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RESEARCH

Partial Duodeno-Ileal Diversion with Magnetic Compression Anastomosis: A Novel Approach for the Treatment of Type 1 Diabetes-Associated Metabolic Derangements in a Porcine Model

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Abstract

Background Metabolic surgery has shown effectiveness in the management of some patients with type 2 diabetes (T2D). However, the evidence for metabolic surgery in type 1 diabetes (T1D) remains scarce. This pilot study aimed to evaluate the feasibility, safety, and metabolic impact of partial duodeno-ileal diversion (PDID) using a novel magnetic compression small bowel anastomosis (MCA) system in a T1D porcine model.

Methods Ten adult Yorkshire pigs were subjected to intravenous infusion of streptozotocin (STZ) to induce T1D. Diabetic pigs were randomized to either PDID via MCA or control with no operation. The proximal magnet was placed in the duodenum, and the distal magnet was inserted into the distal ileum about 40 cm proximal to the ileocecal valve through a small enterotomy, and magnetic coupling ensued. Procedural feasibility (MCA device coupling efficiency, anastomotic patency) and safety (e.g. burst pressure, device-related complications, survival) were evaluated. Postoperative changes including fasting plasma glucose (FPG), body weight, Homeostatic Model Assessment of Insulin Resistance [HOMA-IR]) were assessed periodically up to 6 weeks postoperatively. Histopathologic and immunohistochemical changes in the distal ileum and pancreas were also evaluated.

Results Five adult Yorkshire pigs underwent successful PDID via MCA, and 5 unoperated counterparts served as controls. One pig in each group died soon after induction, likely due to STZ toxicity. Anastomotic magnets were expelled per rectally within 14 days of PDID without any complications. In postoperative week 3, FPG normalized to a mean of 5.13 (±0.618) mmol/L in the PDID group and remained stable, whereas in the control group, mean FPG levels were persistently elevated at a mean of 30.28 (±3.168, $p<0.001$) mmol/L. The PDID group had a mean HOMA-IR value of 0.892 (±0.220), in contrast to the control group's mean of 6.056 (±0.803, $p<0.001$). Histopathological examinations showed satisfactory tissue healing at the anastomotic sites of all pigs in the PDID group, focal hyperplasia of beta cells in the pancreas of all pigs that underwent PDID, and increased immunostaining for synaptophysin, glucagon-like peptide-1 and proinsulin in the distal ileum and pancreatic tissues in the PDID group, as compared with the controls.

Conclusions PDID via MCA is safe and effective in optimization of glycemic control in this STZ-induced T1D porcine model. Further preclinical validation and evaluation of metabolic changes in response to this novel intervention in different large animal models of T1D is needed before clinical trials in humans.

Keywords Partial duodeno-ileal diversion · Type 1 diabetes · Magnetic compression small bowel anastomosis · Porcine model of diabetes · Metabolic intervention

Extended author information available on the last page of the article

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Introduction

Diabetes mellitus is one of the most important public health problems worldwide with 589 million adults living with diabetes in 2024 [1]. Among those, over 9.5 million individuals had T1D, including 1.9 million children and adolescents. T1D is an autoimmune disorder characterized by immune-mediated destruction of pancreatic beta cells, resulting in dependency on insulin injections.

Despite advancements in insulin therapies and monitoring technologies, optimal glycemic control remains challenging for many patients with diabetes mellitus. Bariatric surgery is a well-recognized treatment option for patients with both T2D and obesity; however, its use in patients with T1D is heavily debated [2, 3]. It was widely believed that the improvements in glycemic control after bariatric surgery were primarily due to weight loss, which created hesitation in considering bariatric or metabolic procedures for patients with T1D. However, recent studies have suggested that the remission and improvement of T2D following bariatric surgery may be influenced by factors independent of weight loss, notably changes in gastrointestinal hormones [4–6]. While evidences for bariatric surgery in T1D patients with obesity are limited,[2,5] two meta-analyses in T1D patients with obesity have shown significant reduction in daily insulin requirement in association with significant postoperative BMI reduction [3]. However, in terms of glycemic control, the decrease in average HbA1c levels observed in both meta-analysis studies were either only modest or statistically insignificant.

In addition to the widely recognized bariatric procedures such as RYGB and sleeve gastrectomy, which primarily focus on weight reduction, there are emerging surgical techniques that may produce similarly significant metabolic benefits through minimally invasive approaches. In particular, the duodenum has become a target for treating metabolic dysfunction via endoscopic or surgical procedures. Duodenal mucosal resurfacing, is an endoscopic procedure that has been shown to improve glycemic control and insulin resistance in people with T2D, irrespective of BMI changes [7]. Recent studies have reported the use of minimally invasive magnetic compression anastomosis (MCA) to achieve a controlled and partial proximal-to-distal small bowel diversion (jejuno-ileostomy bipartition, duodeno-ileostomy bipartition) [8–12].Partial duodeno-ileal diversion (PDID) is a novel technique that allows a portion of proximal intestinal contents including duodenal chyme, gastric acids, bile acids and pancreatic secretions to bypass most of the length of the small intestine while still enabling sufficient nutrient absorption in the diverted section. As a result, this diversion may utilize the essential mechanisms that contribute to the glucoregulatory and incretin benefits observed in conventional metabolic surgery. Furthermore, maintaining sufficient nutrient flow through the bypassed section of small bowel mitigates potential adverse effects such as malnutrition and bacterial overgrowth, that are commonly linked to more extensive gastrointestinal reconstructions in traditional metabolic surgery. Pioneering works from others have demonstrated that PDID resulted in significant weight loss and improved glycemic control in both human subjects [11, 12] and animal models [13–15]. This study aimed to assess the feasibility of establishing a PDID utilizing a novel MCA device in a streptozotocin induced T1D porcine model. The objectives of this study were two fold: first, to establish the feasibility and safety of the MCA device to create a functional PDID; second, to assess the metabolic impact of PDID in a porcine model of T1D diabetes.

Methods

Porcine Model of Induced Diabetes

Adult Yorkshire pigs were selected for the development of a T1D model due to their susceptibility to streptozotocin (STZ) manifesting in a phenotype that resembles human T1D, and the animals' anatomical and physiological similarities to humans. This porcine model was used for evaluating the effectiveness of PDID created by the novel MCA system, given that the device and procedure have been demonstrated to be safe and feasible in normal healthy pigs during a previous unpublished pilot study. To induce diabetes, STZ at 130 mg/kg was intravenously infused over 3–4 h for ablation of pancreatic β-cells, as reported previously [16, 17]. Prior to STZ administration, a normal diet was introduced, comprising 200 g of fructose daily, and this diet continued throughout the study period after the induction [18]. The criteria for successful establishment of the diabetic model included a fasting plasma glucose (FPG) level of > 7 mmol/L. A total of 10 pigs received STZ whilst an additional pig was chosen to be a normal control without administration of STZ. FPG levels in all pigs were measured one day before and after STZ induction. Two pigs died soon after STZ induction, likely due to STZ toxicity. FPG levels in the remaining nine pigs were monitored continuously for 3 days after STZ administration, and subsequently twice weekly for 6 weeks, and metabolic alterations were evaluated (Fig. 1).

Fig. 1 Representative figures of the control diabetic pigs without PDID (*left*) and diabetic pigs underwent PDID (*right*). Control diabetic pigs appeared emaciated and weak, with wasting and frailty. In contrast, diabetic pigs received PDID recovered well and appeared healthy

Magnetic Compression Anastomosis System

PDID is established using a novel MCA system that enables self-centering and self-aligning of the circular magnetic discs during the coupling process (Fig. 2). The device is composed of a pair of symmetrical circular magnetic discs with reciprocating convex and concave profiles and axial symmetry that ensures perfect self-centering and self-alignment for the formation of a robust small bowel anastomosis. Each magnetic disc features a rare-earth magnetic core (outer diameter is 19 mm, inner diameter is 9.6 mm, height of the center point to the horizontal plane is 6.6 mm) made of neodymium-iron-boron that is contained in a specially engineered polycarbonate shell. Each pair of symmetrical magnetic discs measure 22.2 mm in outer diameter. The reciprocating convex-concave profiles of the coupling surfaces creates a gradient of compressive forces. When brought into proximity, the magnetic discs will self-center and self-align for a perfect coupling, resulting in magnetic compression of the intervening small bowel walls with a gradient of compression forces that is maximal in the center and lessened towards the periphery. The main pressure (N50 strength) is applied on the inner side of the discs to induce ischemic necrosis of the intervening small bowel walls at the center, while the surrounding small bowel walls towards the periphery will experience less pressure to facilitate inflammation and tissue healing. This magnetic device forms a surface field of approximately 2100 Gauss (G), causing pressure necrosis and perforation irrespective of device geometry. For up to 7 days, the inner bowel walls at the central core will necrose, while the surrounding bowel wall at the outer circumference remodels and heals. Following successful establishment of the small bowel anastomosis, the paired magnets naturally detach from the fully matured anastomotic site and will pass through the gastrointestinal tract in the fecal stream.

Surgical Procedure

Four adult Yorkshire pigs with fully developed diabetes after STZ induction were randomly assigned to undergo PDID utilizing the MCA device. The remaining four diabetic pigs acted as controls. The PDID group of pigs were matched with the diabetic control group of pigs in terms of body weight and FPG before assignment, and other laboratory tests results were not known at the time of assignment to avoid selection bias (Table 1). Following induction of general anesthesia, a midline laparotomy was performed. The proximal magnet was positioned in the distal duodenum through a small enterotomy. The distal magnet was placed in the distal ileum again through a small enterotomy at around 40 cm proximal to the ileocecal valve. The enterotomies were then closed using interrupted absorbable sutures. The duodenum and the distal ileum were then approximated, allowing for magnetic coupling of the pair of magnetic discs. The abdomen was then irrigated, and the abdominal wall was closed in layers. Postoperatively, the animals were monitored closely following standard veterinary protocols.

Postprocedural Care and Assessment

Postoperatively, the animals were closely monitored and resumed on soft diet after a 12-hour recovery period. Diet was gradually increased based on tolerance of the animals. Consumption of food and fluids were meticulously monitored and recorded. Pain management was implemented with analgesics including oxymorphone at a dosage of

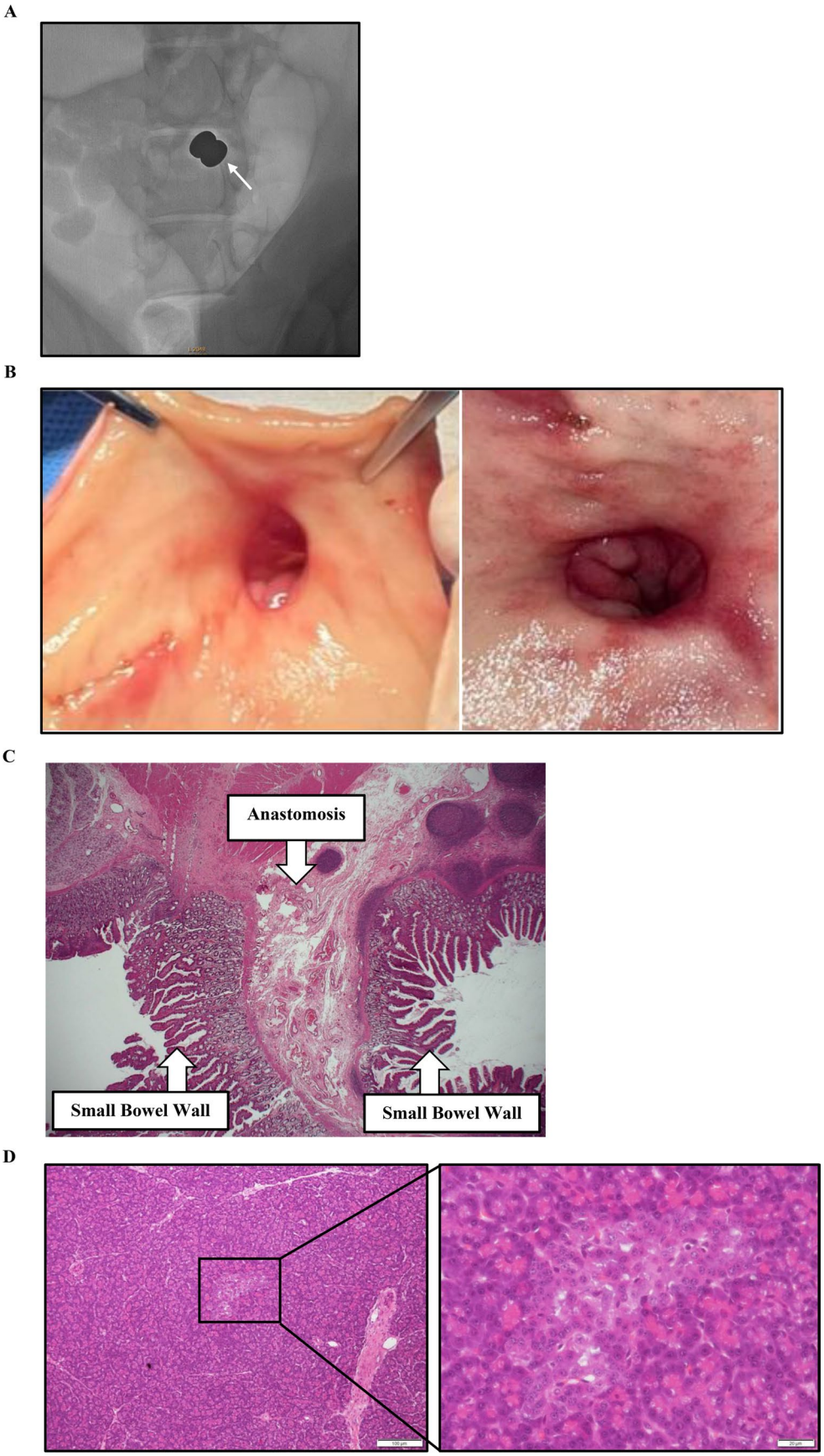

Fig. 2 (**A**) A representative roentgenogram showed precise coupling of both magnets. (**B**) Widely patent anastomosis at 6 weeks after surgery. Mucosal surfaces of all anastomoses exhibited signs of healthy healing with minimal scarring. (**C**) H&E staining of anastomotic site demonstrates remarkable tissue healing, exhibiting no signs of necrosis, fibrin, or neutrophil clusters, along with only minimal chronic inflammation. (**D**) H&E staining of pancreatic islet with focal hyperplasia and overall decreased concentration of islet cells. 100× (*left*) and 400× (*right*) magnification shown. Within the pancreatic parenchyma, the concentration and distribution of islets of Langerhans was decreased, while those present were hyperplastic

Table 1 Baseline demographics of the experimental animals

Characteristics	PDID Group	Diabetic Control Group	*p*-value
Yorkshire pig, *n*	4	4	-
Sex, % male	100%	100%	$p=1$
Median weight, kg (range)	49 (46–55.5.5)	45 (41.5–51.1)	$p=0.202$
Median FPG before STZ induction of diabetes, mmol/L (range)	4.3 (4.3–4.3)	4.75 (4.3–5.4)	$p=0.137$
Median FPG before PDID, mmol/L (range)	18.65 (7.7–31.4)	17.75 (10.2–25.3)	$p=0.823$

FPG fasting plasma glucose, *PDID* partial duodeno-ileal diversion, *STZ* streptozotocin

0.15 mg/kg, and buprenorphine at a dosage ranging from 0.01 to 0.03 mg/kg, both administered intramuscularly, in accordance with established veterinary protocols adopted at the animal research facility. This analgesic regimen was maintained for a minimum of three days following the surgical procedure. Abdominal X-ray was performed on all animals 5 days after surgery to assess and confirm successful placement of the device. To verify the expulsion of the paired magnetic discs, the cages and fecal matter were routinely inspected. Animals were euthanized after a survival period of six weeks, or sooner if complications necessitated euthanasia. Following this, a gross dissection was carried out, and specimens containing the small bowel anastomotic sites were subjected to histopathological examination and evaluation of burst pressure. Throughout the study animals were evaluated for signs of weight loss, malabsorption, and malnutrition, with formal assessments conducted twice weekly. This study was approved by the Animal Research Ethics Committee of the Guangdong Science and Technology Department, Guangdong Provincial Government, PRC, and the Chinese University of Hong Kong, Shenzhen, School of Medicine (License No.: SYXK 2023 − 0228).

Perioperative Blood Sampling and Metabolic Evaluations

Blood samples were collected from both the diabetic control and PDID groups prior to the surgical procedures and postoperatively twice weekly for six weeks. Plasma insulin concentrations were quantified using the Porcine Insulin ELISA Kit (Shanghai Enzyme-Linked Biotechnology Co., Ltd., China), while plasma glucose levels were measured using a glucose analyzer (Mindray Medical International Inc., China). HOMA-IR was calculated using the formula [fasting glucose (mmol/L) × fasting insulin (μU/mL)]/22.5. Tissue samples obtained from the pancreas and distal ileum at and beneath the anastomotic sites were collected and sent for histopathological examination and semi-quantitative immunohistochemical analysis for expression of proinsulin, glucagon like peptide 1 (GLP-1), and synaptophysin, an indicator of neuroendocrine differentiation.

Histopathological Analysis

Tissue samples from the pancreas and the small bowel anastomotic sites were collected at post-mortem examination and fixed in 10% neutral buffered formalin, then submitted to City University Veterinary Diagnostic Laboratory (CVDL, City University of Hong Kong) for histopathologic examination. After fixation, a board-certified veterinary pathologist examined all the samples macroscopically, and representative sections were cut into blocks for routine processing and embedding in paraffin wax. The 4-μm-thick sections were stained with hematoxylin and eosin (H&E).

Immunohistochemistry

For immunohistochemical analysis, selected paraffin sections of ileum, colon and pancreas were cut at 4μm and attached to charged slides (Leica BOND Plus Slides, Leica Microsystems Limited, Hong Kong). All sections were processed in the same manner that included peroxide blocking for 10 minutes, 3,3'-diaminobenzidine (DAB) and post antibody marking with bond polymer refined detection for 8 min, and antibody incubation for 15 min, before hematoxylin counter-staining for 5 min. For immunostaining of ileum samples, antigen retrieval was performed using Bond ER1 solution for 20 min at room temperature. Sections were then incubated with a primary polyclonal antibody against glucagon-like peptide 1 (GLP1) at a dilution of 1:200. Normal porcine gastrointestinal tract was used as positive control. Other antibodies used for immunostaining of ileum included mouse anti-pig synaptophysin polyclonal antibody at 1:200; (Dako, Tokyo, Japan) following antigen retrieval with Bond ER1 for 30 min; normal porcine adrenal medulla was used as positive control. For proinsulin staining of pancreas, a mouse polyclonal antibody at 1:300 (Dako,, minutes; normal porcine pancreas was used as positive control. For all tissue sections and analyses, the primary antibody substituted with the respective antibody diluent served as the negative control. All stained histopathology slides were reviewed by specialist veterinary pathologists. The tissue sections were examined under brightfield microscopy coupled to a digital image capture system (Olympus BX46, Hamamatsu Photonics K. K., Hamamatsu, Japan). The

images were processed using the Image-Pro Plus 6.0, Media Cybernetics, Rockville, Maryland USA. To determine the frequency of immunoreactive cells, photomicrographs of the slides were captured, and the cell count was conducted in 10 random unit areas (each unit measures 223 µm high and 300 µm wide = total area of 66900 μm^2 (0.0669mm^2 × 10 fields of this size = 0.669 mm^2) of the tissue samples.

Statistical Analysis

All quantitative data were evaluated for distribution. Descriptive statistics were generated to characterize the baseline distribution of the area under the curve (AUC) and other metabolic markers, presented as mean ± standard deviation (SD). Inferential statistical analysis was performed to compare the means of the diabetic control and PDID groups for each marker. The primary test was the independent samples t-test, chosen for its appropriateness in comparing two mutually exclusive, independent groups. Prior to analysis, the underlying assumptions of the t-test were formally tested. Normality of the data within each group was assessed via the Shapiro-Wilk test, and the assumption of homogeneity of variances was examined using Levene's test. If both assumptions were met, a standard t-test was reported. In cases where Levene's test indicated unequal variances ($p < 0.05$), Welch's t-test was utilized. For variables that violated the normality assumption, the non-parametric Mann-Whitney U test was applied as a robust alternative. All tests were two-tailed, and a p-value < 0.05 was established as the threshold for statistical significance. Beyond p-values, the magnitude of the difference between groups was quantified using Cohen's d as a measure of effect size. Effect sizes were interpreted using the established conventions: 0.2 (small), 0.5 (medium), and 0.8 (large). To translate statistical findings into clinical context, biological significance was evaluated by calculating the mean percentage reduction in AUC post-intervention. The biological significance analysis was carried out using mean AUC reduction and individual response analysis to show the clinical interpretation of metabolic impact.

Results

Procedure and Device Feasibility and Safety

Ten adult Yorkshire pigs were successfully induced to have diabetes using STZ intravenous infusion. The median time from STZ infusion to full establishment of diabetes was two days. Five pigs underwent PDID successfully using the novel MCA device, and 5 pigs matched in FPG and body weight were assigned as diabetic control. Pigs that underwent PDID appeared healthy and well after recovery, whereas control animals with diabetes appeared emaciated and weak, with wasting and frailty (Fig. 1). One pig each in the PDID and the diabetic control group subsequently died soon (within 12 h) after induction due to excessive STZ sensitivity. Postoperatively, all surviving animals resumed a normal oral diet. Abdominal X-ray indicated perfect coupling of the magnetic discs and accurate device placement in all 4 pigs in the PDID group (Fig. 2A). All magnets were expelled without any complications in all animals within 14 days after the procedure. Postoperative recovery was uneventful and without device-related complications including intestinal obstruction or anastomotic leak. Following euthanasia at 6 weeks, postmortem dissection was performed and the specimens containing the anastomotic site were obtained for histopathological examination and assessment of burst pressure. All anastomotic sites healed well and remained widely patent (Fig. 2B). Histological examination of the anastomotic sites showed good healing with no signs of inflammation or stricture. Burst pressure tests were performed on 3 anastomosis specimens. The average burst pressure for the magnetic small bowel anastomosis was 659.37 mmHg and no leakage was observed at all the anastomosis sites. H&E staining of the anastomotic sites revealed good tissue healing with no necrosis, fibrin or neutrophil aggregates, along with minimal chronic inflammation. (Fig. 2C) Histopathological analysis of pancreatic tissues in all the diabetic pigs (both control and PDID groups) displayed diffuse edema in the interlobular stroma, along with areas of scattered hemorrhage and a reduced concentration and distribution of the islets of Langerhans. However in the PDID group of pigs there were signs of significant islets cells focal hyperplasia and enlargement. (Fig. 2D).

Metabolic Trajectories and Outcomes: Analysis of HOMA-IR and Fasting Plasma Glucose

HOMA-IR and FPG levels were assessed at weeks 3 and 6 (Fig. 3). At pre-induction, baseline HOMA-IR values were 0.984 for the diabetic control and 1.251 for the PDID group, respectively ($p = 0.65$, NS). Following STZ induction of diabetes at Week 0, HOMA-IR increased in both groups to 2.228 for the diabetic control and 2.188 of PDID group, indicating an initial impairment in insulin action consistent with the T1DM state. Subsequently, the diabetic controls exhibited a significant and persistent marked increase in HOMA-IR, reaching 6.056 by Week 3 and 6.750 by Week 6, demonstrating the development of severe insulin resistance. In contrast, the PDID group showed a significant improvement in insulin sensitivity following the intervention, with HOMA-IR significantly reduced to 0.892 by Week 3 and further to 0.805 by Week 6, reaching values at or below their

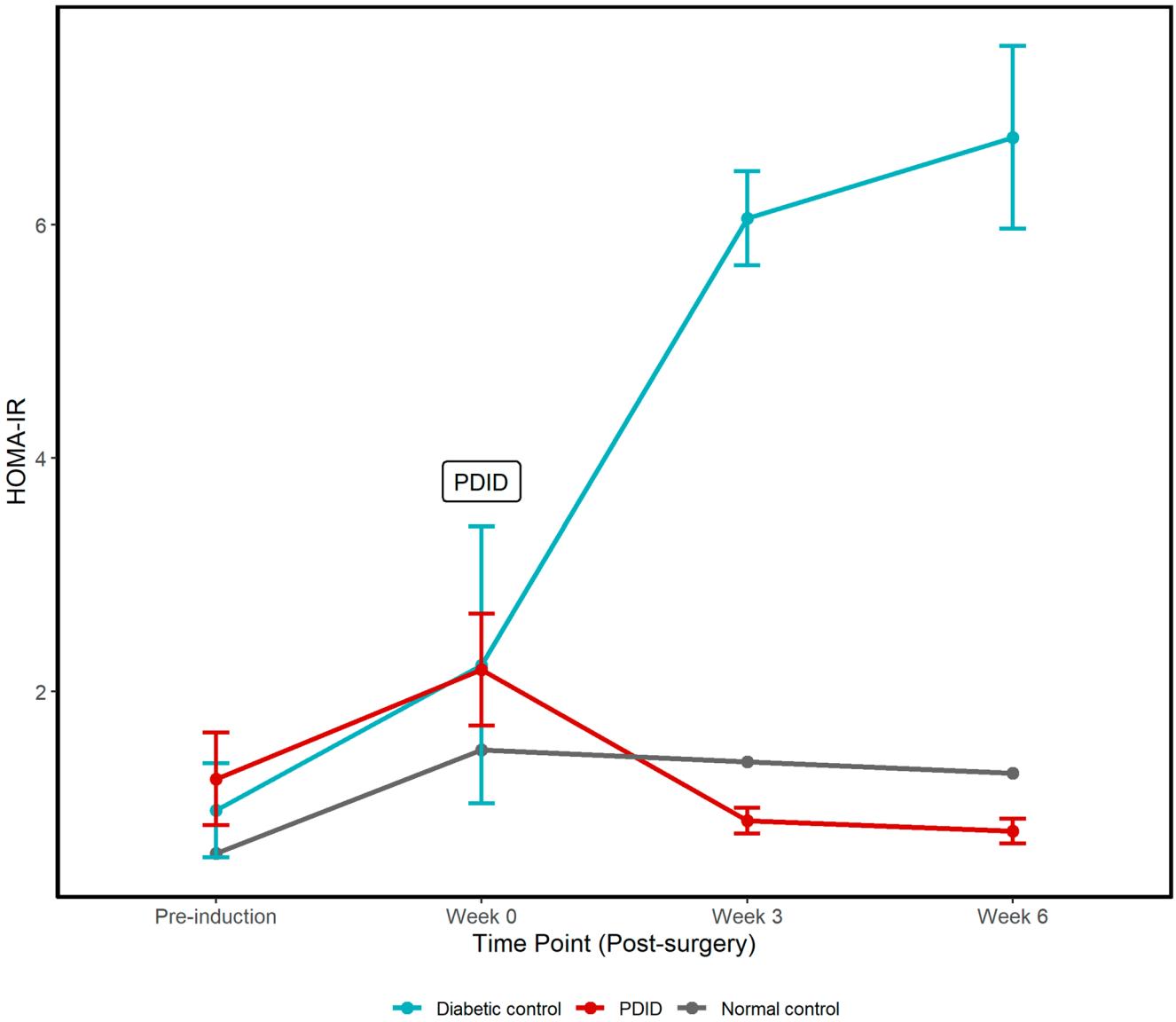

Fig. 3 Alterations in metabolic trajectory and outcomes assessed by HOMA-IR in the PDID and the control groups across 4 time points: Pre-induction, Week 0 (before surgery), Week 3 (after surgery), and Week 6 (after surgery)

pre-induction baseline. A significant reduction in FPG levels was seen in the PDID group, compared with the diabetic control group (Fig. 4).

Metabolic Trajectories and Outcomes: Analysis of Total Glucose Load

The glucose AUC was analyzed from baseline to the 6th week after surgery. Animals in the diabetic control group maintained elevated glycemic exposure (mean AUC = 940.54 ± 85.81 mmol/L·day), whereas the PDID treatment group exhibited a 65.3% reduction in mean AUC (326.11 ± 108.40 mmol/L·day; independent t-test: t (6) = 7.294, $p = 0.0003$, 95% CI = 364–864 mmol/L·day, Cohen's d = 5.65) (Fig. 5). This decrease indicated clinically relevant metabolic improvement, with all animals that underwent surgery exhibiting lower AUC values compared with the lowest diabetic control (surgery max: 472.5 mmol/L·day, diabetic control min: 872.2 mmol/L·day) (Fig. 5).

Immunohistochemical Evidence and Glucoregulatory Protein Expression

Immunohistochemical analysis of synaptophysin in distal ileum demonstrated an increase in the quantity of immunopositive cells from the PDID group, compared with the diabetic control (Fig. 6A). Positive immunostaining for synaptophysin in normal clusters were seen between the transverse and longitudinal smooth muscle layers

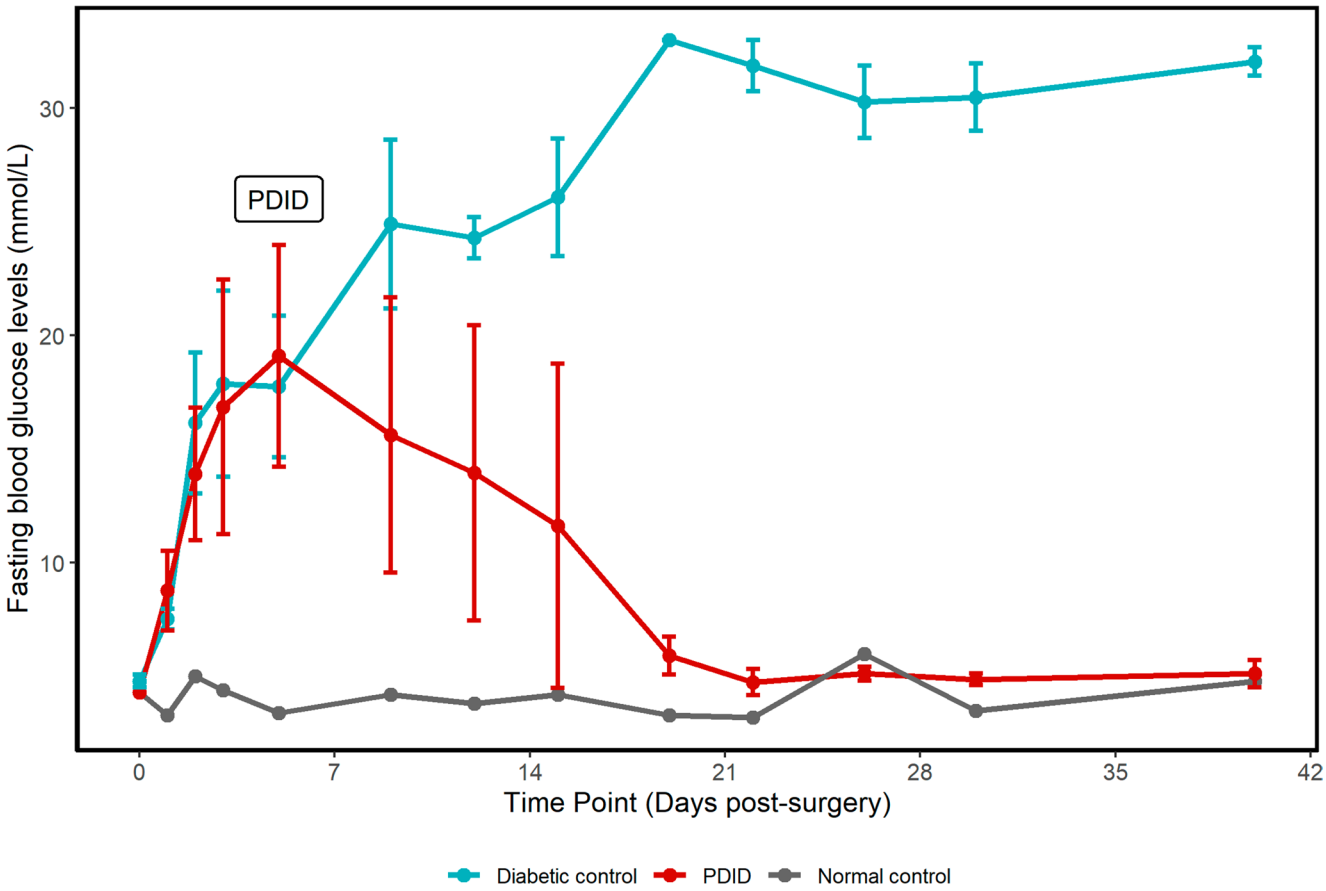

Fig. 4 Alterations in metabolic trajectory and outcomes assessed by fasting plasma glucose levels in the PDID and the diabetic control group

of the ileum. Quantitative analysis yielded a p-value of 0.067 for the difference in synaptophysin-positive cells between groups.

Expression of GLP-1 protein in mucosal epithelial cells of the distal ileum was notably more abundant in the PDID, whereas in the diabetic control group, expression was localized in the superficial enterocytes (Fig. 6B). Quantitative analysis indicated significantly greater number of GLP-1 positive cells in the PDID than the diabetic control group ($p = 0.048$).

Immunostaining for proinsulin indicated a greater abundance of proinsulin-expressing cells in the pancreatic tissue of the PDID than the diabetic control group (mean 101 ± 38 cells vs. 36 ± 16, $p = 0.02$) (Fig. 6C). Proinsulin-positive cells were 178% greater in numbers in the PDID group than in the diabetic control. Cohen's d of 2.20 (exceeding conventional large-effect threshold of 0.8), indicated a clinically substantial effect. All PDID animals exceeded maximum diabetic control values, and the lowest PDID count was 25% higher than highest diabetic control count.

Body Weight Analysis

During postoperative week 2, the PDID group exhibited a mean weight loss of 5.6 kg, similar to that of the normal control pig (5.5 kg). This was most probably related to the intermittent fasting in preparation for blood taking under anesthesia. In contrast, the diabetic control pigs (without PDID treated) had an average weight loss of 13.2 kg over the same period.

Discussion

Long-term insulin replacement therapy has been the cornerstone of glucose management in T1D. The lifelong dependence on exogenous insulin is fraught with challenges in achieving consistent glycemic control and is associated with a high incidence of various debilitating long-term complications [19]. Safe and effective alternative modes of intervention for T1D may potentially be life-changing and bring about beneficial metabolic effects beyond insulin replacement. Metabolic surgery has been shown to be effective in the management of patients with T2D, particularly when

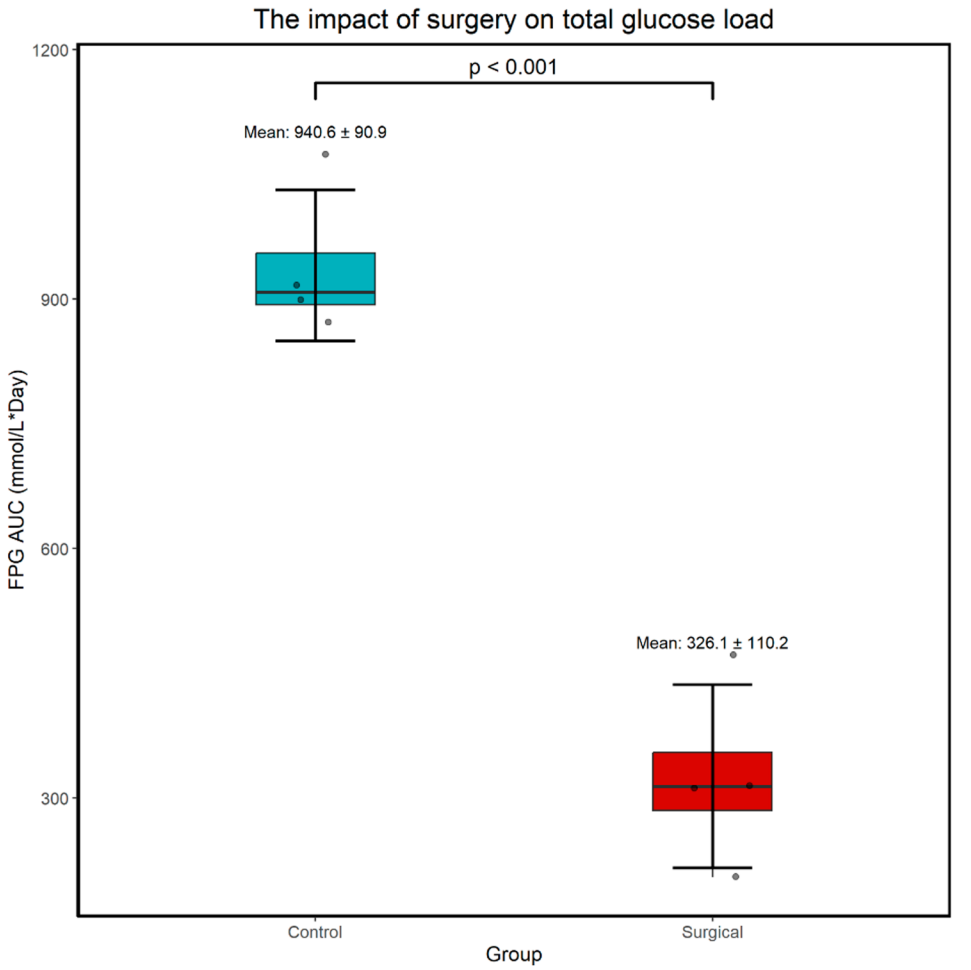

Fig. 5 Impact of PDID on total glucose load in porcine model of T1D. Superimposed individual data points comparing glucose AUC between diabetic control (*blue*) and PDID (*red*) groups ($n=4$ animals per group). Central line denotes median value. Mean ± standard deviation displayed above each group (diabetic control: 940.5 ± 85.8; PDID: 326.1 ± 108.4 mmol/L·day)

	1	2	3	4
Diabetic Control	915.6	1074.2	872.2	900.2
PDID	472.5	204.8	315.4	311.9

associated with morbid obesity. This intervention has multiple beneficial effects, including significant weight loss that contributes to obesity reduction, as well as improvements in systemic metabolism, reduction in insulin resistance, and alleviation of metabolic syndrome [20–22]. While metabolic surgery has been widely recognized and utilized as an effective therapy for T2D with morbid obesity, its application in the management of T1D remains largely investigational and published studies are extremely limited. Currently, metabolic surgery has not been considered a standard or established treatment for T1D because of the traditional understanding that T1D is characterized by absolute insulin deficiency presumably due to autoimmune destruction of pancreatic beta cells. This is not compatible with the prevailing understanding that the primary mechanisms of metabolic surgery targets at beta cell function preservation and reversal of insulin resistance, which are fundamental to T2D pathophysiology. As such, the role of metabolic surgery in the treatment of T1D remains uncertain, and much further research will be needed to document its safety, efficacy, and long-term treatment outcomes in this unique patient group.

A systematic review of the limited number of studies in obese T1D patients undergoing bariatric surgery showed a significant improvement in insulin dependency and marked reduction in HbA1c levels. In addition, there was a significant decrease in BMI following bariatric surgery [23–25]. It may be envisaged that when these obese T1D patients undergo bariatric surgery, the metabolic effects of the surgery procedure may entail not only simple reduction of adiposity but also improvement in glycemic control through other extra-pancreatic mechanisms (e.g. via GLP-1) that remains to be unraveled.

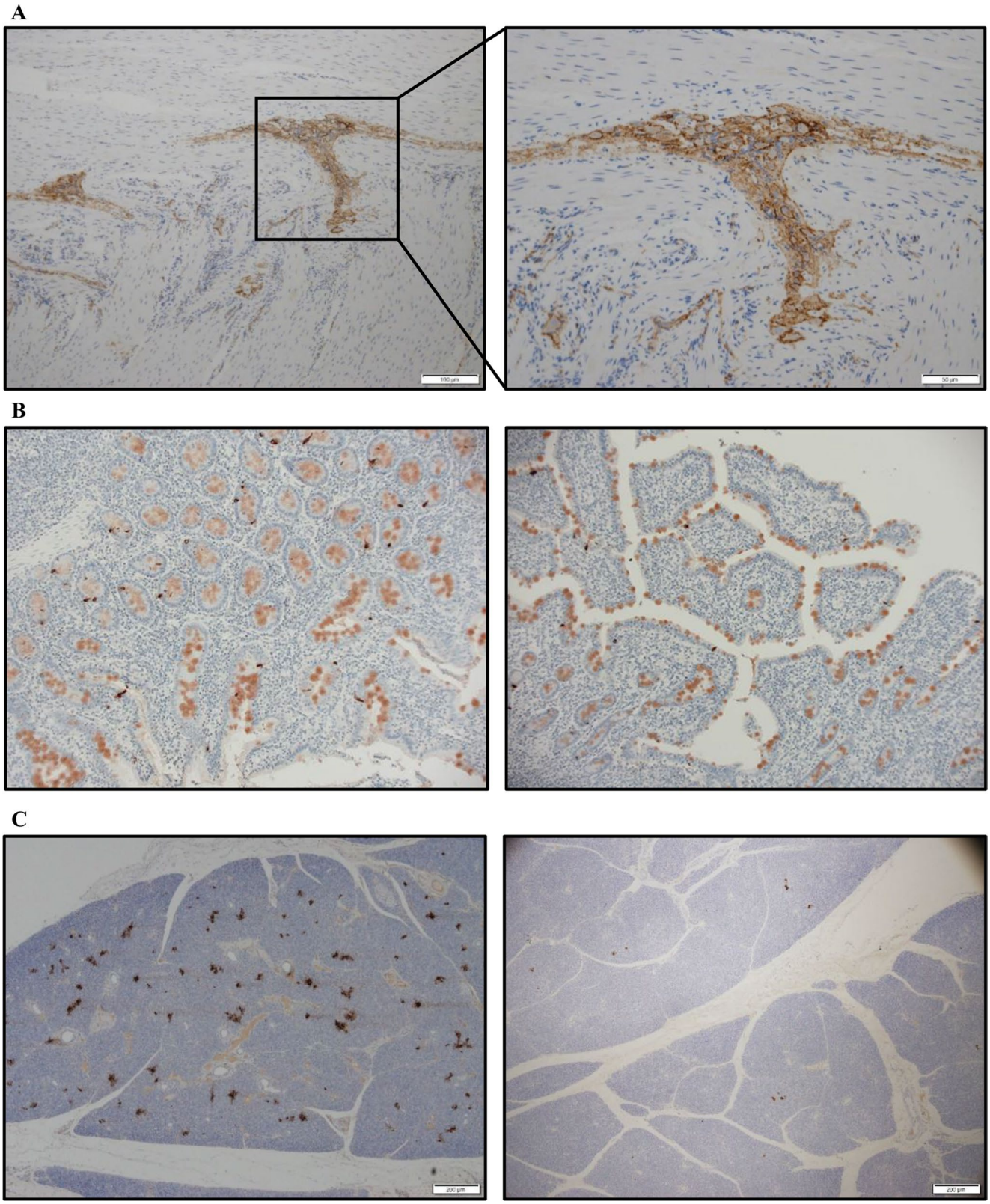

Fig. 6 Immunohistochemical analysis of (**A**) synaptophysin (brown) expression in distal ileum from the PDID group demonstrating neuroendocrine differentiation (100× (*left*) and 200× (*right*) magnification); (**B**) GLP-1 in distal ileum tissue from the PDID (*left*) and control (*right*) groups. 100× magnification shown; (**C**) proinsulin in pancreatic tissue from PDID (*left*) and the diabetic control group (*right*). 40× magnification shown

Conventional bariatric surgeries, such as Roux-en-Y gastric bypass and sleeve gastrectomy, primarily aim at achieving weight loss. In contrast, the innovative minimally invasive PDID using the magnetic compression anastomosis technique entails only a slight alteration of the GI tract with re-routing and early diversion of digestive juices including bile acids and pancreatic enzymes to the distal ileum. As only a small portion of the digestive juices and duodenal chyme are diverted, food digestion and nutrient absorption in the small intestine are largely maintained and unaffected. Ensuring adequate passage of nutrients through the whole length of the small intestine may alleviate side effects including malnutrition and bacterial overgrowth that are often associated with more extensive alteration of the gastrointestinal tract consequent to traditional metabolic surgery. Consequently, one may postulate that the improvement in glucose homeostasis and metabolic enhancements observed following this PDID probably leverages on more fundamental mechanisms that are distinct from weight reduction as seen in traditional metabolic surgeries. Possible weight-independent mechanisms may comprise re-routing of bile acids and digestive juices, vagal manipulation, modulation of secretion of enteric hormones and incretins, and changes in gut microbiomes [5, 26, 27].

The MCA system was designed to ensure that the resulting anastomosis is uniform in size. The compression force exerted between the paired magnets lead to gradual ischemic necrosis of the interposed small intestinal tissues, followed by the natural formation of a fistula. This controlled process minimizes trauma and allows mucosal healing under physiological pressure, greatly reducing the risk of anastomotic leakage. Furthermore, since the compression is circumferential and evenly distributed, the tissue interface is stable and well-apposed, eliminating the need for sutures or staples that can serve as niduses for infection or inflammation. Another distinct advantage of the magnetic compression anastomosis system is its ability to provide very precise and consistent control over the size of the small bowel anastomosis. This contrasts with open surgery where the size of the anastomosis can vary substantially depending on surgeon experience, tissue handling, and intraoperative conditions. This variability can lead to surgical complications such as anastomotic leakage or strictures, as well as metabolic complications including malabsorption, severe diarrhea and malnutrition. Results from this pilot study assessing the safety and efficacy of utilizing a magnetic compression device to establish PDID in a porcine model have been promising. Successful establishment of PDID starting with placement of the magnetic compression device, formation of the small bowel fistula, and timely detachment and expulsion of the magnets in all the studied animals without any complications have proven the procedure's safety and efficacy. As no device-related complications or anastomotic complications have been observed, our results further attested that the magnetic compression device is a safe approach for creating a PDID. In contrast to open surgical anastomoses which are subject to variability in surgical techniques and outcomes, magnetic compression anastomosis offers a high degree of reproducibility and predictability. The design of the magnetic device ensures that each anastomosis is performed with identical geometry, size, pressure, and tissue apposition, regardless of the surgeon or the operative setting. This leads to a much more predictable healing process and more consistent clinical outcomes.

Our study indicates that the magnetic compression PDID procedure may significantly impact the neuroendocrine cells found in the distal ileum. This finding is supported by the results of immunohistochemical staining of the distal ileum with synaptophysin. Enteroendocrine cells, among others, are essential for the regulation of gut hormones such as GLP-1 and peptide tyrosine tyrosine (PYY). Following the surgical intervention, the re-routing of digestive juices and bile acids together with the modified nutrient flow alters the stimulation of these cells, probably resulting in an increased secretion of these hormones that can affect appetite, glucose metabolism, and overall glucose homeostasis.

To our knowledge, this is the first study evaluating the impact of PDID in a porcine model with STZ-induced T1D. Compared with the diabetic control group, the surgical group with PDID exhibited a statistically significant increase in the number of GLP-1 positive cells. While the exact mechanism underlying the remarkable elevation in GLP-1 expression following PDID remains unclear, the notable normalization in fasting plasma glucose and HOMA-IR insulin resistance immediately following surgery suggests a major influence of the PDID procedure. In addition, there was a remarkable increase in synaptophysin positive cells in the distal ileum, as well as a significant increase in proinsulin positive cells in the pancreas following PDID. While the exact mechanisms for the increase expressions in GLP-1, proinsulin and synaptophysin requires much further studies for better elucidation, one may speculate that the increase in GLP-1 expression may potentially be linked to the activation of the intestinal enteroendocrine L cells that are located in the distal ileum as a result to early and direct exposure to a combination of nutrients, bile acids and digestive juices following the duodeno-ileal diversion. Our finding of enhanced immunohistochemical staining of synaptophysin in the distal ileum in the PDID group is supportive of this hypothesis. Enteroendocrine cells, among others, are essential for the regulation of gut hormones such as GLP-1 and PYY. The changes in luminal bile acid pool and composition could increase the activation of colonic Takeda G protein-coupled receptor 5 (TGR5), a bile acid

receptor expressed by intestinal enteroendocrine L cells, which led to endogenous GLP-1 secretion. Indeed, recent studies have shown that TGR5 plays an important role in energy homeostasis, blood glucose and lipid metabolism and is tightly linked with disorders such as steatotic liver disease, obesity and diabetes mellitus. TGR5 agonists have been shown to improve liver steatosis and insulin sensitivity [28], and promote stimulate energy consumption of brown adipose tissue and muscle [29]. This hypothesis is supported by the observation of increased immunostaining for GLP-1 in the distal ileum, and the enriched proinsulin stain in the pancreas of PDID group compared to the diabetes control group suggestive of GLP-1 downstream effects [30]. The lack of elevated plasma GLP-1 levels observed in this study could be attributed to the rapid degradation of GLP-1 by the enzyme dipeptidyl peptidase 4 (DPP-4), resulting in a very short half-life of 1–2 min in the circulation [31]. In addition, increase in GLP-1 expression may induce the proliferation and regeneration of pancreatic β-cells as evidenced by the focal hyperplasia of pancreatic islet cells, and potentially compensate for beta cell destruction in T1D. This may in turn lead to an increase in proinsulin levels in the surgical cohort, as demonstrated by the IHC staining in this current animal study, thereby improving glucose homeostasis by enhancing insulin secretion.

An increased GLP-1 response to food intake has been observed following RYGB surgery and other metabolic interventions, as evidenced by prior studies involving participants with and without T2D [32]. Furthermore, it has also been demonstrated that this augmented GLP-1 response appears shortly after the surgical procedure, persists for several months to years' post-surgery, and is predominantly independent of weight reduction [5, 23, 26–30, 32, 33]. Although the exact factors that initiate the increased release of GLP-1 remain unclear, to the best of our understanding, this is the first demonstration of enhanced GLP-1 expression following PDID procedures in a T1D model. The anatomical alterations and altered luminal contents as a result of PDID may potentially provide a sustained enteroendocrine signaling with increased endogenous release of GLP-1 and induction of beta cell plasticity and regeneration, increase in proinsulin and insulin secretion, and normalization in systemic insulin resistance thereby leading to improved glucose homeostasis.

Notwithstanding the significant findings from this study which may have important implications on our understanding of the pathophysiologic mechanisms and treatment options for T1D, as well as on the possible role of the distal ileum as an alternative control center for glucose homeostasis, the current study does have a number of limitations. Firstly, the sample size is limited. However, this study represents the first proof-of-principle demonstration of an innovative and alternative approach to the intervention of T1D metabolic derangements that could have profound clinical impact on disease management. We plan to apply the same methodology to a wider range of large pig models to deepen our understanding of the pathophysiologic mechanisms and safety in the future. Secondly, our early findings require validation by other researchers, while we collect additional data to further study the changes in gut hormones, circulatory physiology and biomarkers that change in response to the induction of diabetes mellitus and the PDID procedure. Additional studies will allow us to understand the therapeutic limits, safety and long-term side effect profile of PDID in T1D. Thirdly, as this is a porcine model for T1D, the translational potential and applicability to T2D require careful interpretation. Recent first-in-human studies utilizing similar magnetic compression techniques for side-to-side duodenoileal [11] and jejuno-ileal [12] diversion in patients with T2D have reported promising but variable metabolic outcomes. For instance, following duodenoileal partial diversion, 13% of patients discontinued diabetes medications while 46.7% reduced their dosage; conversely, jejuno-ileal partial diversion resulted in 83% of patients achieving HbA1c levels below 6.5% with substantial medication reduction or discontinuation. This contrasts with the uniform glycemic normalization observed in our current study. It must be acknowledged that the STZ-induced porcine model represents an acute, chemically induced injury which differs significantly from the chronic, multifactorial pathophysiology of human diabetes. Consequently, while the PDID procedure holds promise, clinical efficacy in humans may be more variable than that observed in this animal model, and more extensive research is needed to bridge this translational gap.

Conclusions

This preclinical investigation suggests that the use of a magnetic compression anastomosis device for PDID is both safe and effective. Further mechanistic research and in vivo safety and long-term analysis are needed to determine the impact of PDID with early diversion of nutrients and re-routing of bile acids and digestive juices and secretion of various gut hormones on glucose homeostasis, beta-cell regeneration and systemic insulin resistance.

Author Contributions Prof Chung Kwong Yeung acts as the principal investigator for the study, having developed the initial concept and study protocol design, led the review and editing of the manuscript, and performed the surgical procedures on animals. Prof Lung Yi Mak offered guidance on the study protocol and also reviewed and edited the manuscript. Yuzhang Wang played a role in data acquisition and the statistical analysis of the study data, as well as assisting in the execution of the experiments. Dr Biji Sreedhar contributed to the design

and implementation of the study, overseeing its overall direction and taking the lead in drafting the manuscript. Dr Fraser Ian Hill contributed to the formulation of the immunohistological study protocol and the analysis of tissue samples. Prof Hequn Zou provided essential feedback on the manuscript. Prof Howard Chan and Prof Hao Sun acted as co-investigators for the study, offering their insights on the manuscript. Prof Keith Lau and Prof Eric Fung were involved in finalizing the manuscript and offered guidance regarding the study's design. All authors contributed critical feedback that significantly influenced the research, analysis, and manuscript.

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Data Availability All data supporting the findings of this study are available within the paper.

Materials availability Yes

Declarations

Ethics approval and consent to participate This study was conducted in strict accordance with the Guiding Principles for the Review of Registration of Animal Test Studies for Medical Devices Part II: Test Design, Implementation Quality Assurance (released in September 2021). The application and use of laboratory animals for this pilot study has been consented and approved by the IACUC of this facility (IACUC Number: [removed for review]). Laboratory Animal Use License No.: [removed for review]. Issuing authority: [removed for review].

Consent for publication All authors have given their consent for publication.

Competing Interests Prof Chung Kwong Yeung holds the position of Adjunct Clinical Professor at the School of Medicine, Chinese University of Hong Kong, Shenzhen, and is the principal investigator of the study. He is also the founder of iIDEAS Group Holdings Limited, with stock options. Prof Lung Yi Mak holds the position of Clinical Assistant Professor in the Department of Medicine at the University of Hong Kong and has no conflicts to declare. Yuzhang Wang works at the School of Medicine, Chinese University of Hong Kong, Shenzhen, and has no conflicts to declare. Dr Biji Sreedhar is employed by iEMIS (HK) Limited and has no conflicts to declare. Dr Fraser Ian Hill is the Director of the Veterinary Diagnostic Laboratory at the City University of Hong Kong and has no conflicts to declare. Prof Hequn Zou is the Deputy Director of the CUHK-Shenzhen Medical Centre Planning Office at the School of Medicine, Chinese University of Hong Kong, Shenzhen, and has no conflicts of interest to declare. Prof Howard Chan is the Presidential Chair Professor at the School of Medicine, Chinese University of Hong Kong, Shenzhen, and has no conflicts of interest to declare. Prof Hao Sun is Presidential Chair Professor at the School of Medicine, Chinese University of Hong Kong, Shenzhen, with no conflicts of interest to declare. Prof Keith Lau is a Professor in the Division of Life Sciences at the Hong Kong University of Science and Technology and has no conflicts to declare. Prof Erik Fung is a Clinical Associate Professor in the Division of Life Sciences at the University of Hong Kong and has no conflicts to declare.

References

1. International Diabetes Federation. *IDF Diabetes Atlas, 11th Edn.* International Diabetes Federation; 2025.
2. Ashrafian H, Harling L, Toma T, et al. Type 1 diabetes mellitus and bariatric surgery: a systematic review and meta-analysis. OBES SURG. 2016;26(8):1697–704. https://doi.org/10.1007/s11695-015-1999-6.
3. Chow A, Switzer NJ, Dang J, et al. A systematic review and meta-analysis of outcomes for type 1 diabetes after bariatric surgery. J Obes. 2016;2016:1–7. https://doi.org/10.1155/2016/6170719.
4. Breen DM, Rasmussen BA, Kokorovic A, Wang R, Cheung GWC, Lam TKT. Jejunal nutrient sensing is required for duodenal-jejunal bypass surgery to rapidly lower glucose concentrations in uncontrolled diabetes. Nat Med. 2012;18(6):950–5. https://doi.org/10.1038/nm.2745.
5. Czupryniak L, Wiszniewski M, Szymański D, Pawłowski M, Loba J, Strzelczyk J. Long-term results of gastric bypass surgery in morbidly obese type 1 diabetes patients. OBES SURG. 2010;20(4):506–8. https://doi.org/10.1007/s11695-010-0074-6.
6. Hussain A, Mahmood H, El-Hasani S. Can Roux-en-Y gastric bypass provide a lifelong solution for diabetes mellitus? Can J Surg. 2009;52(6):E269–275.
7. van Baar ACG, Holleman F, Crenier L, et al. Endoscopic duodenal mucosal resurfacing for the treatment of type 2 diabetes mellitus: one year results from the first international, open-label, prospective, multicentre study. Gut. 2020;69(2):295–303. https://doi.org/10.1136/gutjnl-2019-318349.
8. Gagner M, Abuladze D, Koiava L, Buchwald JN, Van Sante N, Krinke T. First-in-human side-to-side magnetic compression duodeno-ileostomy with the magnet anastomosis system. Obes Surg. 2023;33(8):2282–92. https://doi.org/10.1007/s11695-023-06708-x.
9. Gagner M, Almutlaq L, Cadiere GB, et al. Side-to-side magnetic duodeno-ileostomy in adults with severe obesity with or without type 2 diabetes: early outcomes with prior or concurrent sleeve gastrectomy. Surg Obes Relat Dis. 2024;20(4):341–52. https://doi.org/10.1016/j.soard.2023.10.018.
10. Bhandari M, Neto MG, Brunaldi VO, et al. Immediately-Patent magnetic duodeno-ileal anastomosis (IMPA-DI): the First-in-Human study. Obes Surg. 2025;35(6):2053–8. https://doi.org/10.1007/s11695-025-07823-7.
11. Gagner M, Abuladze D, Buchwald J, Koiava L, Almutlaq L. First-in-Human side-to-side duodenoileal bipartition for weight loss and type 2 diabetes with the swallowable biofragmentable magnetic anastomosis system. J Am Coll Surg. 2025;241(2):146–59. https://doi.org/10.1097/XCS.0000000000001384.
12. Gagner M, Fried M, Michalsky D, et al. First-in-Human linear magnetic jejuno-ileal bipartition: preliminary results with incisionless, sutureless, swallowable technique. Obes Surg. 2025;35(6):2067–80. https://doi.org/10.1007/s11695-025-07861-1.
13. Gonzales KD, Douglas G, Pichakron KO, et al. Magnamosis III: delivery of a magnetic compression anastomosis device

using minimally invasive endoscopic techniques. J Pediatr Surg. 2012;47(6):1291–5. https://doi.org/10.1016/j.jpedsurg.2012.03.042.
14. Gagner M, Krinke T, Lapointe-Gagner M, Buchwald JN. Side-to-side duodeno-ileal magnetic compression anastomosis: design and feasibility of a novel device in a porcine model. Surg Endosc. 2023;37(8):6197–207. https://doi.org/10.1007/s00464-023-10105-x.
15. Olavarria OA, Chhabra KR, Levi ST, Wilson EB, Hutter MM. Small bowel magnetic compression anastomosis creation for bypass procedures in a porcine model. Surg Endosc. 2025;39(3):2155–63. https://doi.org/10.1007/s00464-025-11575-x.
16. Dufrane D, Van Steenberghe M, Guiot Y, Goebbels RM, Saliez A, Gianello P. Streptozotocin-Induced diabetes in large animals (Pigs/Primates): role of GLUT2 transporter and β-cell plasticity. Transplantation. 2006;81(1):36–45. https://doi.org/10.1097/01.tp.0000189712.74495.82.
17. Von Wilmowsky C, Stockmann P, Metzler P, Harsch IA, Amann K, Schlegel KA. Establishment of a streptozotocin-induced diabetic domestic pig model and a systematic evaluation of pathological changes in the hard and soft tissue over a 12-month period. Clin Oral Implants Res. 2010;21(7):709–17. https://doi.org/10.1111/j.1600-0501.2010.01914.x.
18. Barrière DA, Noll C, Roussy G, et al. Combination of high-fat/high-fructose diet and low-dose streptozotocin to model long-term type-2 diabetes complications. Sci Rep. 2018;8(1):424. https://doi.org/10.1038/s41598-017-18896-5.
19. Inzucchi SE. Diagnosis of diabetes. N Engl J Med. 2012;367(6):542–50. https://doi.org/10.1056/NEJMcp1103643.
20. Ashrafian H, Athanasiou T, Li JV, et al. Diabetes resolution and hyperinsulinaemia after metabolic Roux-en-Y gastric bypass. Obes Rev. 2011;12(5). https://doi.org/10.1111/j.1467-789X.2010.00802.x.
21. Ashrafian H, Darzi A, Athanasiou T. Autobionics: a new paradigm in regenerative medicine and surgery. Regen Med. 2010;5(2):279–88. https://doi.org/10.2217/rme.10.2.
22. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes — 3-year outcomes. N Engl J Med. 2014;370(21):2002–13. https://doi.org/10.1056/NEJMoa1401329.
23. Stier CK. Metabolic surgery in obese patients with type 1 diabetes mellitus. In: *Diabetes*. Vol 63. Amer Diabetes Assoc 1701 N Beauregard St, Alexandria, VA 22311 – 1717 USA; 2014:A513-A513.
24. Dorman R, Rasmus N, Serrot F et al. The role of bariatric surgery in the management of patients with type idiabetes. In: 2012:1321–2.
25. Esteves CM, Costa VA. E, others. Significant improvement in type 1 diabetes mellitus after gastric bypass surgery. Endocr Rev. 2013;34(3 Suppl. 1).
26. Li JV, Ashrafian H, Bueter M, et al. Metabolic surgery profoundly influences gut microbial-host metabolic cross-talk. Gut. 2011;60(9):1214–23. https://doi.org/10.1136/gut.2010.234708.
27. Spector D, Perry Z, Shikora S. Bariatric surgery improves glucose control in obese patients with type 1 diabetes. In: *Obes. Surg*. Vol 20. Springer 233 Spring St, New York, NY 10013 USA; 2010:979–979.
28. Ward DT, Yau SK, Mee AP, et al. Functional, molecular, and biochemical characterization of streptozotocin-induced diabetes. J Am Soc Nephrol. 2001;12(4):779–90. https://doi.org/10.1681/ASN.V124779.
29. Folli F. Lessons from animal diabetes VI. 75th anniversary of the insulin discovery: E. shafrir (ed.) Birkhäuser, Basel, 1996, pp 440. Acta Diabetol. 1996;33(4):276–276. https://doi.org/10.1007/BF00571564.
30. Arison RN, Ciaccio EI, Glitzer MS, Cassaro JA, Pruss MP. Light and electron microscopy of lesions in rats rendered diabetic with streptozotocin. Diabetes. 1967;16(1):51–6. https://doi.org/10.2337/diab.16.1.51.
31. Holst JJ. The physiology of glucagon-like peptide 1. Physiol Rev. 2007;87(4):1409–39. https://doi.org/10.1152/physrev.00034.2006.
32. Yang J, Zhang CZ, Wang JJ, Zhang J. Metabolic improvement effects of jejunoileal side-to-side anastomosis in patients with type 2 diabetes and the glucagon-like peptide-1 mechanism. World J Diabetes. 2025;16(4). https://doi.org/10.4239/wjd.v16.i4.103567.
33. Gäbel H, Bitter-Suermann H, Henriksson C, Säve-Söderbergh J, Lundholm K, Brynger H. Streptozotocin diabetes in juvenile pigs. Evaluation of an experimental model. Horm Metab Res. 1985;17(06):275–80. https://doi.org/10.1055/s-2007-1013518.

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