OBES SURG (2015) 25:2018–2022
DOI 10.1007/s11695-015-1671-1

ORIGINAL CONTRIBUTIONS

Metabolic Outcomes of Laparoscopic Diverted Sleeve Gastrectomy with Ileal Transposition (DSIT) in Obese Type 2 Diabetic Patients

Alper Celik[1,2] · Surendra Ugale[3] · Hasan Ofluoglu[1] · Erol Vural[1] · Eylem Cagiltay[4] · Huseyin Cat[5] · Muharrem Asci[1] · Bahri Onur Celik[1]

Published online: 19 April 2015

Abstract

Background Bariatric surgical techniques are based on mechanical restriction rather than functional restriction. Our purpose is to analyze the outcomes of diverted sleeve gastrectomy with ileal transposition (DSIT) as a mode of functional restrictive therapeutic option for class II and class III obese type 2 diabetes mellitus patients.

Methods A retrospective analysis was performed on data derived from 159 patients with type 2 diabetes mellitus who underwent DSIT between October 2011 and January 2014. Postoperative changes in body mass index (BMI), HbA1c, cholesterol indexes, and triglycerides, as well as complications and mortality rates, were noted and analyzed.

Results The study group consisted of 88 females and 73 males, with a mean age of 51.8 years. Mean duration of hospital stay was 6.4 (range, 4 to 42) days; mean follow-up was 18.3 months, and no mortality was detected. Mean BMI decreased from 39.33 to 25.51 kg/m^2 (excess BMI loss rate was 75.4 %, $p<0.001$). Mean fasting glucose level decreased from 189.8 to 123.5 mg/dl ($p<0.001$), and mean postprandial glucose level decreased from 246.1 to 179.4 mg/dl ($p<0.01$). Mean HbA1c decreased from 9.24 to 6.14 % 1 year after surgery ($p<0.001$). Overall, 88.68 % of patients were off antidiabetic medications at the end of 1 year. Hypertension was diagnosed in 121 of 161 patients preoperatively and resolved in 114 cases (94.2 %, $p<0.001$). Triglycerides decreased from a mean of 210.07 to 125.24 mg/dl, and cholesterol decreased from a mean of 208.34 to 163.23 mg/dl ($p<0.001$ for each).

Conclusion Our results demonstrate that DSIT provided effective remission rates in all components of metabolic syndrome in obese type 2 diabetic patients with acceptable complication and mortality rates.

Keywords Obesity · Diabetes mellitus · Metabolic syndrome · Treatment · Surgery · Laparoscopic diverted sleeve gastrectomy with ileal transposition

Introduction

Obesity and type 2 diabetes mellitus (T2DM) are increasing worldwide [1], and medical treatment fails to provide adequate control in a significant number of obese diabetics [2–4]. Bariatric surgery seems to be the most effective treatment for T2DM in obese patients [5, 6]. On the other hand, surgical treatment has also been associated with reduced rates of cardiovascular events [7] and mortality [8, 9]. Studies investigating the metabolic outcomes of surgical treatment have yielded that adjustable gastric banding [10, 11], gastric bypass [12, 13], biliopancreatic diversion [14–17], and ileal transposition [18] enhance both insulin action and ß-cell function more effectively than the conventional medical therapy [19, 20]. However, all bariatric operations are not identical in terms of indications, pros, and cons. The prototype gastric restrictive

✉ Alper Celik
doktoralper@hotmail.com

1 Department of General Surgery, Taksim German Hospital Metabolic Surgery Clinic, Istanbul, Turkey

2 Department of General Surgery, Yeniyuzyil University Faculty of Medicine, Istanbul, Turkey

3 Bariatric and Metabolic Surgery Clinic, Kirloskar Hospital, Hyderabad, India

4 Department of Endocrinology, GATA Haydarpasa Research Hospital, Istanbul, Turkey

5 Department of Internal Medicine, Taksim German Hospital, Istanbul, Turkey

operation provides a 50 % excess weight loss and diabetic remission rates in the obese population. Sleeve gastrectomy, initially known as a restrictive procedure, also provides intestinal hormonal changes, leads to weight loss rates comparable to gastric bypass (GBP) and diabetic remission rates in between banding and GBP [21]. GBP may lead to restriction and malabsorption of micro- (in general, not macro-) nutrients but most of all to humeral effects: according to some researchers, the latter being the only important long-lasting effects responsible for weight loss maintenance and diabetes remission [13]. Malabsorptive operations, namely biliopancreatic diversion (BPD) and duodenal switch (DS), provide the highest rates of weight control and over 90 % diabetic remission rates in the long-term follow-up [22]. BPD is a malabsorptive procedure; the metabolic effect is dependent not only on weight loss but also on similar humeral effects like after sleeve or bypass, in general, resulting in a more effective diabetes remission. However, not only mild complaints such as abdominal discomfort occur but also serious problems such as critical illness polyneuropathy, a need for total parenteral nutrition, wheelchair dependency, asthenia, and even mortality due to hepatic failure have been reported [23]. Therefore, a need for safe and effective modalities is obvious.

Weight loss, caloric restriction in the early postoperative period, and weight-independent mechanisms triggering favorable metabolic effects contribute to better glucose tolerance [24].

The aim of the present study was to analyze the outcomes of DSIT as a mode of functional restrictive therapeutic option for class II and class III obese T2DM patients. The main outcome measure in the present study was diabetes remission rate at 1 year postoperatively.

Methods

Study Design This study consisted of a retrospective analysis of our prospectively collected data in accordance with our Center of Excellence in Bariatric and Metabolic Surgery credentialing guidelines. For this type of study, formal consent is not required. Patients were diagnosed according to the American Diabetes Association criteria [25]. All patients were informed about the surgical procedure and signed an informed consent about the operation. According to the current protocol, we have evaluated consecutively 159 obese patients with T2DM and BMI >35 kg/m^2, operated in the general surgery department of our tertiary care center from October 2011 to December 2013. All patients were under a follow-up of at least 6 months.

Inclusion criteria were at least 3 years duration of T2DM under stable medical treatment, HbA1c >7 % for more than 3 months, weight stability, defined as no significant change (>3 %) within the last 3 months, and BMI above 35 kg/m^2. Patients were excluded if they had a fasting C peptide level <0.5 ng/ml or antiGAD antibody positivity. Other exclusion criteria included previous major gastrointestinal surgery, pregnancy, inability to tolerate anesthesia, severe eating problems, and patients on medications for eating disorders.

Surgical Procedure All operations are performed by the senior author (AC) laparoscopically. The operation was performed as described in the literature [25]. In brief, we start with a sleeve gastrectomy or fundectomy (depending on the BMI) and progress with duodenal transection 2–3 cm from the pylorus. The sleeved stomach is transferred to the lower abdomen through a transverse meso-colic opening. A single-stay suture is placed 50 cm from the ligament of Treitz, and the cecum is identified. The last 30 cm of ileum is preserved, and a 170-cm segment of a distal ileal segment is prepared for the anastomosis. The first anastomosis is ileo-ileostomy; the second is duodeno-ileostomy, and the third is jejuno-ileostomy. The first and the last anastomoses are done in functional side-to-side manner, and the second anastomosis is done hand-sewn with single-layer continuous 3/0 PDS. All the mesenteric defects are closed one by one using 3/0 polypropylene (Fig. 1).

Outcome Parameters All patients received the same postoperative care within the Center of Excellence guidelines in the outpatient clinic during the 1st, 3rd, 6th, 9th, and 12th month follow-up visits. Their weight, change in BMI, waist-hip circumference, as well as biochemical analysis including mixed-

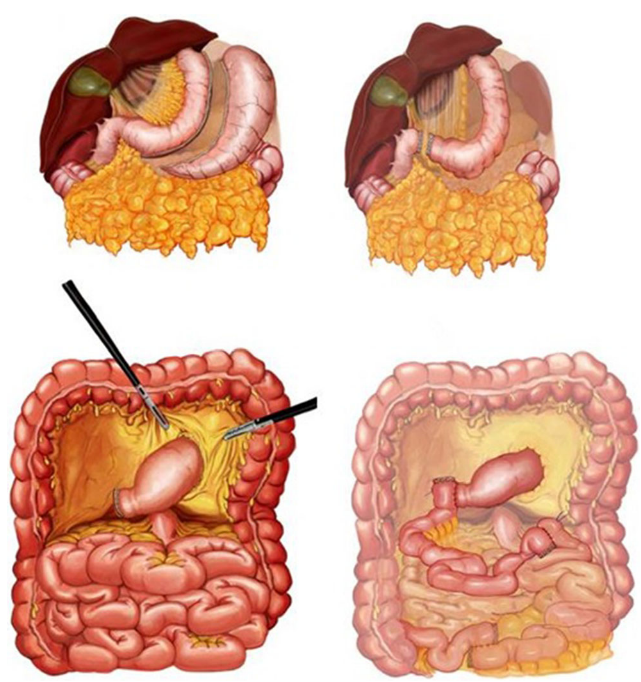

Fig. 1 Illustration of a re-sleeve operation with duodenal diversion, ileal interposition, and cholecystectomy

meal tolerance test (MTT), HbA1c, fructosamine, fasting and postprandial glucose levels, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) cholesterol, triglyceride (TG), kidney and liver function tests, urine analysis, electrolytes, CBC, renin-angiotensin-aldosterone activity, vitamin B_{12}, folate, and vitamin D levels were evaluated. The current study focuses on the changes in BMI, HbA1c, cholesterols, and triglycerides have been outlined.

Statistical Analysis Repeated measures analysis of variance was used to compare the body mass index and HbA1c values among six periods. Least significant difference test was used for the multiple comparisons of the repeated measures analysis of variance. Body mass index and HbA1c values were presented as the mean±standard deviation. A p value <0.05 was considered as statistically significant. Analyses were performed using commercial software (IBM SPSS Statistics, Version 22.0. Armonk, IBM Corp, NY, USA).

Results

The study group consisted of 88 females and 73 males, with a mean age of 51.8 years.

Patients enrolled in the study were severely diabetic with mean BMI of 39.33 (range, 35 to 50.3) kg/m^2, mean T2DM duration of 14.4 (range, 3 to 29) years, and mean HbA1c of 9.24 (range, 5.2 to 15.02) percent. Majority of the patients (n 129, 81.1 %) were on treatment with insulin either alone (n 21, 13.2 %) or in combination with oral antidiabetics (OAD) (n 108, 67.9 %). Only 30 patients (18.86 %) were on OAD treatment. Mean insulin dose was 32 (range, 24 to 160) IU/day. Other medications were antihypertensive drugs used by 76.1 %, dyslipidemics by 73.5 %, and cardiac drugs by 24.7 % of the patients. Mean antihypertensive drug requirement per patient was 1.74 tablets daily. Previous coronary stenting was required in 15 (9.4 %) cases, previous coronary bypass in 18 (11.3 %) cases, and previous carotid stenosis or plaques were present in 23 (14.4 %) cases. In total, 23 patients (14.4 %) had nephropathy and 34 patients (21.38 %) had retinopathy. Patients were engaged only in light physical activity, mostly occupational. In total, 105 patients (66.03 %) were nonsmokers, 24 (15.09 %) were ex-smokers (mean 6.3 years), and 30 (18.8 %) were smokers (one pack/day in average).

All operations are performed laparoscopically. Mean duration of hospital stay was 6.4 (range, 4 to 42) days. Meckel diverticule was diagnosed incidentally in four patients (2.5 %), and a synchronous diverticulectomy was performed. A postoperative course was uneventful in these cases.

Complications seen in eight patients (5.03 %) consisted of a leak from anastomosis (n=3), duodenal stump leak (n=1), intraabdominal bleeding (n=1), intraluminal bleeding (n=1), biliary leak (n=1), and anastomotic stricture (n=1, 0.6 %). Postoperative temporary adverse events that occurred in 19 patients are as follows: nausea and vomiting (n=5), diarrhea (n=4), neuropathy (n=3), anemia (n=3), dehydration (n=2), reflux (n=1), and constipation (n=1). Major surgical complication or mortality was not observed in our series. There were no deaths in our series.

Mean follow-up for the study group was 18.3 months. A total of 144 of 161 patients completed a 1-year follow-up. Seventeen patients were lost to follow-up at the end of 1 year. Mean BMI decreased from 39.33 to 25.51 kg/m^2 (excess BMI loss rate was 75.4 %, p<0.001). There was a significant weight change in all time points examined (p<0.001, each). Mean fasting glucose level decreased from 189.8 to 123.5 mg/dl (p<0.001), and mean postprandial glucose level decreased from 246.1 to 179.4 mg/dl (p<0.01). Mean HbA1c decreased from 9.24 to 6.14 % 1 year after surgery (p<0.001). Overall, 88.68 % of patients were off antidiabetic medications. Change in mean BMI, HbA1c, and their minimum and maximum values are shown in Table 1. Hypertension was diagnosed in 121 of 161 patients preoperatively and resolved in 114 cases (94.2 %, p<0.001). LDL, VLDL, and TG levels have shown marked improvements 1 year after surgery (p<0.001, each). Triglycerides decreased from a mean of 210.07 to 125.24 mg/dl, and cholesterol decreased from a mean of 208.34 to 163.23 mg/dl (p<0.001 for each). HDL levels also showed marked increases 12 months after surgery; however, the difference was not significant (p=0.58) (Table 2).

A total of 89 patients completed 2 years of follow-up. At the end of 2 years, mean BMI was 25.49 (range, 21.14 to 32.90) kg/m^2 (excess BMI loss rate was 74.2 % compared with the baseline, p<0.001). Mean HbA1c was 6.28 (range, 4.9 to 8.7) % 2 years after surgery (p<0.001). A total of 44

Table 1 The change in mean BMI, mean HbA1c, and their minimum and maximum values are depicted

Variable		Mean (min–max)	p value
BMI	Preoperative	39.33±3.66 (35–50.3)	<0.001
	1st month	35.84±3.22 (29.7–46.2)	
	3rd month	32.77±3.11 (27.3–46)	
	6th month	29.34±3.2 (25.6–34.8)	
	9th month	27.56±2.26 (23.8–35.2)	
	12th month	25.51±2.26 (20.3–33.6)	
HbA1c	Preoperative	9.24±1.87 (5.2–15.02)	<0.001
	1st month	7.86±1.3 (5–11.5)	
	3rd month	7.04±1.27 (4.6–12.42)	
	6th month	6.72±1.13 (4.71–10.64)	
	9th month	6.37±0.96 (4.82–10.31)	
	12th month	6.14±0.76 (4.7–8.35)	

BMI body mass index, *HbA1c* hemoglobin A1c

Table 2 The change (in mean±std. deviation) of HDL, LDL, VLDL, and TG levels are shown with their significance

Variable		Mean (min–max)	*p* value
HDL	Preoperative	42 (24–76.8)	0.58
	12th month	50.32 (28.98–77.86)	
LDL	Preoperative	131.06 (56.27–823.3)	<0.001
	12th month	91.61 (50.85–287.08)	
VLDL	Preoperative	42.08 (7.19–205.61)	<0.001
	12th month	25.5 (7.16–72.27)	
TG	Preoperative	210.07 (84.28–1724.1)	<0.001
	12th month	125.24 (56.32–241.09)	

Of note, LDL, VLDL, and TG levels have shown significant decrease ($p<0.001$). Although HDL levels increased after surgery, this increase did not reach a statistical significance ($p=0.58$)

HDL high-density lipoprotein, *LDL* low-density lipoprotein, *VLDL* very low-density lipoprotein, *TG* triglyceride

patients completed 3 years of follow-up. At the end of 3 years, mean BMI was 25.66 (range, 21.94 to 32.13) kg/m^2 (excess BMI loss rate was 72.7 % compared with the baseline, $p<0.001$). Mean HbA1c was 6.19 (range, 5.00 to 8.23) % 3 years after surgery ($p<0.001$).

Discussion

In this study, we attempted to analyze the safety and efficacy of DSIT for obese T2DM patients. Our results have demonstrated that DSIT is a safe and effective procedure in these cases.

Surgical procedures that induce weight loss may provide remission of T2DM in a considerable proportion of morbidly obese patients. Gastrointestinal surgeries can cause improvement in glucose homeostasis via mechanisms beyond restricted food intake and weight loss. Roux-en-Y gastric bypass (RYGB) improves insulin sensitivity independently on weight loss while the metabolic effect of BPD is dependent not only on weight loss but also on similar humeral effects resulting in a more effective diabetes remission [26, 27].

Cellular mechanisms enhancing insulin sensitivity postoperatively are speculative. The surgery is mainly targeted to the pathophysiology of the underlying disease [27, 28]. In our series, resolution of diabetes and its comorbidities, acceptable rates of morbidity, and the absence of mortality and sustained beneficial effects in the postoperative period indicate that DSIT can be a favorable treatment modality. However, the heterogeneity of patient population, complexity of procedure, and associated diseases must be kept in mind during the interpretation of results. Leaks from duodenal stump and anastomosis site are important complications and precautions that should be taken to minimize these hazards. Moreover, more objective, clear, and definite criteria must be established for indications of surgery in diabetic and obese population.

It should be noted that the patients included in the current study are "resistant" type 2 diabetic patients who either have end-organ damage or have failed to reach the metabolic targets despite the best medical treatment. These patients have a long duration of diabetes, and they have already lost a considerable percentage of their insulin reserves and are prone to be affected by glucotoxicity, insulin toxicity, or both. Therefore, a considerable number of our patients are likely to be influenced by the micro and macrovascular complications.

Even in this situation, as demonstrated by our data, the DSIT operation has been shown to pose an over 88.68 % diabetic remission in the severely ill type 2 diabetic patients. Additionally, a successful treatment of hypertension (94.2 % normal blood pressure without medication) and dyslipidemia (92.5 % remission without medication) have been achieved. It should also be kept in mind that DSIT is not a malabsorptive operation.

In the literature, publications on ileal transposition were performed on overweight or non-morbid (BMI< 35 kg/m^2) obese series [24, 26]. The current study is unique since the study population consisted of class II and class III obese patients. Despite this disadvantage, our results are comparable to those achieved with other bariatric surgical procedures. It is noteworthy that these results could be accomplished without causing serious malabsorption.

Limitations of this study include the retrospective design, lack of a control group, and not using a specific measure for the assessment of quality of life. Moreover, feasibility of this surgical procedure on a large scale seems to be limited due to the restricted availability of facilities needed to perform such a complex surgical intervention. Above all, the data in the present study remain preliminary and at least medium-term outcomes of weight loss, diabetes control, and metabolic side effects should be collected before a wider embrace of the DSIT should occur.

In conclusion, type 2 diabetes is a dynamic, heterogenous, and multifactorial disease. For each patient, effective control of all components of metabolic syndrome is of paramount importance. DSIT operation seems to be a reliable, safe, and effective alternative option for those with resistant disease and who fail to achieve the goals of therapy despite the best medical treatment. In this aspect, the integration of DSIT operation with the medical treatment can lead to better clinical outcomes in the management algorithm of type 2 diabetes.

Conflict of Interest No conflict of interest.

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

Human and Animal Rights The study has been approved by the appropriate institutional and/or national research ethics committee and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Funding The authors declare that they have no funding.

References

1. American Diabetes Association. The dangerous toll of diabetes. http://www.diabetes.org/diabetes-statistics/dangerous-toll.jsp.
2. Vaag AA. Glycemic control and prevention of microvascular and macrovascular disease in the Steno 2 study. Endocr Pract. 2006;12:89–92.
3. Bermudez DM, Pories WJ. New technologies for treating obesity. Minerva Endocrinol. 2013;38:165–72.
4. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Eng J Med. 2012;366:1567–85.
5. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med. 2009;122:248–56.
6. Vetter ML, Cardillo S, Rickels MR, et al. Narrative review: effect of bariatric surgery on type 2 diabetes mellitus. Ann Intern Med. 2009;150:94–103.
7. Romeo S, Maglio C, Burza MA, et al. Cardiovascular events after bariatric surgery in obese subjects with type 2 diabetes. Diabetes Care. 2012;35:2613–7.
8. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357:741–52.
9. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357:753–61.
10. Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA. 2008;299:316–23.
11. Bradley D, Conte C, Mittendorfer B, et al. Gastric bypass and banding equally improve insulin sensitivity and ß cell function. J Clin Invest. 2012;122:4667–74.
12. Camastra S, Gastaldelli A, Mari A, et al. Early and longer term effects of gastric bypass surgery on tissue-specific insulin sensitivity and beta cell function in morbidly obese patients with and without type 2 diabetes. Diabetologia. 2011;54:2093–102.
13. Habegger KM, Heppner KM, Amburgy SE, et al. GLP-1R responsiveness predicts individual gastric bypass efficacy on glucose tolerance in rats. Diabetes. 2014;63(2):505–13.
14. Mari A, Manco M, Guidone C, et al. Restoration of normal glucose tolerance in severely obese patients after biliopancreatic diversion: role of insulin sensitivity and beta cell function. Diabetologia. 2006;49:2136–43.
15. Camastra S, Manco M, Mari A, et al. Beta-cell function in severely obese type 2 diabetic patients: long-term effects of bariatric surgery. Diabetes Care. 2007;30:1002–4.
16. Briatore L, Salani B, Andraghetti G, et al. Restoration of acute insulin response in T2D subjects 1 month after biliopancreatic diversion. Obesity (Silver Spring). 2008;16:77–81.
17. Briatore L, Salani B, Andraghetti G, et al. Beta-cell function improvement after biliopancreatic diversion in subjects with type 2 diabetes and morbid obesity. Obesity (Silver Spring). 2010;18:932–6.
18. De Paula AL, Stival AR, Halpern A, et al. Improvement in insulin sensitivity and ß-cell function following ileal interposition with sleeve gastrectomy in type 2 diabetic patients: potential mechanisms. J Gastrointest Surg. 2011;15:1344–53.
19. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;366:1577–85.
20. Dixon JB, le Roux CW, Rubino F, et al. Bariatric surgery for type 2 diabetes. Lancet. 2012;379:2300–11.
21. de Hollanda A, Ruiz T, Jiménez A, Flores L, Lacy A, Vidal J. Patterns of weight loss response following gastric bypass and sleeve gastrectomy. Obes Surg. 2014. doi:10.1007/s11695-014-1512-7.
22. Yu J, Zhou X, Li L, et al. The long-term effects of bariatric surgery for type 2 diabetes: systematic review and meta-analysis of randomized and non-randomized evidence. Obes Surg. 2015;25(1):143–58.
23. Willaert W, Henckens T, Van De Putte D, et al. Life-threatening side effects of malabsorptive procedures in obese patients necessitating conversion surgery: a review of 17 cases. Acta Chir Belg. 2012;112:268–74.
24. Astiarraga B, Gastaldelli A, Muscelli E, et al. Biliopancreatic diversion in nonobese patients with type 2 diabetes: impact and mechanisms. J Clin Endocrinol Metab. 2013;98:2765–73.
25. Members of the expert committee on the diagnosis and classification of diabetes mellitus: report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 2003;26:S5–S20.
26. DePaula AL, Macedo AL, Rassi N, et al. Laparoscopic treatment of metabolic syndrome in patients with type 2 diabetes mellitus. Surg Endosc. 2008;22:2670–8.
27. Gagner M. Surgical treatment of nonseverely obese patients with type 2 diabetes mellitus: sleeve gastrectomy with ileal transposition (SGIT) is the same as the neuroendocrine brake (NEB) procedure or ileal interposition associated with sleeve gastrectomy (II-SG), but ileal interposition with diverted sleeve gastrectomy (II-DSG) is the same as duodenal switch. Surg Endosc. 2011;25:655–6.
28. Rubino F, Gagner M. Potential of surgery for curing type 2 diabetes mellitus. Ann Surg. 2002;236:554–9.