| Table 1. | Diabetic Patients (N=111) | Non-diabetics (N=120) | p-value |
|---|---|---|---|
| **Age (years)** | 58.5±14.7 | 52.0±17.8 | 0.003 |
| **Gender Females n (%)** | 63(56.8) | 75(63.0) | 0.332 |
| **Number of histology slides per patient** | 1(1-2) | 1(1-2) | - |
| **BMI (kg / m²)** | 30.8±8.0 | 23.8±5.56 | <0.001 |
| **Smoking** | 8(7.2) | 11(9.2) | 0.588 |
| **Alcohol Use** | 23(20.7) | 37(31.4) | 0.067 |
| **Comorbidities** | | | |
| Hypertension | 87(78.4) | 27(22.5) | <0.001 |
| Hyperlipidemia | 82(73.9) | 35(29.2) | <0.001 |
| Non-alcoholic fatty liver disease | 10(9.0) | 2(1.7) | 0.013 |
| **Insulin therapy** | 59(53.56) | 0 | <0.001 |
| **Oral hypoglycemics** | 73(65.8) | 0 | <0.001 |
| **Fasting Glucose** (mmol/L) | 159.77±65.4 | 92.0±11.6 | <0.001 |
| **HbA1c level** | 7.8±1.2 | 5.2±0.4 | <0.001 |
| **CBC markers** | | | |
| WBC (x10⁹/L) | 7.3±2.4 | 6.3±2.3 | 0.003 |
| Hgb (g/dL) | 12.3±2.1 | 13.2±2.0 | 0.003 |
| Hct (%) | 37.5±5.6 | 39.7±5.0 | 0.003 |
| Platelets (x10⁹/L) | 241.6±80.6 | 249.8±90.9 | 0.490 |
| Neutrophils (x10⁹/L) | 4.8±2.2 | 6.8±23.4 | 0.405 |
| Lymphocytes(x10⁹/L) | 1.8±0.9 | 1.9±3.5 | 0.679 |
| Monocytes(x10⁹/L) | 0.5±1.9 | 0.7±2.2 | 0.372 |
| Eosinophils(x10⁹/L) | 0.2±0.1 | 0.2±0.1 | 0.189 |
| Basophils(x10⁹/L) | 0.03±0.02 | 0.1±0.2 | 0.303 |
| **Lipid Profile** | | | |
| Total Cholesterol (mg/dL) | 174.2±55.4 | 192.0±45.3 | 0.049 |
| LDL (mg/dL) | 89.3±40.6 | 101.4±39.0 | 0.096 |
| HDL (mg/dL) | 51.3±17.7 | 71.2±26.1 | <0.001 |
| Triglycerides(mg/dL) | 175.0±127.2 | 109.1±83.8 | 0.001 |

Table 1. Baseline characteristics of the diabetic and non-diabetic cohorts.

**Figure 1.**

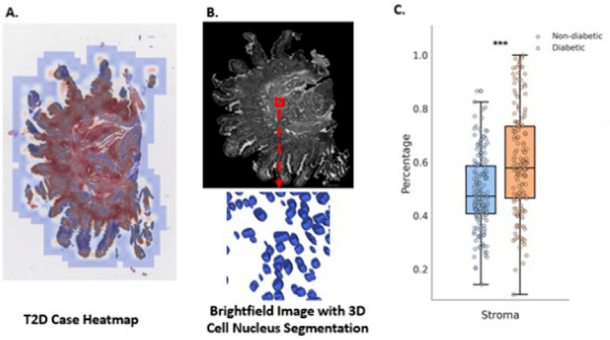


Figure 1. A) Heatmap displaying lymphocyte hotspots and lamina propria stroma expansion (shown in red) associated with T2D, B) Brightfield image showing 3D reconstruction and cellular segmentation of the lamina propria, C) Box plot illustrating increased lymphocyte hotspots and lamina propria expansion in T2D.

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### The Current Insights in Bariatric Endoscopy CLINICAL OUTCOME OF THREE DIFFERENT TECHNIQUES OF ENDOSCOPIC GASTROPLASTY. RESULTS AT 18 MONTHS FOLLOW-UP FROM A SINGLE CENTER, RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic Gastroplasty (EG) is an endoscopic therapy to treat obese patients focusing on gastric body remodeling. We considered three different techniques: Endoscopic Sleeve Gastroplasty (ESG), Endoluminal Vertical Gastroplasty (EVG), and distal Primary Obesity Surgery Endoluminal (POSE2). Aims & Methods: This was a single center, randomized controlled trial (ClinicalTrials.gov NCT04854317) of obese patients who underwent EG (through ESG or EVG or POSE2) or a low-calorie Mediterranean diet (1600 and 1400 Kcal/day). Outcomes included technical success rate, serious adverse event rate, and efficacy of the three EG procedures at inducing weight loss, improving obesity related comorbidities and quality of life (QoL), compared to diet. Results: From July 2020 to May 2022, 240 obese (body mass index 37.5±3.5 kg/m$^2$) patients (mean age 46±10 years; females 87.8%; obesity class II 58.3%; hepatic steatosis as the main comorbidity in 70%) underwent EG (through ESG, EVG or POSE2, with 60 patients for each procedure, 180 patients in total) or a low-calorie diet (60 patients). In the EG group the technical success rate was 100%. The serious adverse event rate was 1.1%. The follow-up visit was attended by 100/180 (55.6%), 48/180 (26.7%) and 19/180 (10.6%) patients at 6, 12 and 18 months, respectively. They experienced 16.1±6.1%, 13.7±9.0% and 14.1±11.0% total body weight loss (TBWL) and 39.7±15.4%, 35.3±23.4% and 34.7±27.3% excess weight loss (EWL) at 6, 12 and 18 months, respectively, with no significant difference among the three techniques in both parameters ($p>0.62$ in TBWL% and $p>0.94$ in EWL% ANOVA tests) at 18 months follow-up. Concerning the low-calorie diet group, 31/60 (52%), 13/60 (22%) and 4/60 (6%) patients attended their 6, 12 and 18 months follow-up; they experienced 1.1±4.7% TBWL ($p<0.001$ versus EG group) and 2.3±9.8% EWL ($p<0.001$ versus EG group) at 18 months. Ninety seven of one hundred (97.0%), 37/48 (77.1%) and 16/19 (84.2%) patients achieved at least 5% TBWL, while 86/100 (86.0%), 32/48 (66.6%) and 15/19 (78.9%) achieved at least 25% EWL in the EG group at 6, 12 and 18 months follow-up, compared to 4/31 (12.9%), 1/13 (7.6%) and 0/4 (0%), and 3/31 (9.7%), 1/13 (7.6%) and 0/4 (0%) in the diet group, at 6, 12 and 18 months. Fatty liver disease, hypertension, hyperlipidemia, diabetes, and obstructive sleep apnea improved after the EG procedure at 18 months, while no improvement was observed in the diet group. Also, the QoL measured by EQ-5D test improved at 18-month follow-up ($p<0.01$) in the EG group, while no significant improvement was detected in the diet group. Conclusion: EG through ESG, EVG and D-POSE are technically feasible and safe, and appear to be effective for the treatment of obese patients, compared to diet, at a medium term follow-up.

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### The Current Insights in Bariatric Endoscopy DUODENAL RECELLULARIZATION VIA ELECTROPORATION IN POORLY CONTROLLED TYPE 2 DIABETES

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Background: In the evolving treatment landscape for T2D, the duodenum, a key site for nutrient sensing and glucose metabolism regulation, presents a compelling target for new therapeutic approaches that seek to improve insulin sensitivity and glucose homeostasis. One promising technology involves the endoscopic application of pulsed electric fields to induce duodenal cell regeneration. Duodenal recellularization via electroporation (ReCET™, Endogenex Inc.) is a non-thermal, non-

pharmacologic intervention that selectively targets mucosal and submucosal cells inducing irreversible electroporation that is followed by re-epithelialization of the duodenal surface with the intent of improving glucose metabolism. This first-in-human study evaluates the safety, feasibility and preliminary efficacy of ReCET in T2D patients inadequately controlled on glucose lowering medications. Method: This is an ongoing multicenter, open-label, treatment-only study. Key eligibility criteria are 18-70 years of age, history of T2D for ≤10 years, HbA1c of 7.5%-11.0%, BMI of 24 – 40 kg/m2, C-peptide ≥ 333 pmol/l, and on 1-4 non-insulin GLMs. The primary endpoint is the incidence of device- or procedure-related serious adverse events (SAEs) at 12 wks. Secondary endpoints include technical success and changes in glycemic control at 24 wks. Patients are followed for 48 wks, with endoscopic follow up at 4 wks. The GLMs are maintained stable for ≥12 wks before and ≥24 wks after the procedure. Results: Fifty-one patients have been enrolled and treated with two versions of catheters (Table 1). Technical success was 100%, with a mean treated length of 11.2 ± 2.7 cm, and median procedure time of 68 min (IQR 46 – 88). No device/procedure-related SAEs occurred. Incidence of device/procedure-related adverse events (AEs) were less frequent with the Gen 2 vs. Gen 1 device (10/21 vs 23/30, p<0.05). The most reported AEs were sore throat 49% (25/51) and transient diarrhea 22% (11/51). AEs were mild (76%) or moderate (24%) in severity. At 4 wks, the treated areas showed complete healing, were mostly unidentifiable endoscopically with no signs of stricture, ulceration, or other significant findings. Glycemic control was significantly improved post-procedure from baseline with a trend towards greater effectiveness with double Tx and with the Gen 2 device (Figure 1). Mean change in HbA1c was -1.7% at 24 wks from baseline with the Gen 2 device. Follow up in the Gen 2 treated group is ongoing. In patients treated with the Gen 1 device, improvement in glycemic effect was maintained at 48 wks in the double Tx group. Conclusions: Endoscopic therapy using the ReCET system is safe and has demonstrated a clinically meaningful improvement in glycemic control in T2D patients uncontrolled on medications in this feasibility study.

**Table 1. Baseline Characteristics**

| | Gen 1 Device | | Gen 2 Device | |
|---|---|---|---|---|
| | Single Tx | Double Tx | Double Tx | Total |
| N | 12 | 18 | 21 | 51 |
| Age (yrs) | 50.5 ± 9.5 | 51.5 ± 8.8 | 55.4 ± 5.5 | 52.9 ± 7.9 |
| Male (%) | 66.7% | 77.8% | 76.2% | 74.5% |
| BMI (kg/m²) | 30.1 ± 4.8 | 32.2 ± 3.0 | 31.4 ± 3.1 | 31.4 ± 3.5 |
| HbA1c (%) | 8.8 ± 0.9 | 8.6 ± 1.0 | 8.8 ± 0.9 | 8.8 ± 0.9 |
| FPG (mmol/L) | 9.1 ± 1.3 | 10.2 ± 2.5 | 10.6 ± 2.6 | 10.1 ± 2.3 |
| HOMA-IR | 2.6 ± 1.5 | 3.3 ± 1.7 | 2.3 ± 1.4 | 2.7 ± 1.5 |
| T2D duration | 5.1 ± 3.0 | 5.8 ± 2.6 | 5.6 ± 2.2 | 5.6 ± 2.5 |
| **Background GLMs (n, %)** | | | | |
| Metformin | 12 (100%) | 16 (89%) | 21 (100%) | 49 (96%) |
| Sulfonylureas | 6 (50%) | 5 (28%) | 0 (0%) | 11 (22%) |
| SGLT2i | 6 (50%) | 12 (67%) | 11 (52%) | 29 (57%) |
| GLP-1a | 3 (25%) | 1 (6%) | 1 (5%) | 5 (10%) |
| DPP4 | 1 (8%) | 5 (28%) | 8 (38%) | 14 (27%) |
| **No. of background GLMs** | | | | |
| 1 | 3 (25%) | 5 (28%) | 7 (33%) | 15 (29%) |
| 2 | 4 (33%) | 6 (33%) | 8 (38%) | 18 (35%) |
| 3 | 3 (25%) | 6 (33%) | 6 (29%) | 15 (29%) |
| 4 | 2 (17%) | 1 (6%) | 0 (0%) | 3 (6%) |

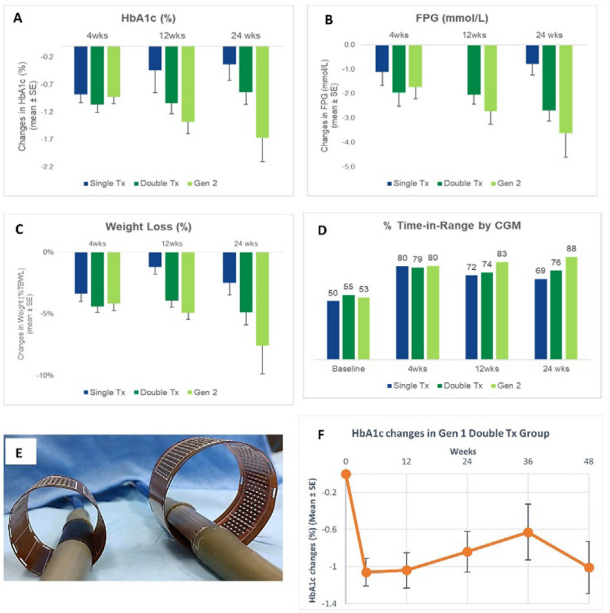


Figure 1. Improvement in in HbA1c (A) and FPG (B) post procedure from baseline showed an energy-dose response; (C) Weight loss post procedure showed an energy-dose response; (D) Mean Time-in-Rage by CGM at baseline and at follow up; (E) The Gen 2 catheter (right) accommodates a bigger diameter and has more electrodes on the flex circuit than the Gen 1 catheter (left). (F) Improvement in glycemic control was maintained at 48 wks in the double Tx group using the Gen 1 device).

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## The Current Insights in Bariatric Endoscopy

## EFFECT OF ENDOSCOPIC GASTRIC REMODELING ON HISTOLOGIC METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS (MASH) AND LIVER FIBROSIS: A 12-MONTH PROSPECTIVE OBSERVATIONAL STUDY

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Background: Metabolic dysfunction-associated steatohepatitis (MASH) is traditionally treated with lifestyle modification. Nevertheless, most patients are unable to achieve the 10% total weight loss (TWL) threshold required for fibrosis regression. Endoscopic gastric remodeling (EGR) is an effective weight loss procedure. This study aims to assess the effect of EGR on histologic features of MASH and portal pressure. Methods: This was a 12-month prospective study. Inclusion criteria were obesity and biopsy-proven MASH with at least stage 1 fibrosis. Exclusion criteria included decompensated cirrhosis. Subjects underwent EGR using an endoscopic plication device to reduce the gastric volume. Single-session endoscopic ultrasound-guided liver biopsies (EUS-LB) and endoscopic ultrasound-guided portosystemic pressure gradient measurements (EUS-PPG) were performed before and 12 months following EGR. Liver histology was assessed using the NASH CRN classification. The primary outcome was the efficacy of EGR in treating MASH with liver fibrosis assessed using FDA standards. This included the proportion of subjects who experienced 1) an improvement in liver fibrosis by at least one stage without worsening of MASH or 2) a resolution of MASH without worsening of liver fibrosis at 12 months. Secondary outcomes included changes in NAFLD activity score (NAS), non-invasive tests (NITs) for fibrosis and steatosis, and PPG at 12 months compared to baseline. Additionally, weight loss efficacy and safety were assessed. ClinicalTrials.gov