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The rapid effects of sleeve gastrectomy on glucose homeostasis and resolution of diabetes mellitus

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Abstract

Aims: Type 2 diabetes caused by obesity is increasing globally. Bariatric surgical procedures are known to have positive effects on glucose homeostasis through neurohormonal action mechanisms. In the present study, we aimed to investigate the factors influencing glucose homeostasis independent of weight loss after the laparoscopic sleeve gastrectomy (LSG).

Methods: Patients who underwent LSG for morbid obesity in a 3-year period were evaluated. Data on demographics, clinical characteristics (duration of diabetes, resected gastric volume, antral resection margin) and laboratory parameters (preoperative and postoperative blood glucose on fasting, preoperative HbA1c levels and first-year HbA1c levels) were retrospectively reviewed. Effect of patients' body mass index (<50 kg/m^2, ≥50 kg/m^2), first-year excess weight loss (EWL%) rates, age (≥50 years, <50 years), duration of diabetes (≥5 years, <5 years) and antral resection margin (≥3 cm, <3 cm) on postoperative blood glucose profile and diabetic resolution status were investigated.

Results: Total of 61 patients constituted the study group. There were 40 female and 21 male patients with an average age of 43.8 ± 10.5 years (19-67 years). Preoperatively, mean BMI, blood glucose levels and HbA1c were 48.8 ± 8.5 kg/m^2, 133.6 ± 47.4 mg/dL and 7.4 ± 1.1, respectively. The mean blood glucose level at the postoperatively 5th day was 88.0 ± 16.3 mg/dL (median: 84 mg/dL) ($P < .001$). Fifty-nine out of 61 patients improved their glycaemic control.

Conclusions: It is noteworthy that LSG can control blood glucose levels in short term after surgery regardless of weight loss. Therefore, LSG should be preferred at earlier stages in the treatment of obesity-related T2DM in order to prevent T2DM-related complications.

KEYWORDS
diabetes mellitus, laparoscopic sleeve gastrectomy, obesity, resolution of diabetes

1 | INTRODUCTION

Obesity-related type 2 diabetes mellitus (T2DM) is a global ever-growing health problem, a significant burden on healthcare systems and healthcare costs.[1] Obesity is an important factor in the onset of T2DM. Therefore, weight loss has a therapeutic importance for success in T2DM treatment. In these patients, lifestyle changes and medications are the main factors for controlling the diabetes. Problems in compliance with long-term drug use and maintaining weight loss limit the role of these treatment methods.[2]

The development of minimally invasive laparoscopic techniques has provided immense progress in bariatric surgery, and many randomized controlled trials have shown that bariatric surgery reduces cardiovascular risk factors along with successful glycaemic control.[3,4] Operative results are remarkable in patients with long-term uncontrolled T2DM.[5] Similarly, a randomized controlled study conducted by Schauer et al[5] demonstrated that bariatric surgery in combination with medical therapy is more effective than medical therapy alone for improving T2DM outcomes for patients with body mass index (BMI) from 27 to 43 kg/m^2.

Out of a host of bariatric operations for morbid obesity, laparoscopic sleeve gastrectomy (LSG) has been the most frequent surgical procedure worldwide. LSG involves removing almost all of the fundus and creating a tube-shaped stomach with a capacity of 60-100 mL, which in turn limits the capacity for food intake. LSG was originally defined as a first step of biliopancreatic diversion with duodenal switch (BPDDS), but today it is preferred as a well-tolerated stand-alone bariatric surgical procedure.[6,7]

We noticed that in patients with obesity-related diabetes, blood glucose levels decreased in the first days after LSG. Therefore, we performed a retrospective analysis documenting the improved blood glucose levels after LSG, which was observed before losing significant weight in 61 morbidly obese patients with T2DM. The main focus of our study is to reveal the effect of LSG on glucose homeostasis in the very early postoperative period and to investigate the factors that may cause this effect.

2 | MATERIALS AND METHODS

Data of obese patients who underwent LSG between 2013 and 2016 at a tertiary referral hospital in Istanbul/Turkey were reviewed. The study protocol was approved by the Local Institutional Review Board of University of Health Sciences Sisli Hamidiye Etfal Education and Research Hospital (approval code 877). Informed consent was obtained from all subjects, and all methods were carried out in accordance with the relevant guidelines and regulations of institutional review board.

2.1 | Study population and design

Sixty-one morbidly obese patients with a diagnosis of T2DM were included in the study. The patients were included in this study if the following criteria were met: (a) BMI > 40 kg/m^2, (b) uncontrolled T2DM after 6 months of medical therapy (HbA1c > 6.5%), and (c) the absence of contraindications for bariatric surgery. Exclusion criteria were as follows: (a) history of duodenal or proximal jejunal intervention, (b) patients with malabsorptive syndrome, and (c) patients who did not attend recall visit or lost to follow up. Data related to patients' demographics (age, sex, BMI), laboratory results (blood glucose level and HbA1C level) and duration of T2DM were recorded. HbA1c level below 6.5% without the need of antidiabetic treatment for 1 year or blood glucose level of fasting below 100 mg/dL was considered as diabetes resolution.[8]

The parameters used for effectiveness of LSG and weight loss were BMI and excess weight loss ratio (EWL%).

Preoperative blood glucose levels and serum HbA1c, fasting blood glucose and HbA1c level at postoperative 1st, 2nd, 3rd, 4th, 5th days and 1th, 3rd, 6th, 9th and 12th months were recorded. First-year EWL% and surgical findings were also recorded. Effects of patients' BMI (<50 kg/m^2, ≥50 kg/m^2), 1st-year EWL%, age (≥50 years, <50 years), duration of T2DM (≥5 years, <5 years), resected gastric volume (RcGV) and antral resection margin (ARM) (≥ 3 cm, <3 cm) on postoperative fasting blood glucose level and T2DM resolution status were investigated.

2.2 | Statistical analysis

SPSS Statistics ver. 15.0 (Chicago, SPSS Inc) was used for statistical analysis. While data for continuous variables were reported as mean ± standard deviation (SD), median, minimum and maximum, categorical variables were presented as number and percentages. Friedman test was used for comparison of numerical variables in dependent groups. Wilcoxon test with Bonferroni correction was performed for subgroup analyses. Chi-square test was performed for comparison of independent group. A statistical P value of .05 or lesser was considered significant.

3 | RESULTS

3.1 | Study patients

Totally, 61 patients of which 40 were female and 21 were male were included in this study. The mean age of the patients included was 43.8 ± 10.5 years (19-67 years). Preoperatively, the mean ± SD BMI, blood glucose level and HbA1c of the patients were 48.8 ± 8.5 kg/m^2 (range: 40.1-100.9 kg/m^2), 133.6 ± 47.4 mg/dL and 7.4 ± 1.1% (median: 6.9%), respectively (Table 1).

3.2 | Glycaemic control

The mean blood glucose level on fasting was 88.0 ± 16.3 mg/dL (median: 84 mg/dL) on the 5th postoperative day (P < .001) (Tables 2

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TABLE 1 Demographics and clinical characteristics of the patients

		Mean ± SD/Min-Max (Median)	n (%)
Mean Age (y)		43.8 ± 10.5/19-67 (42)	
Age (y)	<50		41 (67.2)
	≥50		20 (32.8)
Duration of T2DM (y)		5 ± 2.6/1-14	
Duration of T2DM (y)	<5		31 (50.8)
	≥5		30 (49.2)
RcGV (cc)		1718.7 ± 434.8/1150-2200 (1600)	
ARM (cm)		3.7 ± 1.8/2-8 (3)	
ARM (cm)	<3		39 (63.9)
	≥3		22 (36.1)
Height (cm)		164.5 ± 9.0/150-186 (164)	
Preoperative weight (kg)		132.1 ± 26.2/100-295 (130)	
Preoperative BMI (kg/m^2)		48.8 ± 8.5/40.1-100.9 (46.9)	
Preoperative HbA1c		7.4 ± 1.1/6.5-11.6 (6.9)	
Preoperative fasting blood glucose level (mg/dL)		133.6 ± 47.4/90-318 (116)	
1st-year EWL%		96.6 ± 18.2/61-175 (95)	
Resolution of T2DM	No		2 (3.3)
	Yes		59 (96.7)

Abbreviations: ARM, Antral resection margin; BMI, Body mass index; RcGV, Resected gastric volume; T2DM, Type 2 diabetes mellitus.

and 3). The postoperative first-year blood glucose levels of the patients in the study group are shown in Table 2. Postoperative HbA1c level at the 1st year was 5.7 ± 0.8% (median: 5.6%), and comparison of preoperative and postoperative 1st-year HbA1c was shown in Figure 1.

3.3 | Diabetes medications

The mean T2DM duration of the patients was 5 ± 2.6 years (range: 1-14 years). There was no statistically significant difference between the groups with diabetes duration ≥5 years and <5 years in terms of T2DM resolution (p:0.238). Fifty-nine patients ceased all medication for diabetes in the 1 year follow-up period. None needed increased dosage of antidiabetic therapy. Two patients, whose T2DM did not improve, continued using insulin in the postoperative period, albeit a lower dose of insulin. T2DM was improved in 59 out of 61 patients (Table 1).

3.4 | Weight loss

Although the mean EWL% at the end of the first month was only 28 ± 8.4%, the rate of decrease in blood glucose was 20% (mean ± SD: 104.4 ± 38.6 mg/dL) in the first month and the blood glucose level reached normal limits in 48 (78.6%) patients during the first month ($P < .001$). At 1st year of follow-up, the mean ± SD EWL% was 96.6 ± 18.2%, and blood glucose levels decreased by 35% and HbA1c decreased by 23% during this period (Table 2).

We evaluated that T2DM improved in 59 patients (96.7%). Although preoperative HbA1c levels were higher in other 2 patients (3.3%) who had no improvement in T2DM, preoperative HbA1c levels and early postoperative improvement were not

TABLE 2 Follow-up fasting blood glucose level and 1st-year HbA1c

			Mean ± SD	Min-Max	Median
HbA1c	1st year		5.7 ± 0.8	5-9.5	5.6
Fasting blood glucose (mg/dL)	Preoperative		133.6 ± 47.4	90-318	116
	Postoperative				
		1st day	174.4 ± 43.7	112-297	165
		2nd day	126.8 ± 43.7	86-396	117
		3rd day	100.9 ± 27.7	63-196	94
		4th day	92.3 ± 23.9	64-179	85
		5th day	88.0 ± 16.3	62-155	84
		1st month	104.4 ± 38.6	72-348	94
		3rd month	96.9 ± 27.5	75-277	91
		6th month	95.2 ± 47.8	65-413	87
		9th month	90.2 ± 27.7	66-240	84
		1st year	86.8 ± 23.1	72-213	82

TABLE 3 The *P*-values after Bonferroni correction

	P
Po day 1 – Pr	<.001
Po day 2 – Pr	.236
Po day 3 – Pr	<.001
Po day 4 – Pr	<.001
Po day 5 – Pr	<.001
Po month 1 – Pr	<.001
Po month 3 – Pr	<.001
Po month 6 – Pr	<.001
Po month 9 – Pr	<.001
Po month 12 – Pr	<.001

Note: Comparison of postoperative fasting blood glucose with preoperative blood glucose.

Bonferroni correction $P < .0026$.

Abbreviations: Po, Postoperative, Pr, Preoperative.

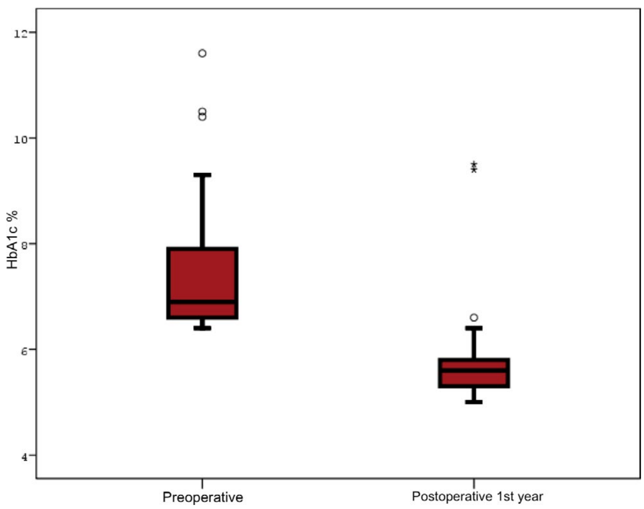

FIGURE 1 HbA1c levels at preoperative period and postoperative 1st year

statistically relevant. In this study, no difference was found in terms of changes in blood glucose levels, improvement of T2DM and EWL% of patients according to age groups. In terms of surgical technique, we did not find a relationship between the RcGV or ARM and improvement of T2DM (p:0.495 and p:0.531, respectively) (Table 4). No complication was detected related to surgical procedure.

4 | DISCUSSION

Management of T2DM in obese patients is difficult. HbA1c level below 7% was defined by the current American Diabetes Association as a primary goal of diabetes treatment.[9] Many studies show that the majority of people with diabetes have difficulty managing their own drug regimens. Even if the recommended drug regimes are followed,

TABLE 4 Effect of demographics and surgical findings on resolution of T2DM

		Resolution of T2DM				
		No		Yes		
		n	%	n	%	
Age (y)	<50	0	0.0	41	69.5	0.104
	≥50	2	100	18	30.5	
Duration of T2DM (y)	<5	0	0.0	31	52.5	0.238
	≥5	2	100	28	47.5	
RcGV (cc)	≤1500	0	0.0	28	47.5	0.495
	>1500	2	100	31	52.5	
ARM (cm)	<3	2	100	37	62.7	0.531
	≥3	0	0.0	22	37.3	
BMI (kg/m^2)	<50	2	100	40	67.8	1.000
	≥50	0	0.0	19	32.2	

Abbreviations: ARM, Antral resection margin; BMI, Body mass index; RcGv, Resected gastric volume; T2DM, Type 2 diabetes mellitus.

these targeted HbA1C levels may not be achieved.[10,11] Bariatric surgical procedures are accepted as an effective method in the treatment of obesity-related T2DM.[4]

In our study, laparoscopic sleeve gastrectomy provides dramatic improvement in blood glucose level within the first postoperative week, regardless of weight loss. In parallel with similar studies, there is no correlation between improvement in blood glucose level and EWL% for the early postoperative period.[12,13] This result supports that the improvement in blood glucose level within early postoperative period may be due to the neurohormonal effects of sleeve gastrectomy.

Prior case series have found that the duration of T2DM prior to surgery affects the remission rates; a less robust improvement in glucose level is seen in those patients who have had T2DM for a long duration and who have high dosage of insulin requirements preoperatively.[5,14] Contrary to the other published data, in our present study, duration of diabetes or plasma glucose levels did not predict the change in glucose at 1 and 3 months or remission of type 2 DM. A striking result of our study is that 96.7% of patients do not need antidiabetic drugs during the 1 year after surgery. This is a similar result to our previous work.[15] In a systematic review written by Gill et al,[16] partial and complete remission rates of T2DM at 13 months of follow-up after LSG were reported as 26.9% and 66.2%, respectively. However, in this study, it is not clear which mechanisms the difference between diabetes resolution rates depends on.

It has been recently reported that BMI level in the preoperative period did not predict T2DM remission rate postoperatively. T2DM remission occurs without significant weight loss as known by bariatric surgeons.[17] In our study, T2DM resolution rates were similar for patients with a BMI ≥ 50 and < 50 kg/m.[2] Therefore, while BMI cannot be used as a measure of metabolic abnormalities, the concept of considering the cut-off value of BMI as a strict criterion for potential effects of bariatric surgery on T2DM resolution is also controversial.[18]

In this study, the rate of weight loss did not correlate with remission of T2DM. This result concurs with recent studies reporting 84.2% T2DM resolution without significant change of %EWL and fat distribution.[19,20] This remission can be explained by additional factors known to improve glucose homeostasis. Sista et al[21] stated that LSG lowers blood glucose level through hormonal mechanisms in the early postoperative period, while preserving this improvement with weight loss effect in the late postoperative period. Lowering of blood glucose level before significant weight loss is a similar finding to other studies in the literature of gastric bypass surgery. Hormonal changes occurring with the removal of the fundus reveal the importance of the stomach in glucose metabolism.[22] In the late postoperative period after bariatric surgery, the most effective factor on glucose homeostasis is the breaking down of insulin resistance related with weight loss, which lead beta cells to rest and recover.

The first metabolic event seen after LSG is the reduction in the plasma concentration of ghrelin due to the removal of the ghrelin-secreting cells in the fundus. Increasing resected gastric volume (RcGV) suggests that the more ghrelin-secreting cell is resected and the more plasma ghrelin level will decrease. Therefore, a larger RcGV is thought to reduce peripheral insulin resistance and have a regulatory effect on insulin release. Although some authors stated that RcGV > 1200 mL was more effective on T2DM resolution,[23] in our study, no statistically significant difference was detected between groups with RcGV > 1500 mL and ≤1500 mL in terms of blood glucose homeostasis. The lowest RcGV in our study was 1150 mL. Similar to our study, Singh et al[24] reported a T2DM resolution rate of 82.9%, regardless of the amount of RcGV with a cut-off of 1700 mL in their prospective study.

Laparoscopic sleeve gastrectomy is a purely restrictive operation with no malabsorptive effect. Improvement in blood glucose levels after malabsorptive procedures occurs within days without significant weight loss.[17] Although this is not observed in restrictive procedures, review of the literature has shown that LSG has a comparable T2DM amelioration rate in the early postoperative period at rates similar to RYGB.[15,16,25]

While endocrinologists recommend nutritional regulation and strict diet at the initial stage of the disease to prevent catastrophic consequences that can be observed if T2DM is not controlled, surgical intervention performed at early stages of T2DM is likely to be more effective. Since LSG has positive effects on T2DM unrelated with weight loss in the early period, it should be considered as a treatment option in order to prevent T2DM-related microvascular and macrovascular complications in obese patients in the early period of the disease. The key positive effects of LSG on T2DM independent of weight loss has led to the development of interventional T2DM treatments that do not cause weight loss. In addition, at later stages, LSG also has a positive effect on the recovery of pancreatic beta cell functions with its weight loss effect.

Although fulfilling the sample-size requirement, a relatively small number of patients were the main limitation of this study. Despite this, we conclude that LSG should be considered as a potential primary treatment option in patients with diabetes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

EB, CK, SÖ, OG and MM conceived and designed the study; involved in data collection and processing; analysed and interpreted the data; and wrote the manuscript. EB and CK performed literature search. EB, CK and MM critically reviewed the manuscript.

DATA AVAILABILITY STATEMENT

There are no new data associated with this manuscript.

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REFERENCES

1. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK [published correction appears in Lancet. *Lancet*. 2011;378(9793):815-825.
2. Moyer VA; U.S. Preventive Services Task Force. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2012;157(5):373-378.
3. Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2013;347:f5934.
4. Guo X, Liu X, Wang M, Wei F, Zhang Y, Zhang Y. The effects of bariatric procedures versus medical therapy for obese patients with type 2 diabetes: meta-analysis of randomized controlled trials. *Biomed Res Int*. 2013;2013:410609.
5. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. *N Engl J Med*. 2017;376(7):641-651.
6. Saber AA, Elgamal MH, McLeod MK. Bariatric surgery: the past, present, and future. *Obes Surg*. 2008;18(1):121-128.
7. Lee WJ, Almulaifi A, Tsou JJ, Ser KH, Lee YC, Chen SC. Laparoscopic sleeve gastrectomy for type 2 diabetes mellitus: predicting the success by ABCD score. *Surg Obes Relat Dis*. 2015;11(5):991-996.
8. National Collaborating Centre for Chronic Conditions (UK). Type 2 diabetes in adults: management (update). 2019. Available at https://www.nice.org.uk/guidance/ng28. Last accessed December 2019
9. . American Diabetes Association. Standards of medical care in diabetes–2013. *Diabetes Care*. 2013;36 Suppl 1(Suppl 1);S11-S66.
10. Calvert MJ, McManus RJ, Freemantle N. Management of type 2 diabetes with multiple oral hypoglycaemic agents or insulin in primary care: retrospective cohort study. *Br J Gen Pract*. 2007;57(539):455-460.
11. Juarez DT, Ma C, Kumasaka A, Shimada R, Davis J. Failure to reach target glycated a1c levels among patients with diabetes who are

adherent to their antidiabetic medication. *Popul Health Manag*. 2014;17(4):218-223.

12. Papailiou J, Albanopoulos K, Toutouzas KG, Tsigris C, Nikiteas N, Zografos G. Morbid obesity and sleeve gastrectomy: how does it work? *Obes Surg*. 2010;20(10):1448-1455.
13. Salinari S, Bertuzzi A, Asnaghi S, Guidone C, Manco M, Mingrone G. First-phase insulin secretion restoration and differential response to glucose load depending on the route of administration in type 2 diabetic subjects after bariatric surgery. *Diabetes Care*. 2009;32(3):375-380.
14. Vetter ML, Cardillo S, Rickels MR, Iqbal N. Narrative review: effect of bariatric surgery on type 2 diabetes mellitus. *Ann Intern Med*. 2009;150(2):94-103.
15. Mihmanli M, Isil RG, Bozkurt E, et al. Postoperative effects of laparoscopic sleeve gastrectomy in morbid obese patients with type 2 diabetes. *Springerplus*. 2016;5:497.
16. Gill RS, Birch DW, Shi X, Sharma AM, Karmali S. Sleeve gastrectomy and type 2 diabetes mellitus: a systematic review. *Surg Obes Relat Dis*. 2010;6(6):707-713.
17. 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(17):1577-1585.
18. Sjöholm K, Anveden A, Peltonen M, et al. Evaluation of current eligibility criteria for bariatric surgery: diabetes prevention and risk factor changes in the Swedish obese subjects (SOS) study. *Diabetes Care*. 2013;36(5):1335-1340.
19. Silecchia G, Boru C, Pecchia A, et al. Effectiveness of laparoscopic sleeve gastrectomy (first stage of biliopancreatic diversion with duodenal switch) on co-morbidities in super-obese high-risk patients. *Obes Surg*. 2006;16(9):1138-1144.
20. Rizzello M, Abbatini F, Casella G, et al. Early postoperative insulin-resistance changes after sleeve gastrectomy. *Obes Surg*. 2010;20(1):50-55.
21. Sista F, Abruzzese V, Clementi M, Guadagni S, Montana L, Carandina S. Resolution of type 2 diabetes after sleeve gastrectomy: a 2-step hypothesis. *Surg Obes Relat Dis*. 2018;14(3):284-290.
22. Cai J, Zheng C, Xu L, et al. Therapeutic effects of sleeve gastrectomy plus gastric remnant banding on weight reduction and gastric dilatation: an animal study. *Obes Surg*. 2008;18(11):1411-1417.
23. Sista F, Abruzzese V, Clementi M, Carandina S, Amicucci G. Effect of resected gastric volume on ghrelin and GLP-1 plasma levels: a prospective study. *J Gastrointest Surg*. 2016;20(12):1931-1941.
24. Singh JP, Tantia O, Chaudhuri T, Khanna S, Patil PH. Is resected stomach volume related to weight loss after laparoscopic sleeve gastrectomy? *Obes Surg*. 2014;24(10):1656-1661.
25. 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(3):248-256.e5.

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