lower rates with the single-catheter than with the dual-catheter (Table). AEs were mostly mild to moderate; no SAEs were reported with the dual-catheter. With the single-catheter, one patient experienced a SAE (increased C-reactive protein), possibly related to the procedure and one experienced a severe AE (angina due to increased oxygen demand) with unknown relation to device/procedure. No device/procedure related UADEs were reported in either study. Two patients in the dual-catheter and no patients in the single-catheter studies experienced hypoglycemic events (none required rescue action). Most common AEs were gastrointestinal disorders which generally occurred within 0-3 days of the procedure and were resolved, except diarrhea in one patient (single-catheter) which remained unresolved until the patient withdrew consent. **Conclusion:** The procedure success was comparable between the dual- and single-catheters, with numerical reduction in the procedure time and AEs using the single-catheter.

Table. Comparative Frequencies of AEs in Patients treated With Dual-vs Single-Catheter System[a]

	Dual-catheter n (%)	Single-catheter n (%)
N[b]	28	23
Overall AEs	24 (85.7)	18 (78.2)
Overall SAEs	0 (0.0)	1 (4.3)
Severe AE	0 (0.0)	1 (4.3)
Overall procedure related AEs[c]	16 (57.1)	12 (52.1)
- Possibly procedure related	9 (32.1)	4 (17.4)
- Probably procedure related	7 (25)	5 (21.7)
- Definitely procedure related	7 (25)	3 (13.0)
Device/procedure related SAEs[d]	0 (0.0)	0 (0.0)
Device/procedure related UADEs	0 (0.0)	0 (0.0)
Overall hypoglycemia[e]	2 (7.1)	0 (0.0)
Most frequent AEs by System Organ Class, n (%)[f]		
Gastrointestinal disorders[g]	17 (60.7)	13 (56.5)
Musculoskeletal and connective tissue disorders	8 (28.6)	3 (13.0)
Respiratory, thoracic and mediastinal disorders	6 (21.4)	0 (0.0)
General disorders and administration site conditions	5 (17.9)	3 (13.0)
Metabolic and nutrition disorders	4 (14.3)	2 (8.7)
Infections and infestations	4 (14.3)	2 (8.7)
Injury, poisoning and procedural complications	3 (10.7)	1 (4.3)

[a] Data over 24 weeks for the dual-catheter group and over 12 weeks for the single-catheter group. [b] N = total number of patients in the safety population defined as patients who received ≥1ablations. [c] Patients were counted more than once in the sub-categories where applicable. [d] SAEs classified by investigators as definitely or probably related to device/procedure are included. [e] Defined as blood glucose level <3.1 mmol/L or hypoglycemic events that require third party assistance. [f] AEs with >5% frequency in any study. [g] Most common (>5%) gastrointestinal disorders in any study were abdominal pain, diarrhea, nausea and constipation.

Mo1935

GLU *CAG*+ ON LIKE PEPTIDE-1 (GLP-1) AFTER ROUX-EN-Y GASTRIC BYPASS: A META-ANALYSIS TO CLARIFY IMPACT OF SURGICAL TECHNIQUE AND OPTIMAL MEASUREMENT STRATEGY

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Background: Roux-en-Y gastric bypass (RYGB) is an effective treatment for type 2 diabetes mellitus (T2DM). Glucagon-like peptide-1 (GLP-1) is a gut hormone, secreted by the ileum and colon, that is important to glucose homeostasis. It has been hypothesized that GLP-1 may play an important role in T2DM remission after RYGB. **Aim:** To assess serum GLP-1 level and its predictors after RYGB. **Methods: Study Design:** A systematic review and meta-analysis. **Data Sources:** Searches included MEDLINE, EMBASE, Web of Science and the Cochrane Central Register of Controlled Trials databases through August 1, 2016. **Study Selection:** Randomized clinical trials, cohort studies and case series that reported pre- and post-RYGB GLP-1 levels. **Data Extraction and Synthesis:** Independent data extraction, quality assessment and risk-of-bias assessment were performed. Data were pooled using a fixed-effects model or a random-effects model if there was statistical heterogeneity. **Main Outcomes and Measures:** Primary outcome was the change in postprandial GLP-1 levels after RYGB compared to baseline pre-RYGB levels. Secondary predefined outcomes included the changes in fasting glucose levels, fasting insulin levels and fasting GLP-1 levels after RYGB compared to pre-RYGB levels. Meta-regression analysis to determine predictors of changes in GLP-1 levels was performed. Outcomes were reported using Hedge's g. **Results:** Twenty-four studies with a total of 368 patients were included in the meta-analysis. Mean age ranged from 36 to 52 years old. Mean body mass index (BMI) prior to RYGB ranged from 32.1 to 51.9 kg/m^2. Postprandial GLP-1 levels significantly increased after RYGB (Hedge's g = 1.29 [1.15,1.43] (p<0.0001)) (Figure 1), while fasting GLP-1 did not significantly change (p=0.23). Peak postprandial GLP-1 levels gave the most consistent results (I^2 of 9.11). Fasting glucose and insulin levels significantly decreased after RYGB with Hedge's g of -0.85 [-0.98,-0.71] (p<0.0001) and -0.97 [-1.31,-0.63] (p<0.0001), respectively. A meta-regression analysis showed that Roux limb length was a significant predictor for amount of