Partial jejunal diversion using an incisionless magnetic anastomosis system: 1-year interim results in patients with obesity and diabetes

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Background and Aims: Most patients with type 2 diabetes mellitus have obesity. Studies show that bariatric surgery is superior to medical treatment for remission of type 2 diabetes mellitus. Nevertheless, very few patients undergo surgery, and a less-invasive endoscopic alternative is desirable.

Methods: This was a single-arm first-in-human pilot study designed to evaluate the technical feasibility, safety, and clinical performance of the incisionless magnetic anastomosis system (IMAS) to create a partial jejunal diversion (PJD). Ten patients with obesity and type 2 diabetes mellitus, prediabetes, or no diabetes were enrolled. A PJD to the ileum was attempted in all patients under general anesthesia. The IMAS was delivered through the working channel of a colonoscope, with laparoscopic supervision. The patients were not required to participate in an intensive lifestyle/diet management program. Endoscopic visualization of the anastomosis was obtained at 2, 6, and 12 months. Patient weight, glycemic profile, and metabolic panels were acquired at 0.5, 1, 2, 3, 6, 9, and 12 months.

Results: A PJD was created in all patients with no device-related serious adverse events. The anastomosis remained widely patent in all patients at 1 year. Average total weight loss was 14.6% (40.2% excess weight loss at 12 months). A significant reduction in glycated hemoglobin level was observed in all diabetic (1.9%) and prediabetic (1.0%) patients, while reducing or eliminating the use of diabetes medications.

Conclusions: Permanent anastomosis for PJD was created in all patients with the IMAS. This resulted in improvement in measures of hyperglycemia and progressive weight loss. (Clinical trial registration number: NCT02839512.)

INTRODUCTION

Population-based data on obesity in the United States for 2013 to 2014 from the National Health and Nutrition Examination Survey (NHANES) show the prevalence of body mass index (BMI) >30 kg/m^2 to be 35.2% among men and 40.5% among women,[1] with an overall crude prevalence of class 3 obesity (BMI ≥40 kg/m^2; morbid obesity) of 7.7%.[1] Obesity is associated with a number of well-defined cardiometabolic risk factors, including

Abbreviations: BMI, body mass index; GIP, gastric inhibitory peptide; GLP-1, glucagon-like peptide-1; HbA_{1c}, glycated hemoglobin; IMAS, incisionless magnetic anastomosis system; NHANES, National Health and Nutrition Examination Survey; PJD, partial jejunal diversion; PYY, peptide YY; TWL, total weight loss.

DISCLOSURE: *Dr Lautz and Dr Simonson have served on an advisory panel and are stock/shareholders in GI Windows. Dr Ryou and Dr Thompson have served on an advisory panel and are board members and stock/shareholders in GI Windows. All other authors disclosed no financial relationships relevant to this publication.*

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increased glycated hemoglobin (HbA_{1c}) and fasting glucose levels[2] and comorbidities such as type 2 diabetes, hypertension, and increased all-cause mortality.[3] With respect to diabetes specifically, NHANES data for 2012 show the prevalence to be 12.3%, or 28.9 million Americans,[4] and the prevalence of prediabetes to be 37%, or an estimated 86 million Americans.[4]

Regarding the nexus between obesity and type 2 diabetes, a survey conducted in secondary care diabetes clinics in the United Kingdom found the prevalence of obesity to be considerably higher in patients with type 2 diabetes (60.1%) compared with that in the general population (13.6%) or in patients who had type 1 diabetes (17.0%).[5] Based on data from the Framingham Offspring Study, the risk of type 2 diabetes increased significantly with an increase in obese-years, defined as BMI multiplied by the number of years living with obesity; for every additional 10 obese-years, the risk of type 2 diabetes increased by about 7% ($P < .001$).[6] Neeland et al,[7] using data from the Dallas Heart Study, found that excess visceral fat and biomarkers of insulin resistance in obese patients were independently associated with the development of prediabetes and type 2 diabetes. Lifestyle modification alone has limited effectiveness, and patients usually regain most of their lost weight within 1 to 2 years. Medical therapies are typically prescribed for short periods of time and may cause side effects that reduce compliance and, as a result, their potential value.[3] In contrast, bariatric surgery generally offers effective and durable weight loss.[3,8]

Bariatric endoscopy remains an emerging concept in obesity management. Many of these procedures rely on temporary implants. An endoscopic procedure that delivers permanent anatomic alteration, without relying on retention of a foreign material, would represent a paradigm shift. In 1892, the first compression cholecysto-intestinal, GI, entero-intestinal anastomosis was described by Murphy.[9] Kanshin et al[10] in 1978 were the first to report the creation of a sutureless side-to-side anastomosis during GI surgery, using simple mechanical compression produced by a steady magnetic field. Previously, magnetic compression devices had to be delivered completely assembled, usually requiring an open surgical field. The few endoscopic procedures that were performed used small solid magnets because of size limitations of the narrow upper esophageal sphincter, and were plagued by short-term patency issues.

Our group has developed a self-assembling magnetic system to overcome these limitations. The system was initially used to create a gastrojejunal anastomosis in a porcine model.[11] This was subsequently modified to include a nitinol exoskeleton, allowing the device to be delivered in a linear configuration through an endoscope channel, and then change configuration into a large-caliber octagon (incisionless magnetic anastomosis system [IMAS]; GI Windows, West Bridgewater, Mass) (Fig. 1). These endoscopically delivered "smart" magnets were then used in a porcine model to create a side-to-side anastomosis with enteral diversion.[12,13]

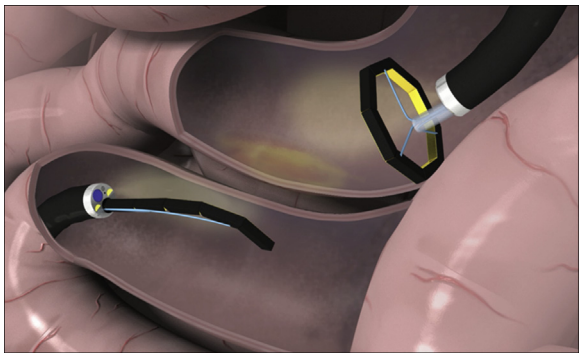

Figure 1. Deployment of the octagonal self-forming magnet device with the deployment tool. The magnet device incorporates an exoskeleton that directs self-assembly. The device can be delivered in a linear configuration using an endoscope working channel, at which time the device self-assembles into an octagonal ring when fully deployed.

This partial jejunal diversion (PJD) allows a portion of ingested nutrients and digestive fluids to circumvent most of the small bowel. Because the native path remains open, this procedure is unlike a jejuno-ileal bypass, which creates a blind defunctionalized segment of small intestine, which may result in a number of serious adverse events. Instead, the result is enteral diversion, with the metabolic effects anticipated to be more similar to the hindgut mechanisms seen with biliary pancreatic diversion, biliary pancreatic diversion with duodenal switch, or ileal transposition surgery.[14,15] These procedures cause food and digestive enzymes to enter the ileum early, leading to increased secretion of glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and other gut hormones, which leads to improved glucose homeostasis and weight loss. Similarly, the IMAS diverts food and digestive fluids, whereby some bypasses the jejunum and is diverted directly to the ileum and likely uses similar mechanisms.

The aim of this first-in-human pilot study was to assess the technical feasibility, safety, and clinical performance of the IMAS in creation of a PJD.

METHODS

Study design and patients

This was an open, prospective, single-arm pilot study with a primary focus on patients with obesity and type 2 diabetes or prediabetes, designed to evaluate the safety, technical feasibility, and clinical performance (including metabolic effects) of the IMAS when used to create a dual-path intestinal diversion. The study was conducted

at one site, the University Hospital of Ostrava, in Ostrava, the Czech Republic. The study was conducted with approval of the institution's Ethics Committee and the State Institute for Drug Control, the regulatory authority for the Czech Republic on April 17, 2014. Informed consent was obtained from each study participant prior to enrollment (Clinical trial registration number: NCT02839512).

Potential participants with obesity, with or without diabetes, were screened for enrollment by behavioral, nutritional, and medical evaluations. Men and non-pregnant women aged 18 to 65 years with a BMI of 30 to 50 kg/m^2 were eligible. Those with a BMI between 30 and <35 kg/m^2 must have had at least one clinically significant, well-controlled obesity-related comorbidity (eg, diabetes, hypertension, dyslipidemia, sleep apnea) to qualify for entry. Key exclusion criteria included a BMI >50 or <30 kg/m^2; type 1 diabetes; use of more than 2 oral anti-diabetic medications, insulin, a dipeptidyl peptidase 4 inhibitor, or a GLP-1 agonist; previous abdominal surgery; and hypersensitivity to nickel (the exoskeleton of the magnet device consists of a nickel-titanium alloy).

Procedure and assessments

Individuals who met the inclusion and exclusion criteria and completed all evaluations were enrolled in the study and underwent endoscopic evaluation to assess adequacy of bowel approximation. IMAS placement was attempted if all criteria were met. With the patient under general anesthesia, pairs of self-assembling magnets (IMAS) were delivered by a deployment tool advanced through a colonoscope channel into the terminal ileum and proximal jejunum, via simultaneous colonoscopy and enteroscopy, respectively (Fig. 2). Laparoscopic ports were placed in each patient after the deployment of the magnets to measure the exact position of the connection relative to the ligament of Treitz and ileocecal valve. In addition, a strict time limit of 40 minutes was imposed for attempted magnetic coupling, because distention of the small bowel with a prolonged attempt could compromise laparoscopic assistance if needed. In these cases, laparoscopic graspers were used to assist with coupling. After device placement, patients were advised to consume a liquid/soft diet for the first 2 weeks, with no specific dietary restrictions thereafter. An abdominal radiograph was performed within 48 hours of the procedure to confirm the position of the magnets and was typically completed before discharge the day after the procedure per protocol. The patients were provided with a plastic strainer that sits in the toilet and a magnetic wand to assist with magnet retrieval. An upper GI series was performed 2 weeks after the procedure to confirm anastomotic patency and device passage. Follow-up endoscopies were performed at 2, 6, and 12 months after device placement to confirm patency of the anastomosis. Patients will be re-evaluated periodically for up to 36 months.

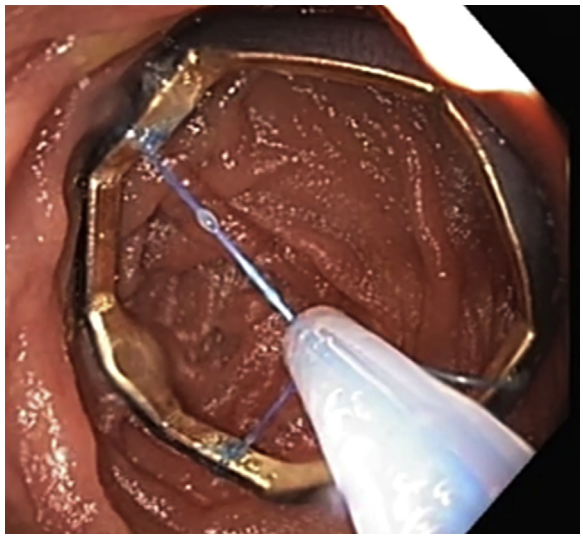

Figure 2. Endoscopic view of the deployed magnet in a patient's jejunum.

The primary endpoints were technical feasibility, defined as device deployment through the endoscope channel, successful engagement of the IMAS, patency of the anastomosis, and device-related serious adverse events. Secondary endpoints included percent total loss of body weight, percent excess weight loss, and decrease in HbA_{1c} at 12 months (for the diabetic cohort). A mixed meal tolerance test was performed at baseline, 2 months, and 6 months after the procedure. Blood samples were obtained before and at regular intervals up to 120 minutes after ingestion of the mixed meal for measurement of glucose, insulin, C-peptide, GLP-1, PYY, ghrelin, and gastric inhibitory peptide (GIP) to evaluate the impact of the procedure on glycemic indices and gut hormones.

Hormonal and biochemical assays

For determination of gut hormones (glucose-dependent insulinotropic peptide [GIP, total], glucagon-like peptide 1 [GLP-1, active], and PYY), blood samples (1 mL) were collected into Eppendorf tubes with 10 μL of dipeptidyl peptidase 4 inhibitor (Millipore, Billerica, Mass), 1 μL of protease inhibitor cocktail (Sigma-Aldrich, St. Louis, Mo), and 10 μL of Pefabloc SC (Roche Diagnostics, Mannheim, Germany). Serum concentrations of total ghrelin, GLP-1, GIP, and PYY were measured in duplicate using a bead-based multiplex assay kit (MILLIPLEX MAP Human Gut Hormone Panel, Merck, Darmstadt, Germany), in conjunction with flow-based protein detection on a Bio-Plex MAGPIX instrument (Bio-Rad, Hercules, Calif). Serum concentrations of glucose and HbA_{1c} were measured by the standard methods (AU 5420, Beckman Coulter, Brea, Calif).

TABLE 1. Summary of key patient demographics

	Value (SD)
Mean age (years)	48.1 (±10.5)
Gender	
Male	6
Female	4
Mean daily caloric intake (kcal)	1896.3 (±721.5)
Mean weight at baseline (kg)	120.9 (±17.8)
Mean BMI (kg/m^2)	41.1 (±4.3)
T2DM/prediabetes/no diabetes	4/3/3
Mean age at diabetes onset (years)	43.0 (±4.4)
Mean baseline HbA1c (%)	
4 with diabetes	7.8 (±2.5)
3 with prediabetes	6.1 (±0.3)
Mean baseline fasting glucose (mg/dL)	
4 with diabetes	177 (±107.4)
3 with prediabetes	119 (±2.5)

SD, Standard deviation; *BMI*, body mass index; *T2DM*, type 2 diabetes mellitus; *HbAc1*, glycated hemoglobin.

Statistical analysis

Because this was a pilot study, there were no statistical hypotheses. Descriptive statistics were used to provide an overview of safety and efficacy results. A paired *t* test (for continuous variables), Wilcoxon signed rank test (for data that were not normally distributed), or the McNemar test (for categorical data) was computed to compare follow-up outcomes with baseline values to aid in interpretation. Nominal *P* values associated with each statistical test were reported, but no statistical significance level was assigned and the study was not powered to determine any statistical significance for any of the endpoints.

RESULTS

Patient demographics

A total of 14 patients were enrolled between October 2014 and March 2015, and 10 underwent successful IMAS placement. Three of the 14 patients failed screening (2 withdrew consent and the third was found to have lung disease, an exclusionary comorbidity). The IMAS was not placed in the first 2 patients who had advanced to endoscopic evaluation, because of an inability to approximate the appropriate loops of bowel. This was thought to be a result of bowel distension from using air insufflation (instead of CO_2) through the colonoscopes during this initial evaluation. These patients did not experience any adverse events. The procedure was modified to permit only CO_2 insufflation during endoscopic evaluation and device placement. Subsequently, a total of 10 consecutive patients underwent endoscopic evaluation and attempted IMAS placement, including one of the patients who had a previous failed endoscopic evaluation. Patient demographics are summarized in Table 1. The study population was 60% male, had a mean age of 48 years (range, 22−58 years), and a mean baseline BMI of 41 kg/m^2 (range, 34.7−46.2 kg/m^2). Four patients had type 2 diabetes, 3 had prediabetes (HbA_{1c} 5.7%−6.4% and fasting glucose >100 mg/dL), and 3 did not have diabetes. Of the 4 with diabetes, 3 were receiving oral medications and 1 was treated with diet alone. All patients have completed 1 year follow-up clinic visits.

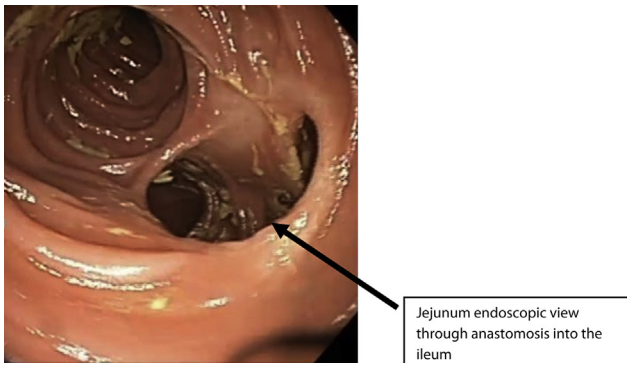

Figure 3. Endoscopic appearance of the intestinal anastomosis 12 months after the procedure.

Technical feasibility

Endoscopic delivery of the IMAS into the desired segments of bowel was successfully accomplished through the colonoscope channel in all 10 patients. The mean procedural duration from placement of the first colonoscope to removal of the second colonoscope was 115 minutes (mean duration was 131 minutes for the first 5 procedures and 98 minutes for the last 5 procedures). The target zone for placement of the 2 IMAS was 50 to 100 cm proximal to the ileocecal valve in the ileum and 50 to 100 cm distal to the ligament of Treitz in the jejunum. Laparoscopic visualization of the anastomosis site was also accomplished in all cases, with confirmation of limb lengths. Because of established time limits, laparoscopically assisted magnet coupling was used in the first 6 cases, but was not required in 2 of the last 4 cases. Laparoscopic and fluoroscopic images were compared in real time, and all magnets were confirmed to be in a fully anti-mesenteric position.

Patients were able to resume normal daily activities within a mean of 1.7 days after the procedure (range, 1−3 days). Initial evaluation of the anastomoses was performed at 2 weeks via an upper GI series with small-bowel follow-through. A patent anastomosis was seen in all patients, with no evidence of leak or perforation. Magnets were expelled on average 13 days after placement (range, 8−28 days) in all but 1 patient. In that patient (the first placement procedure), the bowel tissue

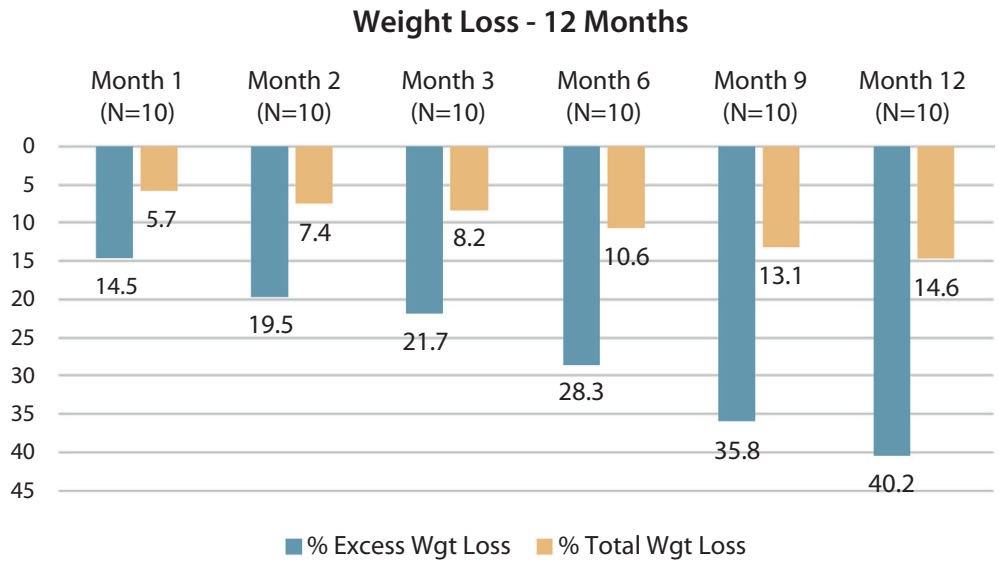

Figure 4. Percent excess weight loss and total weight loss from baseline to month 12.

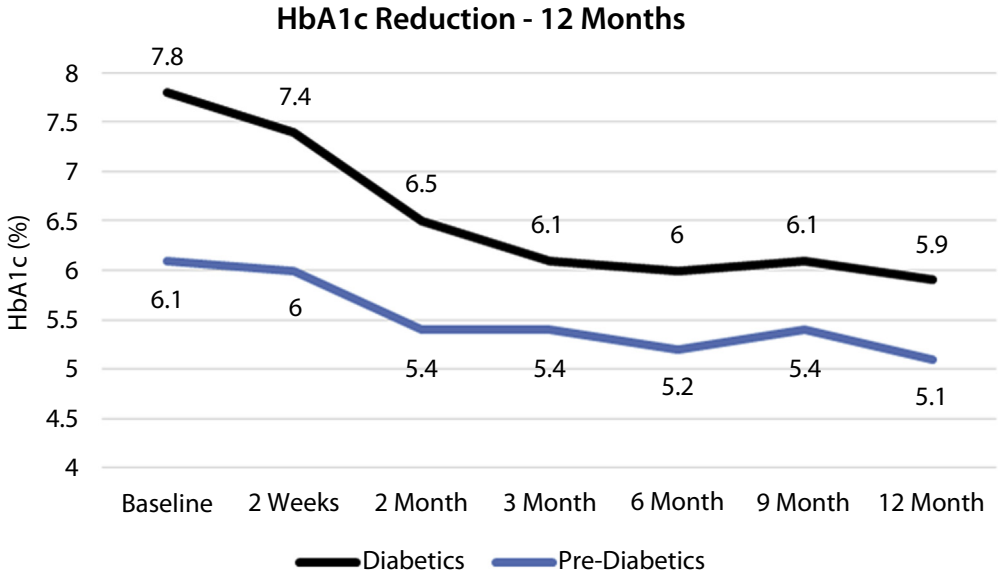

Figure 5. Change in glycated hemoglobin (HbA1c) from baseline for patients with diabetes (n = 4) and patients with prediabetes (n = 3) over 3, 6, 9, and 12 months. Average reduction in HbA1c was 1.9% in the diabetic cohort and 1.0% in the prediabetic cohort, bringing the value into the normal range for the latter.

had been sutured (this was not done for any of the other cases), and the magnet was retrieved endoscopically on day 123 without difficulty or subsequent adverse events. Presence of the IMAS and its later expulsion were well tolerated with no adverse events. Upper endoscopy at 2, 6, and 12 months confirmed patent anastomoses with healthy-appearing mucosa in all cases (Fig. 3). No abnormal scarring, fibrosis, significant change in size, or other technical sequelae have been observed during this 12-month follow-up.

Clinical outcomes

Overall, patients experienced a gradual progressive weight loss as depicted in Figure 4. The mean baseline weight of the study population was 120.9 ± 17.8 kg, which was reduced to 103.7 ± 21.5 kg at 12 months (P = .0014), with a mean total weight loss (TWL) of 14.6% (range, 0.3%–41.8%). The mean excess weight loss at 12 months was 40.2%, and 8 out of 10 patients had more than a 20.6% excess weight loss. These 8 patients had a mean TWL of 17.8%. The remaining 2

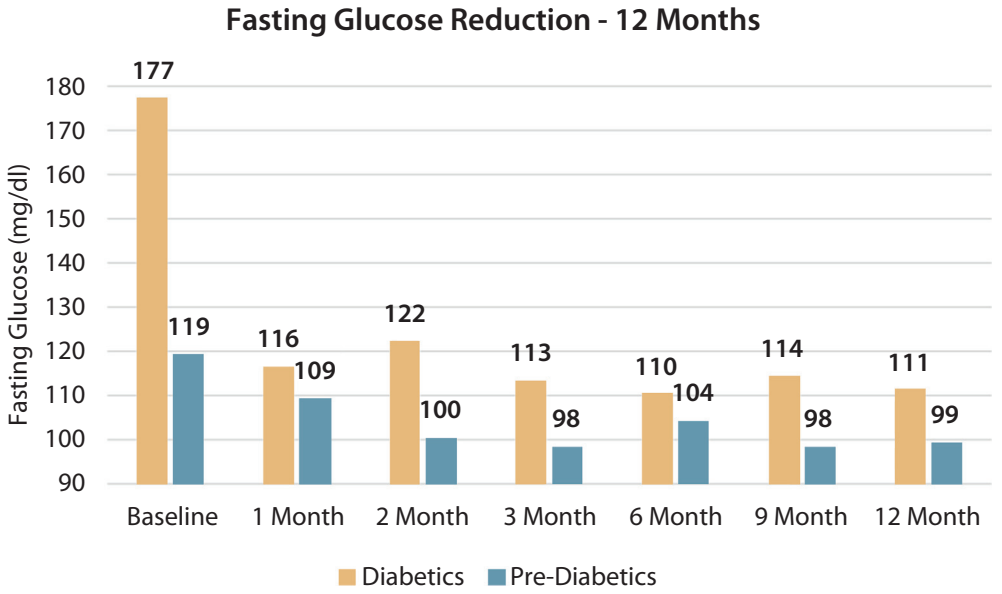

Figure 6. Change in fasting glucose level from baseline for patients with diabetes (n=4) and patients with prediabetes (n=3) over 1, 2, 3, 6, 9, and 12 months. Fasting glucose decreased by 37% in the diabetic cohort and 17% in the prediabetic cohort, bringing the value into the normal range for the latter.

TABLE 2. Mixed meal tolerance test results at baseline, month 2, and month 6*

Parameter	AUC baseline, mean (SD)	AUC week 8, mean (SD)	*P* value† (baseline to month 2)	AUC month 6, mean (SD)	*P* value† (baseline to month 6)
Glucose (mmol/L•minute)	1056 (465)	864 (250)	.028	807 (148)	.008
C-Peptide (pmol/L•minute)	167,065 (43,607)	126,802 (34,625)	.021	131,398 (39,309)	.14
Insulin (pmol/L•minute)	76,579 (34,913)	41,254 (35,364)	.008	46,623 (35,311)	.008
GLP-1 (pmol/L•minute)	2399 (3312)	3376 (3639)	.09	1560 (678)	.86
Ghrelin (active) (pmol/L•minute)	1855 (980)	1858 (735)	.77	2007 (803)	.31
GIP (pmol/L•minute)	7565 (3432)	4809 (1856)	.015	6259 (1987)	.21
PYY (pmol/L•minute)	6838 (2799)	8585 (1835)	.028	7943 (1994)	.24

AUC, Area under the curve; *SD*, standard deviation; *GLP-1*, glucagon-like peptide 1; *GIP*, gastric inhibitory peptide (glucose-dependent insulinotropic polypeptide); *PYY*, peptide YY.

*Nine patients with obesity: 4 with type 2 diabetes mellitus, 2 with prediabetes, 3 did not have diabetes; 1 patient with prediabetes did not have a mixed meal tolerance test at baseline.

†Wilcoxon signed rank test.

patients were weight stable (ie, lost within 0.3% to 3.7% of their starting weight).

The mean baseline HbA_{1c} of the diabetic population was 7.8%±2.4%, which was reduced to a mean of 5.9%±0.5% at the 12-month follow-up. This represents a mean change from baseline of −1.9% for the patients with diabetes in the study (Fig. 5). The mean baseline fasting glucose in the patients with diabetes was 177±93 mg/dL, which was reduced to a mean of 111±10 mg/dL at the 12-month follow-up (Fig. 6).

Mixed meal tolerance test results are available for 9 of 10 patients. For each analyte measured, the mean area under the curve was determined, and results between the baseline and the 2 follow-up time points were compared (Table 2). The results demonstrate significant reductions in postprandial insulin and glucose levels at 2 and 6 months, and a significant increase in PYY activity at 2 months.

Safety

Overall, the IMAS procedure was well tolerated. There were no unanticipated device-related adverse events. There was one procedural adverse event that met the definition of serious that was unrelated to the study device. The patient sustained inadvertent penetration of the gastric serosa during insertion of a trocar that was placed to facilitate introduction of a laparoscope. The serosal site was sutured, and the event was not associated with any additional adverse events. As shown in Table 3, procedure-related adverse events were primarily GI in

TABLE 3. Adverse events occurring in >10% of patients by system organ class/preferred term and severity system organ class/preferred term

	Mild, n (%)	Moderate, n (%)	Severe, n (%)
Gastrointestinal disorders			
Abdominal distension	3 (30)	0 (0)	0 (0)
Abdominal pain*	9 (90)	1 (10)	0 (0)
Constipation	1 (10)	1 (10)	0 (0)
Diarrhea	5 (50)	5 (50)	0 (0)
Nausea	10 (100)	0 (0)	0 (0)
Vomiting	2 (20)	0 (0)	0 (0)
Investigations			
Vitamin D decreased	2 (20)	0 (0)	0 (0)
Metabolism and nutrition disorders (total events)			
Iron deficiency	3 (30)	1 (10)	0 (0)
Magnesium deficiency	0 (0)	2 (20)	0 (0)
Vitamin B_{12} deficiency	1 (10)	3 (30)	0 (0)
Vitamin D deficiency†	1 (10)	1 (10)	0 (0)

*Pain at the trocar site coded as abdominal pain.
†All 10 patients were deficient in vitamin D at baseline.

nature, and early on they were likely related to the administration of general anesthesia. Trocar site pain (coded as abdominal pain) was also experienced in the early postoperative period by all patients but resolved without intervention. All patients experienced diarrhea after the procedure in the short term. Recurrent diarrhea occurred in 4 patients (40%), and this appeared to be largely related to diet composition. This resolved in all patients with nutritional counseling and dietary changes reducing the amount of simple carbohydrates being consumed, and with a short course of loperamide. All of the patients were deficient in micronutrients at baseline: 10 (100%) of the patients were vitamin D deficient, 3 (30%) had low iron levels, and 2 (20%) had deficiencies of vitamin B_{12} and magnesium. These events were improved at 12-month follow-up using standard oral supplementation. At 12 months, 2 of the 3 patients with iron deficiency, 3 of 10 with vitamin D deficiency, and 1 of 2 with vitamin B_{12} deficiency were still below normal values. At 12 months, magnesium deficiency was present in 2 of 10 patients (0.65 and 0.64 mmol/L), both of whom had subnormal values (<0.70 mmol/L) at baseline. Alanine aminotransferase measurements showed a reduction of 23% at 12 months over baseline values.

DISCUSSION

In this pilot study, we evaluated the technical feasibility, safety, and clinical outcomes of the IMAS when used to perform a PJD. The results provide positive evidence of the effectiveness of the IMAS in creating a durable intestinal diversion and for short- and longer-term safety, as well as evidence of clinical efficacy in patients with type 2 diabetes mellitus and prediabetes.

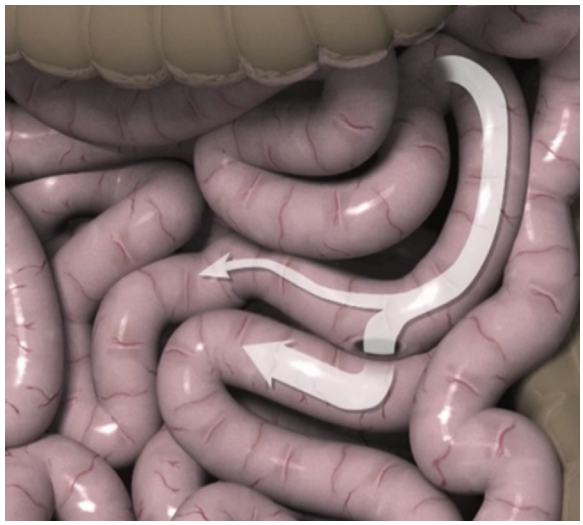

Figure 7. Because the native path remains open, this partial jejunal diversion is dissimilar to a jejuno-ileal bypass (ie, not a blind or defunctionalized segment of small intestine).

All patients who had the IMAS placed developed robust and durable side-to-side anastomoses, and all lost weight. The mean total weight loss for all patients was approximately 17.6 kg, representing a TWL of 14.6%. In addition, all patients with diabetes and prediabetes experienced significant reduction in HbA_{1c} and fasting blood glucose levels, approaching the normal range at 6 months, with further decline in HbA_{1c} at 12 months. Gut hormones, including PYY, GIP, and GLP-1, were also altered, suggesting a metabolic mechanism of action. Unlike a traditional jejunal-ileal bypass, the anatomy created by the IMAS is a PJD that preserves the native pathway for proper nutrient absorption and avoids a blind limb scenario (Fig. 7).

Melissas et al,[16] using a non-obese rat model, found that a simple side-to-side intestinal anastomosis that diverted food and biliopancreatic secretions to the distal small bowel normalized both fasting blood glucose levels and the results of an oral glucose tolerance test compared with results in sham-operated and control animals. Furthermore, Melissas et al[17] followed the clinical results in 6 patients, showing complete remission of diabetes in 3 patients up to 3 years after the procedure. Two other patients remained medication free after the operation, experiencing partial diabetes remission. TWL was 11.9% and the reduction in mean HbA1c was 2%. Fried et al[18] conducted a similar surgical PJD procedure in 15 patients with diabetes, showing a significant reduction in HbA_{1c} (−2.3%) and TWL of 10.3% at 12-month follow-up. Twelve of these 15 patients were on insulin at baseline, suggesting a broader range of patients with diabetes could benefit from these PJD procedures.

Overall, the nature and severity of the adverse events observed in this study were relatively mild and consistent with the altered anatomy. There were no unanticipated adverse events. Nutritional diarrhea in particular was expected,[19] and all 10 patients (100%) reported diarrhea after the procedure. This was self-limited in 6 patients and resolved after dietary management in the remaining 4. There was substantial variability in diet across the study population as a result of an intentional lack of a structured diet plan in the study protocol. The 4 patients with persistent diarrhea had a diet high in simple carbohydrates (bread, creams, and alcohol). The symptoms resolved upon diet correction. Minor postprocedure micronutrient deficiencies were common but reversible with basic supplementation, suggesting that the dual-path diversion was still supplying the entire GI tract with nutrients. Other adverse events that are commonly seen with traditional metabolic surgery were notably absent. There was no leak, hemorrhage, infection/abscess, ulceration, or anastomotic stenosis observed. Furthermore, no patient experienced dumping syndrome, likely because of preservation of the pylorus.[20]

Müeller-Stich et al[21] reported the results of a meta-analysis of 11 studies comparing surgical with medical treatment of type 2 diabetes in 706 patients who were not severely obese. The reviewers concluded that metabolic (bariatric) surgery is superior to medical treatment for short-term remission of type 2 diabetes and its comorbidities. Meek et al[22] recently reviewed the potential benefits of bariatric surgery and concluded that this modality is still the only approach that can induce rapid and sustained weight loss together with beneficial metabolic effects in type 2 diabetes, likely related to postoperative changes in gut hormone concentrations. Cătoi et al[23] reviewed some of the benefits of bariatric surgery and concluded that clinical improvement in glucose homeostasis and type 2 diabetes appears to occur independently from the magnitude of weight loss, which also suggests that other mechanisms are involved. Increased secretion of GLP-1, which results in the potentiation of nutrient-stimulated insulin release, is believed to play a major role.[24,25] Increased production of satiety-promoting hormones, decreased release of hunger-promoting hormones, and reduced food intake, as well as weight loss itself, all likely have implications in this process. In addition to anatomically restricted caloric intake, the beneficial effect of bariatric surgery on weight loss may be related to sustained increases in the satiety-promoting gut hormones such as GLP-1, GIP, and PYY as well as reductions in hunger-promoting factors such as ghrelin.

Limitations of our study include the relatively small number of patients enrolled, all of whom were recruited from a single center, and the fact that there is no control group.

In conclusion, this 1-year interim analysis supports the technical feasibility, safety, and effectiveness of the IMAS, which was demonstrated not only by successful creation of a durable intestinal anastomosis, but with progressive weight loss, without a highly restrictive diet, and improvement in HbA_{1c} and other markers of glycemic control. These interim results also suggest that an endoscopically created PJD may provide a beneficial effect on gut hormones, which appear to play a role in the pathophysiology of type 2 diabetes. Based on these interim results, the PJD created with the IMAS, delivered through a colonoscope, may prove to be a viable treatment option for obese patients with type 2 diabetes. Longer-term (3-year) results from the current study, and additional studies, will further clarify the potential utility of the IMAS in this clinical setting.

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