Compared to Sleeve Gastrectomy, Duodenal–Jejunal Bypass with Sleeve Gastrectomy Gives Better Glycemic Control in T2DM Patients, with a Lower β-Cell Response and Similar Appetite Sensations: Mixed-Meal Study

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ORIGINAL CONTRIBUTIONS

Compared to Sleeve Gastrectomy, Duodenal–Jejunal Bypass with Sleeve Gastrectomy Gives Better Glycemic Control in T2DM Patients, with a Lower β-Cell Response and Similar Appetite Sensations: Mixed-Meal Study

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Abstract
Background Functional studies of how duodenal–jejunal exclusion (DJE) brings a superior glycemic control when added to sleeve gastrectomy in duodenal–jejunal bypass with sleeve gastrectomy (DJB-SG) patients, are lacking. To study this, we compared the appetite sensations and the β-cell response following a standard mixed meal in patients with DJB-SG, versus those with sleeve gastrectomy (SG) alone.
Methods Twenty one patients who underwent DJB-SG and 25 with SG, who participated in mixed-meal tests (MMTT) preoperatively and at 1 year, with complete data were included and compared. Blood glucose, C-peptide, and insulin levels were estimated, along with the visual analogue scale (VAS) scoring of the six appetite sensations, as a part of the MMTT.
Results At 1 year following surgery, compared to SG group, DJB-SG group had greater complete remission rates (HbA1C <6.0 %) of 62 versus 32 % ($p < 0.05$), with similar total body weight loss (25.7 vs. 22 %). There were significantly lower post-prandial blood glucose and lower C-peptide levels during the MMTT in the patients with DJB-SG compared to SG group. There were no significant differences in the appetite sensations (mean VAS) scores between the groups.
Conclusion The addition of DJE component to SG, as in DJB-SG, was associated with higher diabetes remission rates, lower glycemic fluctuations, and lower C-peptide levels. This may point to a β-cell preserving glucose control which could result in longer remission of type 2 diabetes mellitus (T2DM). This effect also may be unrelated to food intake as there were no significant differences in the appetite sensations.

Keywords Sleeve gastrectomy · Metabolic surgery · Duodenal–jejunal bypass · β-cell response · Mixed-meal tolerance test

Introduction

Type 2 Diabetes is currently a serious global problem, growing at epidemic proportions [1]. Metabolic surgery is a new treatment modality and the ideal surgical procedure to treat type 2 diabetes mellitus (T2DM) is still evolving. Given the discoveries of increasing interplay of metabolic and endocrine functions of the gastrointestinal tract, it is now clear that changing the anatomy of stomach and small bowel exert far more complex effects on energy and glucose homeostasis than simple mechanical restriction, or malabsorption. Laparoscopic sleeve gastrectomy (SG) has now become a common bariatric procedure all over the world. Its acceptance is especially high in Asia, because of the concern of missing remnant gastric cancer in gastric bypass patients [2]; however, its efficacy in controlling T2DM is not as effective as gastric bypass procedures [3]. Laparoscopic duodenal–jejunal bypass with sleeve

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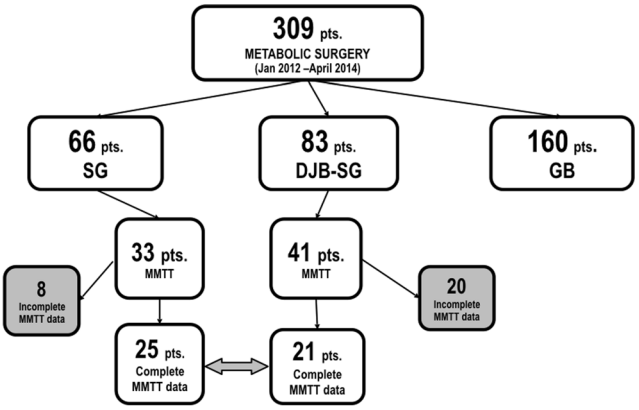
gastrectomy (DJB-SG) is a new metabolic procedure for the treatment of type 2 diabetes mellitus (T2DM) that doubles up the physio-anatomical objectives of a sleeve gastrectomy and a bypass (i.e., duodenal–jejunal exclusion (DJE), see Fig. 2a, b). It has the dual advantage of retaining the pylorus and also avoiding a gastric remnant, unlike gastric bypass procedures [4]. However, some have even questioned the advantage of adding duodenal exclusion to SG [5]. Our previous studies have shown that SG is not as effective in controlling T2DM as the procedures that have a duodenal–jejunal bypass [6]; but, it is still unclear how does the addition of a duodenal–jejunal exclusion to the SG alters the endocrine physiology and gut–brain axis, associated with this better glycemic control.

The aim of this study was to see the functional change of duodenal–jejunal exclusion (DJE) added to the sleeve gastrectomy by comparing the changes in appetite sensations (an indirect measure of caloric intake) and β-cell response (measuring the glucose, C-peptide, and insulin levels) during mixed-meal tolerance test in T2DM patients with duodenal–jejunal bypass with sleeve gastrectomy (DJB-SG) versus those with SG.

Patients and Methods

Patient Selection

This was a retrospective study of prospectively collected data from Diabetic Surgery Study (DSS) Center of the Department of Surgery, Min-Sheng General Hospital, Touyan, Taiwan. It included diabetic patients, clearly documented as poorly controlled T2DM by the endocrinologist after treatment for minimum 6 months, who were referred for metabolic surgery. We started diabetic surgery since 2007 by performing RYGB, SG, and SAGB (single anastomosis (mini) gastric bypass) and began doing DJB-SG since 2011. Between January 2012 and April 2014, a total of 309 patients received metabolic surgery for the treatment of T2DM. (Details of the patient numbers are given in the flow diagram, Fig. 1). These patients had individual counseling sessions by the bariatric nurse and the surgeon describing the nature, advantages, and complications of the two procedures, before they were allowed to finally make a decision regarding the procedure of their choice. Patients with history of previous bariatric surgery were excluded. The proposed study was approved by the human research review board at Min-Sheng General Hospital. The study was then explained to patients who accepted to participate, and appropriate written consents were taken from each before enlisting them. As some patients who could not complete the MMTT (with incomplete data) needed to be excluded, we had 25 patients in the SG group and 21 patients in the DJB-SG groups, respectively, included for the study (Fig. 1). Each patient's basic characteristics and lab work up including other metabolic parameters (Table 1) were recorded preoperatively, and after 1 year of follow-up. The HOMA-IR and HOMA-β were calculated with the fasting glucose and insulin levels using the formulas [7]:



Abbreviations: *SG* sleeve gastrectomy, *DJB-SG* duodenal-jejunal bypass with sleeve gastrectomy, *GB* gastric bypass, *pts.* patients, *MMTT* mixed meal tolerance test.

Fig. 1 Flowchart showing the summary of patients who underwent metabolic surgery between January 2012 and April 2014, with 1-year follow-up

$$\mathrm{HOMA-IR} = [\text{fasting glucose(mmol/L)} \times \text{fasting insulin(mIU/mL)}]/22.5$$
$$\mathrm{HOMA-\beta} = [20 \times \text{fasting insulin(mIU/ml)}]\ /[\text{fasting glucose(mmol/L)}-3.5]$$

Mixed-Meal Tolerance Test (MMTT)

Since diabetic patients have an altered entero-insular axis, the mixed-meal tolerance test (MMTT) was chosen to measure efficacy of the β-cell response in diabetic patients, as it is more physiological compared to OGTT [8, 9] and more reproducible, with lesser adverse effects, compared to other tests. The participants were subjected to mixed-meal tolerance tests (MMTT) preoperatively and 12 months postoperatively. Each participant, after an overnight fast and off anti-diabetic medications on that day, was given standardized mixed meal (Ensure Original, Abbott laboratories, Columbus, Ohio) to

Table 1 Table showing preoperative patient characteristics (mean values with SD) of both the groups with *p* values comparing the two

Variables	DJB-SG ($n=21$)	SG ($n=25$)	*p* value
Age	43.9 (11.2)	44.7(9.1)	0.225
Duration, years	5.8 (3.7)	5.7 (5.2)	0.982
BMI, kg/m^2	35.5 (4.5)	33.5 (4.9)	0.085
Total body weight, kg	95.2 (16.4)	91.5 (17.8)	0.501
Waist circumference, cm	107.6 (10.9)	104.9 (15.4)	0.501
HbA1C, %	9.4 (1.9)	9.3 (2.3)	0.803
C-peptide, ng/ml	3.1 (1.5)	3.8 (1.8)	0.181
Glucose, mg/dl	185.2 (66.1)	198.9 (87.3)	0.873
Blood pressure, mm, Hg			
Systolic	137.6 (12.9)	130.4 (12.8)	0.055
Diastolic	93.1(8.8)	83.8 (10.9)	0.002*
Lipids, mean:			
Total cholesterol, mg/dl	185.2 (66.1)	206.1 (52.7)	0.498
Triglycerides, mg/dl	223.9 (138.9)	244.7 (135.8)	0.902
HDL, mg/dl	45.8 (10.1)	41.3 (7.5)	0.146
LDL, mg/dl	119 (37.5)	132.0 (39.4)	0.374
Insulin, mIU/ml	17.1(14.5)	16.8 (13.4)	0.828
HOMA-IR	7.5(5.9)	8.0 (8.1)	0.844
HOMA-β	101.6 (158.7)	79.5 (77.1)	0.467
Concomitant medicines:			
OHA drug used—(kinds/per person)	1.7(0.6)	1.9(0.9)	0.347
Insulin usage, patients (%)	28.6 %	16 %	0.303

Values within parentheses indicate standard deviation

BMI body mass index, *HbA1C* glycosylated hemoglobin, *HDL* high density lipoproteins, *LDL* low density lipoproteins, *HOMA-IR* homeostasis model assessment - insulin resistance, *HOMA-β* homeostasis model assessment - beta cell function, *OHA* oral hypoglycemic agents

*p value < 0.05

drink in 15 min. Blood samples were drawn at −15, −1, 15, 30, 60, 90, and 120 min, for blood glucose (done by using Hexokinase/ G-6-PDH methodology by ARCHITECT *c* SYSTEMS assay, ABBOTT laboratories, Germany), C-peptide levels (estimated by Chemiflex technology, by ARCHITECT C-Peptide assay, ABBOTT laboratories, Germany), and insulin levels (estimated by Chemiflex technology, by ARCHITECT Insulin assay, ABBOTT laboratories, Germany). The samples were sent to the lab on the same day. Simultaneously, visual analogue scale (VAS) scoring for appetite sensations, were also done as discussed below.

VAS scores of appetite sensations were measured in this study as a tool, indicative of meal initiation and the amount eaten [10], as measuring food intake accurately in humans can be challenging in a clinical setting. These scores seem to correlate well with the gut hormone levels in the circulation [11] and also exhibit a good degree of within-subject reliability and validity [12]. The participants were familiarized with this, prior to the commencement of the study. Six variables of appetite sensations, namely, hunger, fullness, desire to eat, satiation, prospective consumption, and nausea were assessed using paper and pen 100-mm visual analogue scales [13]. We used forms that had 100-mm lines against each of the six variables. On each 100-mm line against the variable, participants were requested to make a measuring mark (from left to right) at a point that best matched how they felt at the time. Each score was determined by measuring the distance in millimeters from the end of the line to the indicated mark, with a digital caliper. The same was repeated with all six variables each time, i.e., at −15, −1, 15, 30, 60, 90, and 120 min after the intake of the mixed meal, and documented.

Surgical Techniques

Laparoscopic Single Anastomosis Duodenal–Jejunal Bypass with Sleeve Gastrectomy (DJB-SG) We performed a simplified DJB-SG procedure with one anastomosis (laparoscopically), and our technique was published previously [14]. The length of the afferent (biliopancreatic) limb bypassed was proximal one third of the small bowel, calculated after measuring the entire small bowel till the ileo-cecal valve (Fig. 2b).

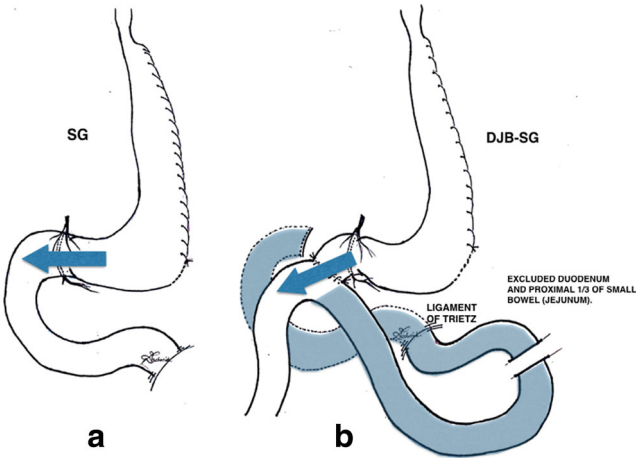


Fig. 2 Sketch showing the difference between laparoscopic sleeve gastrectomy (SG) (**a**) and single anastomosis duodenal–jejunal bypass with sleeve gastrectomy (DJB-SG) (**b**) with the exclusion of the C-loop of duodenum and upper one third of the small bowel (DJE)

Laparoscopic sleeve gastrectomy (SG) Our technique of laparoscopic SG was also described previously [15] (Fig. 2a).

Definition of Complete Remission of T2DM

A patient who had HbA1C of <6.0 % after metabolic surgery, without diabetic medication for 1 year, was defined to have complete remission of T2DM [16].

Statistical Analysis

Preoperative data (MMTT values) of the patients were pooled, as both groups were comparable (Table 1), and the postoperative data of the separate interventions were compared with each other. SPSS version 20.0 for Windows (SPSS Inc, Chicago, IL, USA) was used for all of the statistical analyses. The results for variables were expressed as the mean ± SD. The Student's *t* test and chi-square test were used to compare each variable between DJB-SG and SG groups. Values of $p < 0.05$ were considered statistically significant.

Results

The preoperative characteristics of both groups were comparable in age, sex, duration of diabetes, oral hypoglycemic agents taken, insulin dosage, weight, height, waist-hip ratio, and body weight. A total of 25 patients from the SG group and 21 from the DJB-SG group with complete pre and postoperative data, were included for comparison in this study (Fig. 1). Their mean preoperative BMI, HbA1c, and C-peptide levels were 34.5 kg/m^2, 9.4 %, and 3.5 ng/ml, respectively. All other metabolic parameters (except diastolic pressures) were also comparable (Table 1).

Weight Loss Indicators 1 Year After Surgery

There was weight loss in both the groups (Tables 1 and 2). The percentage of total body weight loss in DJB-SG and SG was 25.7 and 22 %, respectively. However, this difference was not statistically significant (Table 2). There were no differences in their final weights and waist circumferences between the groups (Fig. 3d).

Glycemic Control 1 Year After Surgery

Sixty-two percent (13) in DJB-SG group and 32 % (8) of SG patients, were off all anti-diabetic medications, maintaining a HbA1C of <6 %. DJB-SG group showed greater complete remission ($p < 0.05$) and lower mean HbA1C levels (Fig. 3c). Among those who did not have complete remission, no one in the DJB-SG group required insulin, compared to 4 % (1) in the SG group who needed it and all the rest in both groups had improvement in their glycemic control, with lesser need of anti-diabetic drugs (Fig. 3b, Table 2.)

Glycemic Parameters During Mixed-Meal Tolerance Tests (MMTT), 1 Year After Surgery

Post-Prandial Glucose Levels There was lowering of glucose levels in both groups compared to their preoperative levels. The DJB-SG group, however, had significantly lower premeal glucose levels (<0.05) and lower glycemic surges at 15 min ($p < 0.01$) following the intake of mixed meals, without biphasic pattern or hypoglycemia in both groups (Fig. 4a and Table 3.)

Post-Prandial C-Peptide and Insulin Levels The fasting C-peptide levels were lower than the corresponding preoperative mean, in both groups; however, there was significantly ($p < 0.05$) lower levels of C-peptide during MMTT at 15, 30, 60, 90, and 120 min, in the DJB-SG group compared to SG (Fig. 4b and Table 4.). The insulin levels were also lower (significant at 90 min.) in DJB-SG, compared to SG group (Fig. 4c and Table 3).

Change of Appetite Sensations (VAS) Scores—During MMTT 1 Year After Surgery

The mean preoperative VAS scores of appetite sensations in both groups were pooled. Their 12-month postoperative scores were tabulated separately under SG and DJB-SG groups, respectively. There were no significant differences

Table 2 Table showing 1-year postoperative primary and secondary outcomes (mean values and SD) of both the DJB-SG and SG groups and the *p* values comparing the two. (Δ values indicate the difference of the corresponding pre and postoperative values)

Variables	DJB-SG ($n=21$)	SG ($n=25$)	*p* value
Remission of diabetes, no. (%) (HbA1C < 6.0)	13 (61.9 %)	8 (32 %)	0.043*
BMI, kg/m^2	25.9 (3.3)	25.8 (3.1)	0.813
Δ BMI (kg/m^2)[a]	8.3 (3.6)	7.1 (3.2)	0.159
Total body weight, kg	70.8 (12.0)	70.8 (12.6)	0.722
Total body weight loss % (TWL %)	25.7 (6.8)	22.0 (7.0)	0.082
Waist circumference, cm	87.2 (11.3)	87.1 (8.7)	0.979
ΔWaist (cm)	21.3 (7.2)	16.9 (13.0)	0.119
HbA1C %	6.1 (0.8)	6.8 (1.5)	0.204
ΔHbA1C %	3.1 (1.8)	2.3 (2.1)	0.112
C-peptide ng/ml	1.7 (0.9)	1.8 (0.7)	0.232
ΔC-peptide (ng/ml)	1.7 (1.1)	1.9 (1.6)	0.633
Glucose, mg/dl	99.7 (22.1)	124.1 (48.7)	0.169
ΔGlucose (mg/dl)	77.0 (70.8)	70.6 (80.3)	0.742
Blood pressure, mm Hg			
Systolic	118.3 (23.9)	125.3 (12.8)	0.223
Diastolic	75.7 (15.7)	77.4 (11.9)	0.332
Lipids, mean (SD), mg/dl			
Total cholesterol, mg/dl	180.1 (26.6)	197.7 (58.0)	0.333
ΔTotal cholesterol (mg/dl)	16.4 (36.5)	6.4 (64.5)	0.467
Triglycerides, mg/dl	96.5 (42.4)	124.6 (57.2)	0.225
ΔTriglyceride (mg/dl)	169.4 (216.2)	131.2 (111.1)	0.401
HDL, mg/dl	50.9 (8.2)	47.3 (9.4)	0.243
LDL, mg/dl	108.6 (24.7)	127.7 (38.4)	0.084
ΔLDL (mg/dl)	3.5 (34.3)	0.3 (49.7)	0.777
Insulin, mIU/ml	6.3 (3.3)	4.9 (3.0)	0.130
HOMA-IR	1.7 (0.9)	2.0 (2.9)	0.356
Δ HOMA-IR	5.2 (5.4)	5.7 (7.7)	0.770
HOMA-β	114.9 (146.6) (range: 6.2–726.5)	71.3 (103.8) (range: 3.9–457.2)	0.194
Δ HOMA-β	−96.8(169.8) (range: −726.5 to −2.8)	−2.05 (116.8) (range: −191.6 to 430.9)	0.016*
Concomitant medicines			
Insulin usage, patients (%)	0 %	4 %	0.354
OHA drug used (kinds/per person)	0.2 (0.6)	0.5 (0.8)	0.113

Values within parentheses indicate standard deviation

BMI body mass index, *HbA1C* glycosylated hemoglobin, *HDL* high density lipoproteins, *LDL* low density lipoproteins, *HOMA-IR* homeostasis model assessment-insulin resistance, *HOMA*-β homeostasis model assessment - beta cell function, *OHA* oral hypoglycemic agents

*p value < 0.05(comparison between the two postoperative groups)

[a] Δ = Difference between the mean pre and postoperative values

in all six appetite sensations between SG and DJB-SG groups, 1 year after surgery (Fig. 5a–f and Table 3).

Discussion

This study confirms that DJE added to sleeve gastrectomy (DJB-SG) is a superior metabolic procedure and has a clear advantage over sleeve gastrectomy (SG) alone, both in its mechanism and the rates of remission of T2DM (62 vs. 32 %, $p < 0.05$).

A previous study from our center had already demonstrated that DJB-SG produced better glycemic control compared to SG [6]. Nevertheless, functional studies demonstrating how this additional control is accomplished were lacking in human subjects, although some did exist

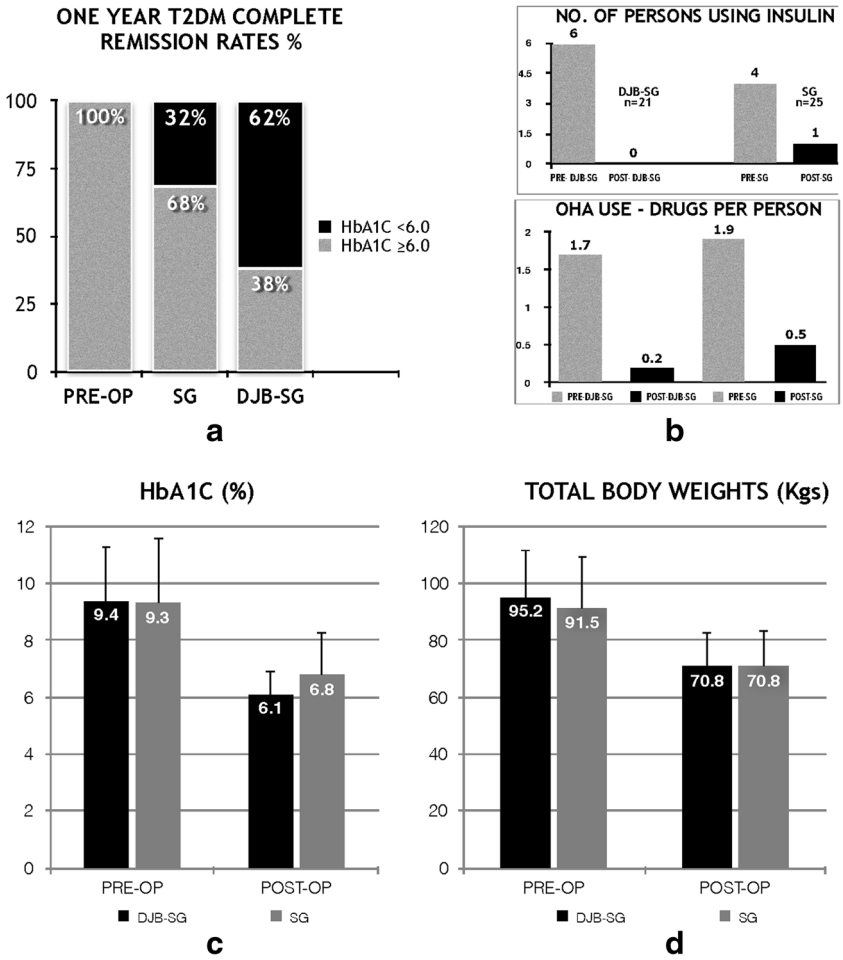


Fig. 3 Bar graphs showing remission rates (%) (**a**), anti-diabetic medications use (**b**), mean HbA1C (%) (**c**), and mean total body weight loss (kg) (**d**), of DJB-SG vs. SG groups, at 1 year after surgery, compared to their preoperative values (see Tables 1 and 2)

in rodent models [17, 18]. Sleeve gastrectomy (SG) by itself is reported to have glycemic control in patients, not only by caloric restriction, but by complex hormonal changes that followed. Some of the proposed pathways are: reduction of ghrelin levels [19], rise in GLP-1 and PYY levels secondary to rapid transit to distal bowel [20], and FXR signaling via bile acids and its effect on gut microbes [21]. On the other hand, duodenal–jejunal exclusion alone, is shown to directly ameliorate type 2 diabetes ('fore-gut' hypothesis), independent of effects on food intake, body weight, malabsorption, or nutrient delivery to the hind-gut [22–24]. Studies comparing duodenal–jejunal bypass (DJB alone) with SG (alone) in ZDF rat models, demonstrated that simple exclusion of duodenal–jejunal portion without gastric manipulation resulted in significantly lower glucose levels following OGTT, without weight loss. At the same time, in spite of the significant weight loss after SG, there was no substantial improvement of glucose tolerance [17].

In our study (DJB-SG vs. SG) both groups of patients had weight loss and improved glucose control. However, DJB-SG group had better remission rate. It seems that the additional effect on glucose homeostasis may also be due to a weight-independent mechanism, as there was no significant difference in their final weights between groups (Fig. 3d).

Better Remissions With DJE is Secondary to Lower Resting and Post-Prandial Glucose Levels Though the glucose levels lowered following both metabolic procedures; at MMTT, there were significantly lower resting glucose levels ($p < 0.05$) and 15-min post-prandial glycemic surge ($p < 0.01$) in the DJB-SG group compared to SG (Fig. 4a). This could explain the cause of lower HbA1C and better remission rates in the DJB-SG group [25]. Moreover, as studies show that prevention of these post-prandial fluctuations of glucose also caused lesser endothelial damage in T2DM patients [26, 27], DJB-SG patients are likely to have this long-term potential clinical benefit on the progressive vascular complications of the disease. However, we need to confirm this in long-term follow-up studies.

Lower β-Cell Response Secondary to DJE β-cells of pancreas respond to glucose challenge by producing insulin and equimolar portions of C-peptide. Lower C-peptide levels seen following mixed meal, in DJB-SG group, compared to that of SG ($p = <0.05$) at 15, 30, 60, 90, and 120 min (Fig. 4b) reflects

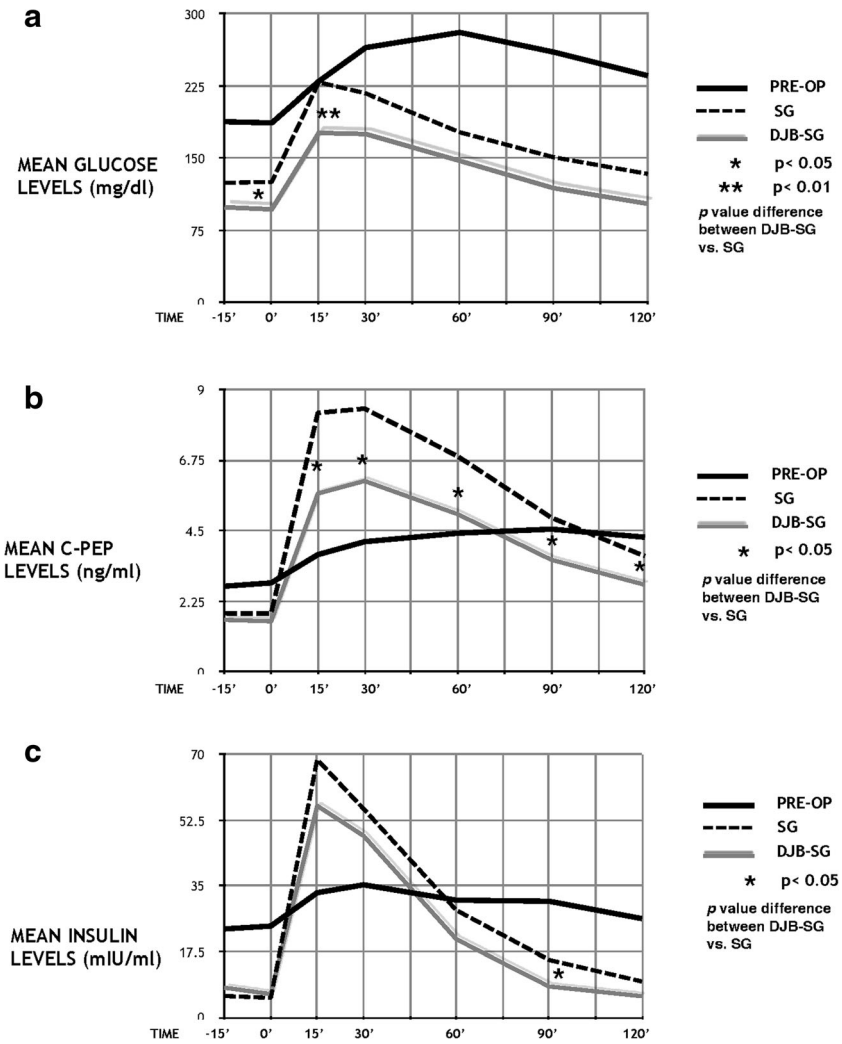


Fig. 4 Mixed-meal tolerance test: graphs showing the mean blood glucose (**a**), C-peptide (**b**), and insulin **(c)** levels, of DJB-SG versus SG groups at 1 year after surgery compared to their preoperative values (see also Table 3)

Table 3 Table showing the preoperative (pooled) and 1-year postoperative mean values of the blood glucose, C-peptide, and insulin levels of both the DJB-SG and SG groups, with the *p* values comparing the latter two

	Time	−15 min	0 min	15 min	30 min	60 min	90 min	120 min
Mean glucose mg/dl								
Preoperative (pooled)		188.3	187.0	230.1	265.2	281.0	260.5	236.0
	SG	124.6	125.5	229.1	217.6	177.3	151.2	133.9
	DJB-SG	99.0	96.9	176.6	175.4	147.5	119.0	102.7
DJB-SG vs. SG	*p* value	0.070	*0.037	*0.006	0.091	0.445	0.591	0.499
Mean C-peptide ng/ml								
Preoperative (pooled)		2.73	2.83	3.74	4.15	4.42	4.55	4.29
	SG	1.87	1.86	8.24	8.38	6.87	4.92	3.69
	DJB-SG	1.67	1.62	5.68	6.08	5.02	3.57	2.77
DJB-SG vs. SG	*p* value	0.070	0.051	*0.021	*0.028	*0.044	*0.015	*0.038
Mean insulin μIU/ml								
Preoperative (pooled)		23.52	24.30	33.17	35.28	31.19	30.90	26.28
	SG	5.76	5.26	68.54	55.55	28.52	15.34	9.63
	DJBSG	7.97	6.27	56.33	48.34	20.79	8.29	5.70
DJB-SG vs. SG	*p* value	0.165	0.440	0.376	0.709	0.504	*0.042	0.187

*p value < 0.05

Table 4 Table showing the preoperative (pooled) and 1 year postoperative mean values of the VAS scores of six appetite sensations of both the DJB-SG and SG groups, with the *p* values comparing the latter two

Hunger rating							
Pooled preoperative mean	4.3	3.4	1.9	1.9	2.4	2.9	3.8
SG mean	3.6	2.4	1.5	2.1	2.4	2.9	3.2
DJB-SG mean	3.0	3.0	1.7	1.8	1.7	2.6	3.1
DJB-SG vs. SG *p* value	0.502	0.146	0.417	0.632	0.349	0.385	0.356
Time	−15′	0′	15′	30′	60′	90′	120′
Fullness rating							
Pooled preoperative mean	1.0	1.0	1.7	1.5	1.2	1.1	1.0
SG mean	0.5	0.5	2.1	2.1	1.6	1.0	1.0
DJB-SG mean	0.3	0.3	1.5	1.7	1.3	0.9	0.6
DJB-SG vs. SG *p* value	0.246	0.223	0.523	0.377	0.450	0.233	0.256
Time	−15′	0′	15′	30′	60′	90′	120′
Desire to eat rating							
Pooled preoperative mean	3.8	3.8	2.5	2.8	3.1	3.5	4.5
SG mean	2.9	2.9	1.1	1.1	1.8	2.5	3.2
DJB-SG mean	3.1	3.8	1.6	1.6	1.7	2.5	3.2
DJB-SG vs. SG *p* value	0.451	0.265	0.916	0.364	0.359	0.468	0.807
Time	−15′	0′	15′	30′	60′	90′	120′
Satiation rating							
Pooled preoperative mean	1.5	1.5	3.7	3.5	3.0	2.4	2.0
SG mean	1.3	1.2	4.1	3.7	2.9	2.2	2.0
DJB-SG mean	1.3	1.3	4.6	4.5	4.0	3.4	2.7
DJB-SG vs. SG *p* value	0.849	0.911	0.360	0.755	0.721	0.579	0.808
Time	−15′	0′	15′	30′	60′	90′	120′
Prospective consumption rating							
Pooled preoperative mean	5.0	5.1	3.6	4.2	3.8	4.1	4.7
SG mean	3.6	3.6	2.2	2.4	2.5	3.0	3.5
DJB-SG mean	3.6	3.6	2.0	2.0	2.2	3.1	3.7
DJB-SG vs. SG *p* value	0.270	0.339	0.322	0.623	0.705	0.664	0.824
Time	−15′	0′	15′	30′	60′	90′	120′
Nausea rating							
Pooled preoperative mean	0.5	0.5	0.7	0.6	0.5	0.3	0.3
SG mean	0.3	0.3	3.3	3.2	2.4	1.2	0.9
DJB-SG mean	0.3	0.3	2.2	2.2	1.5	0.7	0.4
DJB-SG vs. SG *p* value	0.971	0.972	0.972	0.972	0.463	0.759	0.463
Time	−15′	0′	15′	30′	60′	90′	120′

lesser stimulation of β-cells to secrete insulin. Interestingly, as we see better glucose control in spite of lower C-peptide levels, there seems to be a β-cell independent glycemic control with duodenal–jejunal exclusion even in human subjects. Estimation of HOMA-β also showed significantly higher values ($p < 0.05$) in DJB-SG group 1 year after surgery, (Table 2) indicating better β-cell function compared to SG. This intriguing finding is also consistent with the studies in rodent models and needs further investigation.

Several studies in rodent models also indicate that DJB has an alternate (β-cell preserving) mechanism of glucose control. Some mechanisms proposed include: insulin-independent glucose control through jejunal nutrient sensing [28], proliferation of entero-endocrinal cells due to rise in bile acid levels [29, 30] and improved hepatic insulin sensitivity [31]. PET scan studies also confirm an increase in the β-cell mass following DJB than in sleeve gastrectomy [32]. If T2DM is known to worsen due to continuous apoptosis of stimulated β-cells [33, 34], this β-cell preserving, glycemic control mechanism seen in DJB-SG should theoretically result in longer remission rates in T2DM patients. A long-term follow-up of these patients is necessary, before we confirm this in a clinical setting.

Better Remission Rates not due to Differences in the Appetite Sensations Another important finding in our study was that there were no significant differences of appetite sensations between groups at 12 months following the surgery,

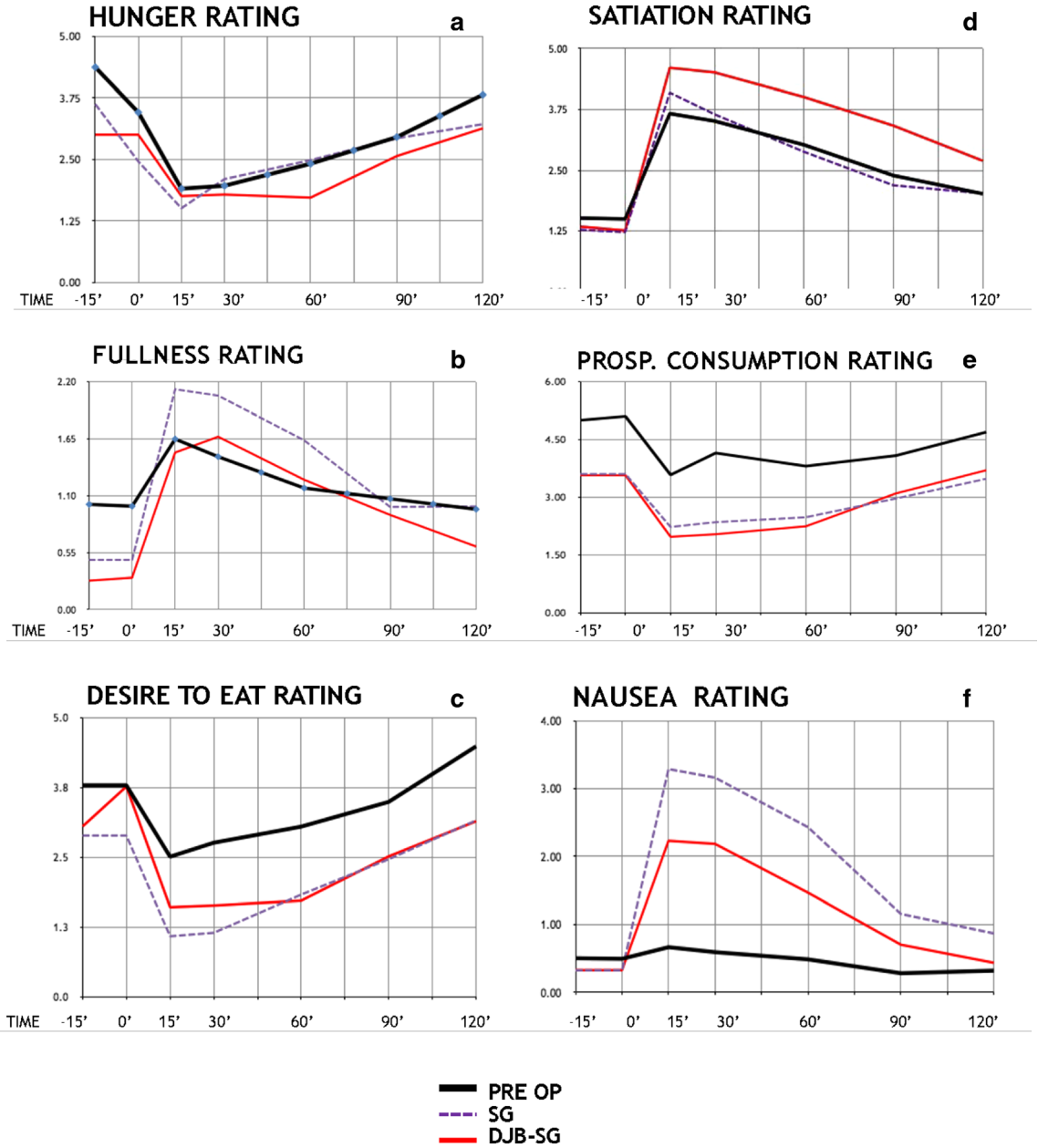


Fig. 5 Graphs showing mean Visual Analogue Scale (VAS) scores of the six appetite sensations (**a**–**f**) during mixed-meal tolerance tests (MMTT) (see Table 4)

indirectly indicative of similar food intake because of the similar gastric (sleeve) restrictive mechanism [17], in both groups (Fig. 4a–f). Though we have not estimated gut hormones in this study, our premise was that these hormonal changes needed to have their final impact on the food intake anyway through appetite sensations [11, 35]. As there was no difference in the same between both groups, it implies that this greater glycemic control in DJB-SG was independent of changes in appetite.

Limitations of this study include small sample size due to exclusion of patients who had any incomplete data of MMTT. A randomized study with a long-term follow-up could have strengthened this evidence further. The ongoing anti-diabetic treatment in patients, unavoidable in a clinical setting, might have influenced glycemic parameters of both groups in the study. Simultaneous estimation of gut hormones could have given additional dimensions to the study.

Conclusion

Addition of DJE to SG, as in DJB-SG patients, gave better remission, lesser post-prandial hyperglycemia, and lower C-peptide levels while improving HOMA-β values at 1 year

follow-up; but produced no difference in appetite sensations following MMTT, compared to SG patients. This may result in positive clinical benefits due to lesser glycemic fluctuations, and longer T2DM remission rates due to β-cell preservation. Randomized clinical trials with longer follow-up and simultaneous gut hormone assessment may further clarify the advantage and role of duodenal–jejunal exclusion in the glycemic control of DJB-SG patients, compared to those with SG.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Ethical Standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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