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Bariatric surgery in the treatment of patients with obesity and type 1 diabetes: A retrospective study of clinical data

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Abstract

Aim: To evaluate the effectiveness and safety of bariatric surgery in patients with coexisting type 1 diabetes and obesity who choose to undergo bariatric surgery for weight management.

Materials and Methods: We conducted a retrospective, longitudinal review of the clinical data of patients with type 1 diabetes, followed up at our centre after bariatric surgery had been performed elsewhere.

Results: Sixty-one patients were included, of whom 51% were women, and 57 (93%) were Emirati Arab, three (5%) were other Arab, and one (2%) was White in ethnic origin. The mean age at surgery was 31 years. A total of 42 patients (69%) underwent sleeve gastrectomy, 17 (28%) gastric bypass, and two (3%) gastric banding. In 48 patients with complete follow-up data, improvements were observed at 12 months in the median (interquartile range [IQR]) values for body mass index (BMI; 38.5 [34.9-40.9] to 26.1 [24.2-29.6] kg/m^2, *P* <0.001), glycated haemoglobin concentration (8.6 [7.8-9.2]% to 7.8 [7.2-8.5]%; *P* <0.001), daily insulin dose (1.0 [0.7-1.2] to 0.8 [0.6-0.9] units/kg/d; *P* <0.001), systolic blood pressure (127 [116-136] to 116 [110-120] mmHg; *P* <0.001), total cholesterol: high-density lipoprotein cholesterol ratio (3.4 [2.9-4.3] to 3.0 [2.6-3.5]; *P* <0.001), and albuminuria. In 32 patients followed up at 3 years, the median (IQR) reduction in BMI was 10.4 (5.9-11.7) kg/m^2, 50% reduced or stopped antihypertensive medication and 58% reduced or stopped lipid-modifying medication. Three patients each reported a single episode of diabetic ketoacidosis; in one case this was due to cessation of insulin treatment.

Conclusions: In our cohort of patients with obesity and type 1 diabetes, bariatric surgery led to significant improvements in weight and cardiometabolic variables, with modest improvements in glycaemia. Few adverse events were reported.

KEYWORDS
bariatric surgery, insulin resistance, observational study, type 1 diabetes, weight control

1 | INTRODUCTION

The prevalence of obesity in individuals with type 1 diabetes is increasing, approaching that observed in people without diabetes.[1,2] Overweight and obesity affect 30% to 50% of patients with type 1 diabetes and features of metabolic syndrome occur in 8% to 40%.[3] Intensive insulin therapy has become standard treatment following the results of the Diabetes Control and Complications Trial (DCCT),[4] but this increases the prevalence of overweight and obesity.[5,6] In the Epidemiology of Diabetes Interventions and Complications (EDIC) study, the prevalence of obesity in the intensive therapy arm increased from 1% at baseline to 31% at the end of follow-up,[5] reflecting a vicious cycle of weight gain and increasing insulin requirements.

The role of bariatric surgery in the treatment of patients with obesity and type 2 diabetes is well established and has been recommended in recent guidelines as a modality of treatment for improvement or remission of disease.[7–11] However, in patients with type 1 diabetes, the role of bariatric surgery for the treatment of obesity is unclear. Increasingly, patients with obesity and type 1 diabetes who have failed to lose weight by other means choose to undergo bariatric surgery. Case series of patients with type 1 diabetes treated with bariatric surgery are emerging,[12–16] but there are limited data regarding longer-term weight loss and related metabolic changes. We evaluated outcomes of bariatric surgery in patients with both obesity and type 1 diabetes who independently chose to undergo bariatric surgery and were subsequently managed at our centre, with specific reference to weight loss, metabolic variables, treatment requirements, and late complications.

2 | METHODS

This retrospective study was performed at the Imperial College London Diabetes Centre (ICLDC) branches in Abu Dhabi and Al Ain, United Arab Emirates. The electronic patient database at ICLDC includes all patients attending the centre and was accessed in January 2020 to identify all patients who had a diagnosis of type 1 diabetes and had previously undergone bariatric surgery. This database includes information on ICLDC patients who sign a consent form upon registration, permitting their anonymized information to be used for research. The study was approved by the ICLDC institutional Research Ethics Committee (ref: IREC053).

Patients were treated with bariatric surgery at multiple different hospitals across the United Arab Emirates and subsequently attended ICLDC for management of their diabetes. All patients were labelled as having type 1 diabetes by their primary physician and were managed with long-term intensive insulin therapy. We further confirmed the diagnosis of type 1 diabetes in these individuals based on either positive autoantibodies (anti-glutamic acid decarboxylase [GAD] and/or anti-islet antigen 2 [IA2]), low or undetectable C-peptide or typical clinical features of type 1 diabetes, including young age at presentation, acute onset of osmotic symptoms and rapid progression to insulin.[17] We excluded patients who did not satisfy these strict criteria for diagnosis of type 1 diabetes as well as those who underwent bariatric surgery before being diagnosed with type 1 diabetes. No data cleaning or inference of missing results was performed. The disposition of the individuals included in the study is presented in Figure 1.

2.1 | Clinical variables

Results are reported according to the American Society of Metabolic and Bariatric Surgery (ASMBS) standardized outcomes reporting.[18] We assessed the following variables at the preoperative visit, at 6 and 12 months postoperatively, and at the most recent visit: weight, body mass index (BMI), systolic blood pressure, glycated haemoglobin (HbA1c), total daily insulin dose and the lipid variables total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides. Biometric variables were recorded by licensed clinical nursing staff. Blood pressure measurements were performed using the Dinamap V100 system (GE Healthcare, Chicago, Illinois). Lipid variables were assessed using electrochemiluminescence immunoassays on the Cobas 8000 platform (Roche, Basel, Switzerland). HbA1c was measured using the Variant II system (Bio-Rad Systems, Hercules, California). Anti-GAD and anti-IA2 antibodies were assayed using ELISA (Euroimmun AG, Lübeck, Germany) and plasma C-peptide was measured using a chemiluminescence assay on the Cobas platform.

The ASMBS criteria for diabetes remission are not applicable to patients with type 1 diabetes, and we therefore examined effects on HbA1c and total daily insulin requirements. Microalbuminuria was defined according to the National Kidney Foundation definition of urinary albumin:creatinine ratio (UACR) of $\geq$3.0 mg/mmol.[19] Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation.[20] We compared outcomes in our group of type 1 diabetes patients against those achieved in individuals with type 2 diabetes included in the STAMPEDE randomized controlled trial.[8,9]

2.2 | Statistical analysis

Statistical analysis was performed using R version 4.0.2 (R Foundation for Statistical Computing). Skewness was assessed using the Shapiro test, and nonparametric tests were used where deviation from the normal distribution was identified. Data are presented as median (interquartile range [IQR]) or mean ± SD. Pairwise testing was used throughout to minimize the effects of interindividual variation, and individuals with missing data at any of the time points studied were excluded from analysis. The paired Wilcoxon signed-rank test was used for nonparametric comparisons of continuous variables. Fisher's exact test was used to compare categorical data. Linear mixed-effects models were used to explore differences between the effects of gastric bypass and sleeve gastrectomy surgery. Statistical significance was assessed at the level of P <0.05. No correction was made for

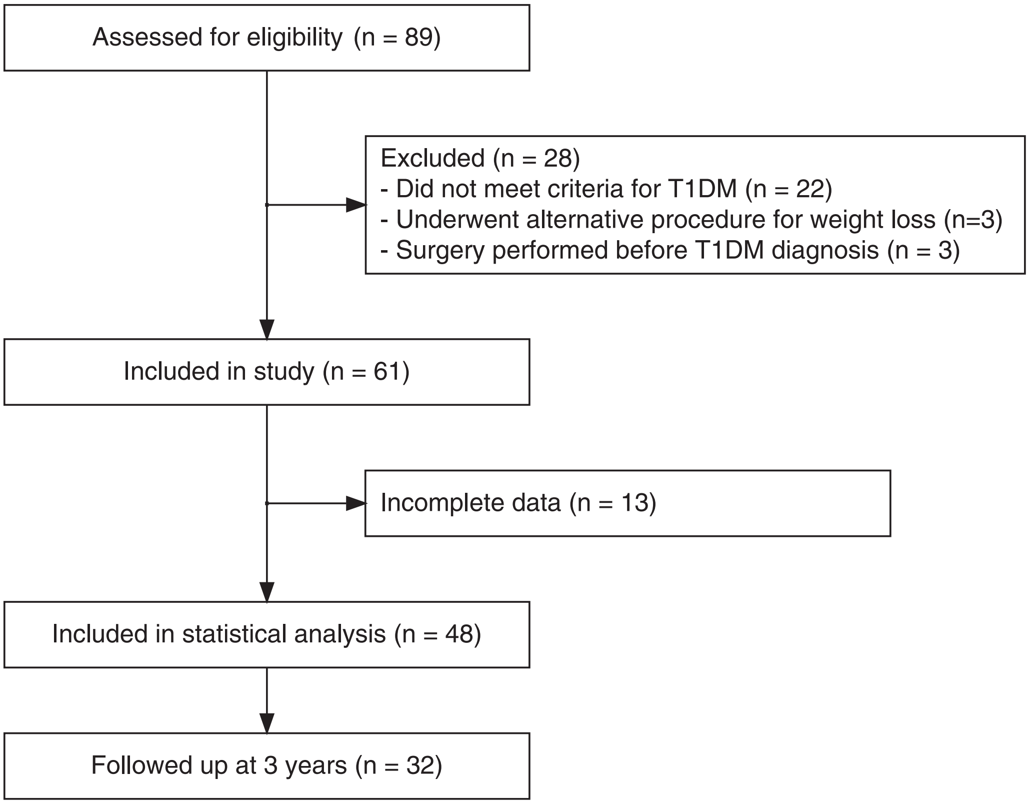

FIGURE 1 Disposition of the individuals included in the study. T1DM = type 1 diabetes mellitus

multiple comparisons due to the exploratory nature of this analysis, although Bonferroni correction for 50 statistical tests would indicate significance at P <0.001.

3 | RESULTS

Our database search yielded 89 patients who underwent bariatric surgery and were labelled as having type 1 diabetes. On further manual review, 28 patients were excluded because they did not satisfy criteria for type 1 diabetes (22), they underwent an alternative endoscopic procedure for weight loss rather than bariatric surgery (3) or bariatric surgery was performed before type 1 diabetes was confirmed (3). Of the remaining 61 patients, 47 had positive anti-GAD and/or anti-IA2 antibodies. In four patients, antibodies were negative but C-peptide was <0.37 nmol/L or undetectable. In the remaining 10 patients, the diagnosis of type 1 diabetes was based on a typical history of acute onset of symptoms, young age and the need for insulin from the time of diagnosis. Details of the criteria used in each case are presented in Table S1.

Thirty-one of the patients (51%) were women. According to their records, 57 (93%) were Emirati Arab, three (5%) were other Arab and one (2%) was White in origin. The mean (range) age at the time of diagnosis of diabetes was 18 (1-45) years, while the mean (range) age at bariatric surgery was 31 (18-51) years. Six patients (10%) used insulin pump systems while 55 (90%) used multiple daily injection therapy. Forty-two patients (69%) underwent sleeve gastrectomy, 17 (28%) gastric bypass and two (3%) gastric banding. Eighteen patients (30%) underwent surgery between 2010 and 2015, while 43 (70%) underwent surgery between 2016 and 2019. The median (range) time from surgery to the last visit assessment was 40 (2-117) months. The timing of follow-up visits followed clinical need, and we therefore took the 6- and 12-month assessments to be the visit times nearest to these time points ± 2 months. Four patients had not been seen for >365 days at the time of database access, and were therefore considered to be lost to follow-up for the purposes of reporting adverse events.

Clinical services were disrupted by the COVID-19 pandemic from March 2020, resulting in a very short duration of follow-up in individuals who underwent surgery shortly before data collection. As a result of this, and schedules of routine clinical screening not being aligned with the study time points, some data were missing at follow-up. Only individuals with complete data preoperatively, and at 6- and 12-month follow-ups were included in statistical analysis (n = 48). No significant effect of sex was detected on any of the variables studied, and therefore only analyses of the entire group are presented. Due to the small number of participants who were not of Arab Emirati origin, we were unable to explore the effects of ethnicity.

3.1 | Weight loss

Biometric values for 48 patients (79%) without missing data are presented in Table 1. The median BMI in this group was 38.5 (34.9-40.9)

TABLE 1 Patient characteristics at baseline, and 6 and 12 months after bariatric surgery, in 48 individuals with complete data

	Preoperative	6-month follow-up	12-month follow-up
Weight, kg	104.0 (93.2-117.5)	82.2 (75.4-90.7) P < 0.001 ***	73.9 (67.8-84.6) P < 0.001 ***
BMI, kg/m^2	38.5 (34.9-40.9)	28.7 (26.9-31.9) P < 0.001 ***	26.1 (24.2-29.6) P < 0.001 ***
SBP, mmHg	127 (116-136)	117 (108-123) P < 0.001 ***	116 (110-123) P < 0.001 ***
HbA1c, %	8.6 (7.8-9.2)	7.8 (7.3-9.0) P = 0.013 *	7.8 (7.2-8.5) P = 0.003 **
TDI, units	98 (75-130)	55 (42-70) P < 0.001 ***	56 (44-73) P < 0.001 ***
TDI units/kg body weight	1.0 (0.7-1.2)	0.7 (0.5-0.8) P < 0.001 ***	0.8 (0.6-0.9) P < 0.001 ***
TC:HDL cholesterol ratio	3.39 (2.92-4.31)	3.16 (2.78-3.91) P = 0.008 **	2.99 (2.55-3.50) P < 0.001 ***
TC, mmol/L	4.50 (3.80-5.12)	4.10 (3.69-4.70) P = 0.023 *	4.05 (3.60-4.51) P = 0.046 *
HDL cholesterol, mmol/L	1.23 (1.08-1.40)	1.21 (1.10-1.50) P = 0.402	1.30 (1.20-1.66) P < 0.001 ***
LDL cholesterol, mmol/L	2.90 (2.30-3.60)	2.65 (2.29-3.20) P = 0.022 *	2.40 (2.13-3.23) P = 0.009 *
Triglycerides, mmol/L	1.10 (0.79-1.33)	0.80 (0.70-1.11) P = 0.002 **	0.75 (0.55-1.02) P < 0.001 ***

Note: Data are expressed as median (interquartile range). Significance assessed with paired Wilcoxon rank-sum tests.
Abbreviations: BMI, body mass index; HbA1c, glycated haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TC, total cholesterol; TDI, total daily insulin dose.
*P <0.05. **P <0.01. ***P <0.001.

TABLE 2 Renal values at baseline and 12 months after bariatric surgery, in 48 individuals with complete data

	N	Preoperative	12 months	P
eGFR (mL/min/1.73 m2)	48	122 (103-135)	122 (108-132)	0.600
Preop eGFR >135 mL/min/1.73 m^2	10	141 (136-146)	134 (132-145)	0.033 *
UACR (preoperative microalbuminuria)	7	12.4 (7.0-20.1)	3.0 (1.3-3.5)	0.023 *
UACR (preoperative albuminuria)	4	140.0 (117.5-268.5)	39.1 (7.2-108.8)	0.100
UACR (any preoperative albuminuria)	11	27.5 (10.8-113.0)	3.6 (2.2-9.3)	0.004 **

Note: Microalbuminuria was defined as urine albumin:creatinine ratio >3.0 mg/mmol; albuminuria was defined as urine albumin:creatinine ratio >30 mg/mmol. Values are expressed as median (interquartile range). Significance assessed with paired Wilcoxon rank-sum test.
Abbreviations: eGFR, estimated glomerular filtration rate; UACR, urine albumin:creatinine ratio.
*P <0.05. **P <0.01.

kg/m^2 preoperatively, 28.7 (26.9-31.9) kg/m^2 at 6 months and 26.1 (24.2-29.6) kg/m^2 at 12 months postoperatively. The median reduction in BMI was 9.2 (5.8-10.8) kg/m^2 at 6 months and 11.4 (9.2-13.1) kg/m^2 at 12 months (P <0.001 for both comparisons). The median weight was 104.1 (93.2-117.5) kg preoperatively, 82.3 (75.4-90.7) kg at 6 months postoperatively and 73.9 (67.7-84.6) kg at 12 months. The median percentage weight loss at 6 months was 23.6 (16.6-27.3)% and at 12 months was 30.5 (25.1-33.8)%. The median percentage of excess BMI loss at 6 months was 69.1 (53.8-84.3)% and at 12 months was 91.4 (69.3-108.6)%. The median percentage excess weight loss was 67.9 (54.0-82.8)% at 6 months and 90.8 (69.3-112.2)% at 12 months postoperatively.

3.2 | Glycaemic control

In the 48 patients with complete data (Table 1), the median HbA1c was 8.6 (7.8-9.2)% preoperatively, 7.8 (7.3-9.0)% at 6 months postoperatively and 7.8 (7.2-8.5)% at 12 months postoperatively (P = 0.013, P = 0.003, respectively). Total daily insulin doses decreased by a median of 44 (27-54)% at 6 months and 40 (24-55)% at 12 months (P <0.001 for both). The median daily insulin requirements adjusted for body weight decreased from 1.0 (0.7-1.2) unit/kg preoperatively to 0.7 (0.5-0.8) unit/kg at 6 months and 0.8 (0.6-0.9) unit/kg at 12 months of follow-up (P <0.001 for both comparisons).

3.3 | Hypertension

In 48 patients with complete data at all time points (Table 1), median systolic blood pressure improved from 127 (116-136) mmHg at baseline to 117 (108-123) mmHg at 6 months and 116 (110-120) mmHg at 12 months postoperatively (P <0.001 for both comparisons). Eight of 18 individuals taking antihypertensive medication preoperatively (44%) had discontinued treatment by 12 months post-surgery. A total of 36 individuals stopped or reduced medication, showed a reduction in systolic blood pressure, or both, and therefore met ASMBS criteria for an improvement in blood pressure at 12 months postoperatively (Appendix S1). Of 30 individuals with prehypertension or hypertension prior to surgery, four met criteria for partial remission and 20 met criteria for full remission of hypertension at 12 months postoperatively, with the limitation that only systolic blood pressure was analysed.

3.4 | Dyslipidaemia

Median lipid parameters for 48 individuals with complete data at all time points studied are presented in Table 1. TC:HDL cholesterol ratio improved from 3.4 (2.9-4.3) preoperatively to 3.2 (2.8-3.9) at 6 months and 3.0 (2.6-3.5) at 12 months postoperatively (P = 0.008, P <0.001, respectively). In the same individuals, significant reductions in LDL cholesterol and triglycerides were seen at both 6 and 12 months postoperatively. HDL cholesterol was not changed at 6 months but increased significantly at 12 months after surgery (P = 0.40, P <0.001, respectively). Seven of twenty-two individuals (32%) initially treated with a lipid-lowering agent had discontinued this treatment at 12 months.

3.5 | Renal complications of diabetes

Values for UACR and eGFR for 48 patients with complete data are presented in Table 2. A significant reduction in UACR was seen in patients with preoperative microalbuminuria (n = 7; P = 0.023) but not

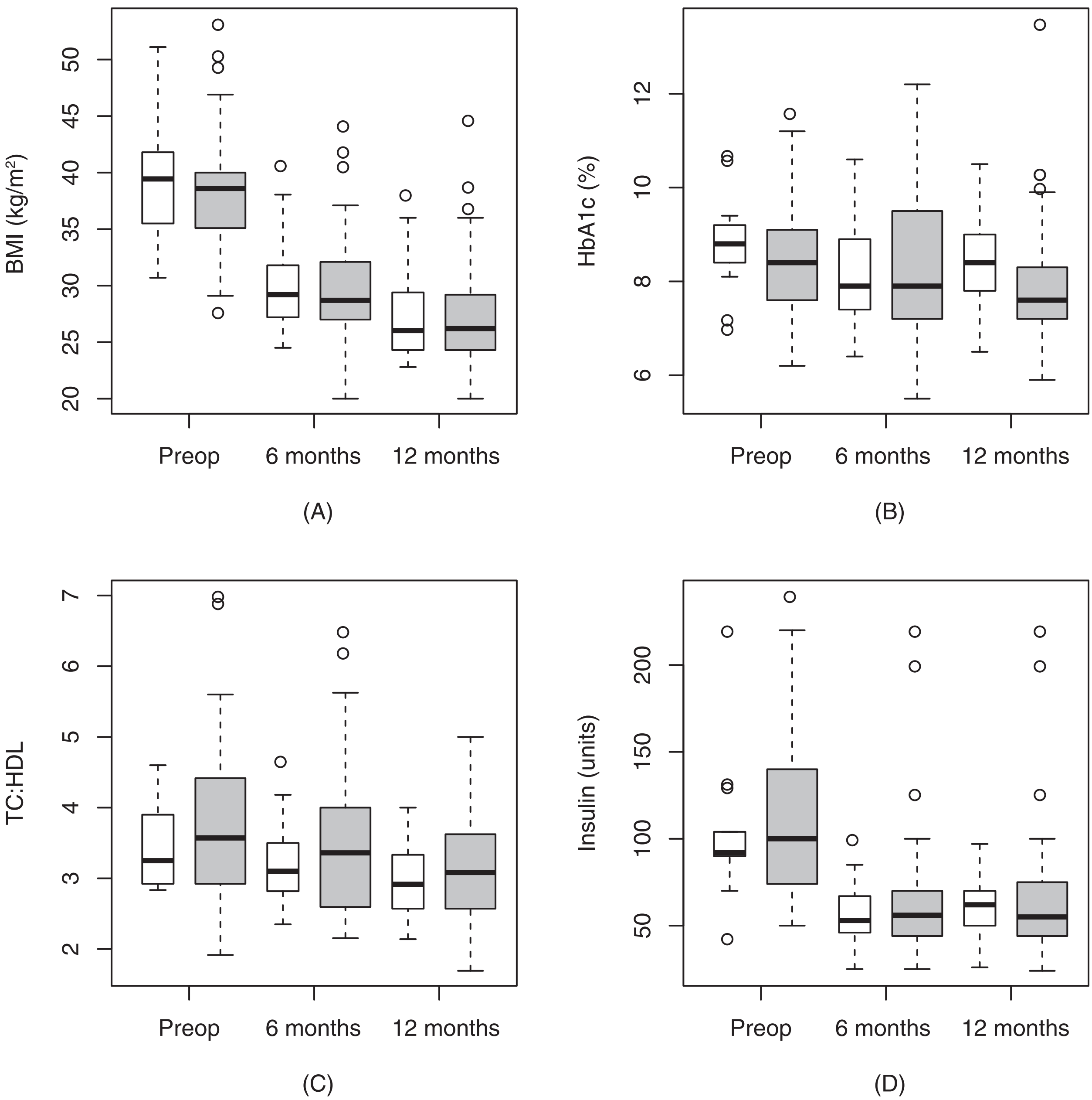

FIGURE 2 Comparison of the effects of gastric bypass and sleeve gastrectomy at 6 and 12 months following bariatric surgery, in individuals with complete data. (A) Body mass index (BMI), (B) glycated haemoglobin (HbA1c), (C) total cholesterol:HDL cholesterol ratio (TC:HDL), (D) total daily insulin dose (units). White denotes bypass procedure, grey denotes sleeve gastrectomy. Tukey plot shows median, interquartile range (IQR), IQR ± 1.5 * IQR. Bar width is proportional to the square root of the number of participants in each group

in individuals with preoperative albuminuria of >30 mg/mmol (n = 4; $P = 0.100$). Combining both groups, there was a significant reduction in UACR at 12 months (n = 12; $P = 0.004$). Patients with a preoperative eGFR of >135 mL/min/1.73 m^2 (n = 10), potentially suggestive of hyperfiltration, demonstrated a decrease in eGFR at 12 months postoperatively ($P = 0.03$). Postoperative eGFR in patients with preoperative eGFR ≤135 mL/min/1.73m^2 (n =38) did not change significantly at 12 months ($P = 0.129$).

3.6 | Patients who completed 3 years of follow-up

Thirty-two patients (53%) were reviewed at 36 months after bariatric surgery. In this group, the median reduction in BMI was 10.4 (5.9-11.7) kg/m^2, and the median reduction in weight was 25.6 (17.5-31.0)%. BMI was not significantly greater than at 12 months postoperatively (median difference 1.2 [−1.1 to 2] kg/m^2; $P = 0.304$). The median insulin dosage was 59 (49-78) units per day at 3 years

TABLE 3 Baseline characteristics and postoperative follow-up data of the Imperial College London Diabetes Centre cohort of patients with type 1 diabetes who had bariatric surgery and those of type 2 diabetes patients in the metabolic surgery arm of the STAMPEDE study[8,9]

Variable	Baseline		12 months		36 months	
	ICLDC	STAMPEDE	ICLDC	STAMPEDE	ICLDC	STAMPEDE
Number of patients	61	100	54	99	32	98
Age, years	31 ± 8	48				
Women, %	51	68	54		50	
Ethnicity, % White Arab Other	2 98 0	73 0 27				
Type of diabetes	Type 1	Type 2				
Diabetes duration at surgery, years	11.9	8.5				
Insulin use, %	100	22				
Dyslipidaemia, %	43	84				
Hypertension, %	31	65				
Albuminuria, %	30	29				
Gastric bypass, n (%)	17 (28)	50 (50)				
Sleeve gastrectomy, n (%)	42 (69)	50 (50)				
Weight, kg	109 ± 18	104	78 ± 14	76.4	79 ± 13	80
BMI, kg/m^2	39 ± 6	37	28 ± 5	27	28 ± 4	29
SBP, mmHg	126 ± 15	135	116 ± 13	132	118 ± 10	134
HbA1c, %	8.5 ± 1.3	9.2	8.0 ± 1.4	6.5	8.3 ± 1.4	6.9
LDL, mmol/L	3.1 ± 0.9	2.5	2.6 ± 0.7	2.6	2.5 ± 0.5	2.6
HDL cholesterol, mmol/L	1.3 ± 0.3	1.2	1.5 ± 0.4	1.5	1.5 ± 0.5	1.5
Triglycerides, mmol/L	1.4 ± 1.5	1.9	0.8 ± 0.3	1.1	0.9 ± 0.6	1.1
Δ weight, kg			−30 ± 12	−27	−27 ± 12	−24
Δ weight, %			−27 ± 9	−27	−25 ± 10	−23
Δ BMI, kg/m^2			−11 ± 4	−9.6	−9 ± 4	−8.3
Δ SBP, mmHg			−9 ± 16	−3.8	−8 ± 16	+1.6
Δ HbA1c, %			−0.6 ± 1.3	−2.3	−0.5 ± 1.4	−2.5
Δ LDL cholesterol, %			−9 ± 28	−14.8	−15 ± 17	−15.7
Δ HDL cholesterol, %			15 ± 22	28.5	19 ± 25	+34.9
Δ Triglycerides, %			−23 ± 46	−43.0	−29 ± 42	−38.7
Stop /↓ lipid Rx					58%	55%
Stop / ↓ aHT Rx					50%	49%

Note: Values are presented as mean ± standard deviation, unless otherwise indicated.
Abbreviations: ↓, reduced dose; aHT, antihypertensive; BMI, body mass index; HDL, high-density lipoprotein; ICLDC, Imperial College London Diabetes Centre; LDL, low-density lipoprotein; Rx, treatment; SBP, systolic blood pressure.

compared with a baseline dose of 100 (74-131) units per day, or 0.84 (0.61-0.99) compared with 1.05 (0.71-1.16) units/d/kg (P <0.001, P = 0.017 respectively). One individual was missing HbA1c data at 36 months; HbA1c in the 31 patients with complete data did not differ significantly from preoperative values (8.7 (7.85-9.25)% preoperatively, 8.4 (7.35-9.3)% at 3 years; P = 0.371).

Analysis of lipid profile is limited by missing data at the 36-month follow-up time point. LDL cholesterol decreased from 2.95 (2.20-3.60) to 2.30 (2.14-2.86) (n = 24; P <0.001) while HDL cholesterol increased from 1.20 (1.08-1.60) to 1.53 (1.20-1.90) (n = 16; P = 0.018). Lipid-modifying agents were reduced or stopped in 11 of 19 patients (58%), while antihypertensive agents were reduced or stopped in 10 of 20 patients (50%) on medical treatment for these conditions preoperatively.

3.7 | Comparison of sleeve gastrectomy with gastric bypass

We compared the outcome of surgery in the individuals without missing data, between 33 patients who underwent sleeve gastrectomy and 13 patients who underwent a gastric bypass procedure. Two patients who underwent gastric banding were excluded from further analysis due to inadequate sample size. The effects of sleeve gastrectomy and gastric bypass surgery on BMI, HbA1c, TC:HDL cholesterol ratio and total daily insulin dose were comparable, as illustrated in Figure 2. In linear mixed-effects models, the effect of time was significant but the interaction between time and procedure type was not significant for each analysis, implying no difference in effect between the two procedures.

3.8 | Comparison with patients with type 2 diabetes in the STAMPEDE study

We compared our results with those of the STAMPEDE study, which examined the effects of bariatric surgery in type 2 diabetes patients, at 1 and 3 years.[8,9] Baseline characteristics of the entire cohort and the STAMPEDE operated group, along with similar comparisons at 1 and 3 years after surgery are presented in Table 3. Our cohort achieved comparable improvements in weight, systolic blood pressure, lipid variables and the number of patients requiring lipid-modifying or antihypertensive medications. The mean improvements in HbA1c, however, were 0.6% and 0.5% at 1 and 3 years in the ICLDC cohort compared to the greater reduction in HbA1c of 2.3% and 2.5% at 1 and 3 years, respectively, in the STAMPEDE participants.

3.9 | Adverse events

In our series, three cases of diabetic ketoacidosis (DKA) were reported by three patients, all of whom were treated with sleeve gastrectomy. In one patient, DKA was precipitated by omission of insulin in the perioperative period despite clear advice from his physician to the contrary.

4 | DISCUSSION

In this cohort of patients with coexisting obesity and type 1 diabetes, we found that bariatric surgery had a modest effect on glycaemic control but was effective in reducing weight and improving metabolic variables associated with cardiovascular risk. Reductions in daily insulin requirements occurred in all patients, while of those who were followed up for 36 months, a large proportion were able to reduce or stop treatment for dyslipidaemia or hypertension and sustained improvements were observed in biometric and metabolic variables.

A systematic review and meta-analysis of all available case series and reports of patients with obesity and type 1 diabetes treated by bariatric surgery published in 2016 identified a total of 107 cases worldwide.[12] A recent large cohort study from Sweden also looked at the long-term benefits and harms of bypass surgery in these patients.[21] Previous studies have tested the use of adjunctive therapies to help with weight loss in patients with type 1 diabetes, including metformin, glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors, all with limited and temporary success.[22–24]

The improvement in glycaemic control in the study cohort was modest and comparable to that previously reported,[12,13,21] albeit in the context of a marked and significant reduction in daily insulin requirement. Possible mechanisms for the improvement in glycaemic control include reduced caloric intake, reduction in obesity-associated insulin resistance and reduction in lipotoxicity.[12] It is crucial to counsel patients with type 1 diabetes and obesity who are contemplating bariatric surgery to expect considerably more modest improvements in glycaemic control than those seen in patients undergoing metabolic surgery for type 2 diabetes and obesity. Patients must also be informed regarding the absolute need to continue lifelong insulin treatment.

Insulin resistance and other features of metabolic syndrome are important contributory factors to the excess risk of atherosclerotic cardiovascular disease in patients with type 1 diabetes. An analysis of the DCCT/EDIC studies demonstrated that weight gain resulting from intensive insulin therapy was associated with insulin resistance and excess risk of atherosclerosis.[25,26] Furthermore, a study based in Scotland[27] identified a very high long-term risk of ischaemic heart disease and cardiovascular mortality in patients with type 1 diabetes. Cardiovascular disease, nephropathy and death are more prevalent in people with type 1 diabetes who have features of metabolic syndrome,[3,26,28] emphasizing the importance of addressing cardiovascular risk factors in these patients.[29] The recent Swedish study showed that bariatric surgery in obese individuals with type 1 diabetes reduced the incidence of cardiovascular mortality.[21] In our cohort, bariatric surgery had beneficial effects on blood pressure, lipid profile, and total daily insulin dose per kilogram of body weight. Although we did not estimate it directly, it seems likely that these changes would be associated with a reduction in insulin resistance.

In our cohort we observed reductions in glomerular hyperfiltration and albuminuria. Diabetic kidney disease is an important complication of type 1 diabetes. Glomerular hyperfiltration is considered to be an early manifestation of diabetic kidney disease and has been shown to be predictive of a more rapid decline in measured GFR in individuals with type 1 diabetes[30,31] as well as in individuals with type 2 diabetes or normoglycaemia.[32] Cohen et al[33] demonstrated that Roux-en-Y gastric bypass surgery (RYGB) achieved remission of albuminuria in 82% of a cohort of individuals with type 2 diabetes, while Bjornstad et al[34] reported higher rates of glomerular hyperfiltration and elevated urinary albumin excretion at follow-up in a study of adolescents with type 2 diabetes receiving medical therapy than in a demographically similar group who underwent RYGB or sleeve gastrectomy. Molitch et al,[35] however, reported that over a median follow-up of 28 years, initial measured GFR >130 mL/min/1.73m^2 was not associated with increased incidence of renal deterioration, expressed as an eGFR <60 mL/min/1.73m^2, in participants in the DCCT/EDIC trial, suggesting that initial glomerular hyperfiltration is not associated with worse clinical outcomes in this group.

In our series, sleeve gastrectomy and gastric bypass had equivalent effects on weight and metabolic variables. With regard to postoperative complications, previous case series have shown that patients treated by gastric bypass can have fluctuations in glycaemic levels which may precipitate DKA or hypoglycaemia, and individuals with type 1 diabetes who undergo bariatric surgery are at increased risk of both hyper- and hypoglycaemic events as well as DKA when compared with matched controls.[12,21,36] DKA can also be precipitated by nausea and vomiting, the stress of surgery as well as abrupt discontinuation of insulin in the context of reduced oral intake in the immediate postoperative period.[36] In our series, all three patients who developed DKA were treated by sleeve gastrectomy.

The 2021 American Diabetes Association guidelines state that "although metabolic surgery has been shown to improve the metabolic profiles of patients with type 1 diabetes and morbid obesity, establishing the role of metabolic surgery in such patients will require larger and longer studies".[11] We report that bariatric surgery in patients with type 1 diabetes resulted in weight reduction and cardiometabolic benefits of similar magnitude to those achieved in patients with type 2 diabetes.[8,9] Similar to patients with type 2 diabetes,[9] we have demonstrated that a weight loss of 21% of baseline weight can be maintained for at least 3 years in patients with type 1 diabetes following bariatric surgery, accompanied by similar benefits with regard to the lipid profile and need for lipid-modifying and anti-hypertensive medications.

Strengths of the present study include the large number of patients followed at a single institution, together with our use of strict criteria for definition of type 1 diabetes. The main limitation was the lack of access to medical notes covering the immediate post-operative period, meaning that postoperative complications such as DKA and hypoglycaemia depended on patient recall and may therefore be underestimated. Bias in adverse event reporting may also have been introduced due to loss to follow-up of a small proportion of the participants, and by missing data at the specific timepoints studied. The analysis of eGFR results should be interpreted with caution since the accuracy of the CKD-EPI equation is limited at higher eGFR values and since we did not measure cystatin-C. Missing data resulted in only a subset of participants being included in statistical analysis, which may have introduced bias since individuals who are more engaged with their follow-up may tend to have better clinical outcomes. We were not able to assess patients' quality of life after surgery, an important consideration which limits the generalizability of our results.

In conclusion, we found that bariatric surgery in patients with obesity and type 1 diabetes, can result in significant and sustained improvements in weight and several cardiometabolic variables, along with reductions in insulin requirements and modest improvements in glycaemic control. These beneficial effects have recently been shown to lead to reduction in cardiovascular events, including cardiovascular mortality.[21] Effects on quality of life have not been established.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

N.M. and M.S. conceived the study and performed data collection. M.S., N.M. and A.B. analysed the data and wrote the manuscript. M.E., M.A., S.S., M.A.H., C.W.I.R. and N.L. contributed to data analysis, edited and revised the manuscript. M.S. is the guarantor of this work and, as such, had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Author elects not to share data

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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