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REVIEW ARTICLE

Bariatric Surgery in Type 1 Diabetes Mellitus: A Systematic Review

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Abstract Bariatric surgery is recognised as an effective treatment strategy for obese patients with type 2 diabetes mellitus. An increasing number of patients with type 1 diabetes mellitus also suffer with obesity and obesity-associated comorbidities but the role of bariatric and metabolic surgery in this group of patients is unclear. This systematic review investigates published English language scientific literature to understand the results of bariatric surgery in obese patients with type 1 diabetes mellitus. We found that these patients can experience significant weight loss and comorbidity resolution with bariatric surgery. Though most patients also see a decline in total insulin requirement, glycaemic control remains difficult. Most of the patients reported in literature have undergone gastric bypass but data is insufficient to recommend any particular procedure.

Keywords Bariatric surgery · Obesity surgery · Gastric bypass · Roux-en-Y gastric bypass · Sleeve gastrectomy · Gastric banding · Biliopancreatic diversion · Type 1 diabetes mellitus

Abbreviations

T2DM	type 2 diabetes mellitus
T1DM	type 1 diabetes mellitus
RYGB	Roux-en-Y gastric bypass
SG	sleeve gastrectomy
BPD	biliopancreatic diversion
LADA	latent autoimmune diabetes in adults
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
GLP-1	glucagon-like peptide 1
PYY	peptide YY

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Introduction

Bariatric surgery is now universally recognised to be an effective treatment strategy for selected obese patients with type 2 diabetes mellitus (T2DM). In comparison, literature on the effect of bariatric surgery on type 1 diabetes, mellitus (T1DM) is somewhat limited. Most of the studies describing any experience with bariatric surgery in T1DM patients suffer with very small sample sizes and there are only three studies comparing the effect of bariatric surgery in T1DM patients with that in T2DM patients [1–3]. This is likely to become an even more important topic in the future with rising prevalence of obesity in patients suffering with T1DM. Approximately 12.6 % of youths with T1DM are obese [K] and up to half of the patients are either overweight or obese [4]. The obesity epidemic and intensive insulin treatment have been held responsible for it [4]. Moreover, it seems T1DM may occur at an earlier age in obese individuals with genetic predisposition and increases the risk of complications [5, 6]. Though typically type 1 DM presents in children and young adults, it can present at any age. There is another variant of type 1 diabetes mellitus called latent autoimmune diabetes in adults (LADA), which typically presents after the age of 30 [1, 7]. Currently, there is no systematic review in scientific literature on this topic. This review systematically examines published English language scientific literature on the effect of bariatric surgery on T1DM, in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Methods

An online search of PubMed, Medline, Embase, and Google Scholar was independently carried out by two researchers using keywords like "bariatric surgery", "metabolic surgery", "gastric bypass" "Roux en Y Gastric Bypass (RYGB)", "Mini Gastric Bypass", "Single Anastomosis Gastric Bypass", "Sleeve Gastrectomy (SG)", "Gastric Banding", "Biliopancreatic Diversion (BPD)", "Duodenal Switch", and "Type 1 Diabetes Mellitus" to identify all articles on the role of bariatric and metabolic surgery in patients with T1DM. Articles were also identified from references of relevant articles. Last of these searches was carried out on 25 June 2015.

A total of 22 articles were identified on the subject of bariatric surgery in type 1 diabetes mellitus. However, a number of them were excluded from cumulative analysis for various reasons. Some articles [8, 9] were excluded, as they did not describe any experience. Czupryniak et al. have published two papers [10, 11] on this topic. However, their latter paper [11] also includes the two cases described in the former [10]; the former study [10] was hence excluded. Similarly, Middlebeek et al. published two articles [12, 13]. However, most patients overlapped between the two studies. So, we included their latter study [13] in cumulative analysis, which also had one more patient than the former [12]. Animal studies and articles [14, 15] were also excluded from the systematic review. There was another study [16] where abstract had mentioned experience with T1DM patients but in reality the patients had T2DM and the description in abstract must have been in error. Finally, 15 articles were included in our cumulative analysis.

Three of these articles compared the results of bariatric surgery between T1DM and T2DM patients. Data from these articles were used to determine cumulative comparative experience in these two groups. We did not use any statistical comparison of data between type 1 and type 2 diabetes groups, as there will be significant risks of error in absence of raw data for any of these studies and their heterogeneous nature. Figure 1 gives a PRISMA flow chart for article selection.

Results

This review identified a total of 15 studies describing experience with various bariatric surgical procedures in patients suffering with type 1 diabetes. Table 1 [1, 2–3, 13, 23, 17–26] lists qualitative characteristics of these studies.

Cumulative Total Experience A total of 15 studies describe bariatric surgery in 89 obese patients with T1DM over a period from August 2000 and May 2013. Out of these, 86.5 % (n=58/67) were females. The mean age was 40.7 years (n=67). The mean weight and BMI was 124 kg (n=24) and 42.6 kg/m^2, respectively. Roux-en-Y gastric bypass accounted for 70 % of the bariatric procedures (n=62/89) in these patients. Sleeve gastrectomy (14.6 %, n=13/89), biliopancreatic diversion (13.5 %, n=12/89), and gastric banding (2.2 %, n=2/89) accounted for the remainder. There was no mortality reported in any of these patients. Complications were reported in 9 patients but we cannot be certain of the denominator as most of these studies focussed on weight loss and diabetic outcomes. Weight loss and comorbidity resolution were satisfactory. It is not possible to provide cumulative numbers for weight loss and resolution in hypertension or dyslipidaemia because of significant variation in reporting methods in different studies. Total insulin requirement improved in almost all studies and requirement in terms of units/kilogram/day improved in 8 out of 15. However, two studies [3, 17] did not show any improvement in insulin requirement expressed per unit weight. Glycaemic control remained unaltered in most patients after surgery, improved in some, and worsened in a few.

Cumulative Comparative Experience Three studies in this review compared the experience with bariatric surgery in T1DM and T2DM patients. Table 2 presents cumulative comparative experience. It is obvious from Table 2 that patients with T1DM have similar weight loss and comorbidity resolution but do not experience the significantly improved glycaemic control seen with T2DM patients.

Discussion

T1DM accounts for about 5–10 % of all cases of diabetes, and its incidence seems to be increasing worldwide [18–21]. It results from an autoimmune destruction of insulin-producing beta cells [22]. A large proportion of patients with T1DM suffer with metabolic syndrome and hypertension, and cardiovascular disease is now the leading cause of death in these patients [23, 24]. It is hence important that treatment strategies aimed at T1DM also address metabolic syndrome and cardiovascular disease risk factors. Bariatric surgery is recognised to be effective for both of these conditions [25, 26].

At the same time, T1DM is a different disease compared to T2DM. Whereas one could reasonably expect weight reduction and altered hormonal milieu, seen with bariatric surgery, to result in significant improvements in insulin resistance, patients with pure T1DM stand nothing to gain from these peripheral changes as the disease process mainly revolves around the pancreas. This has traditionally been the case with T1DM as patients were either normal or underweight. With the advent of obesity epidemic, the landscape of T1DM is changing and now approximately half of these patients are either overweight or obese. Bariatric surgery is recognised as one of the most effective long-term solutions for obesity.

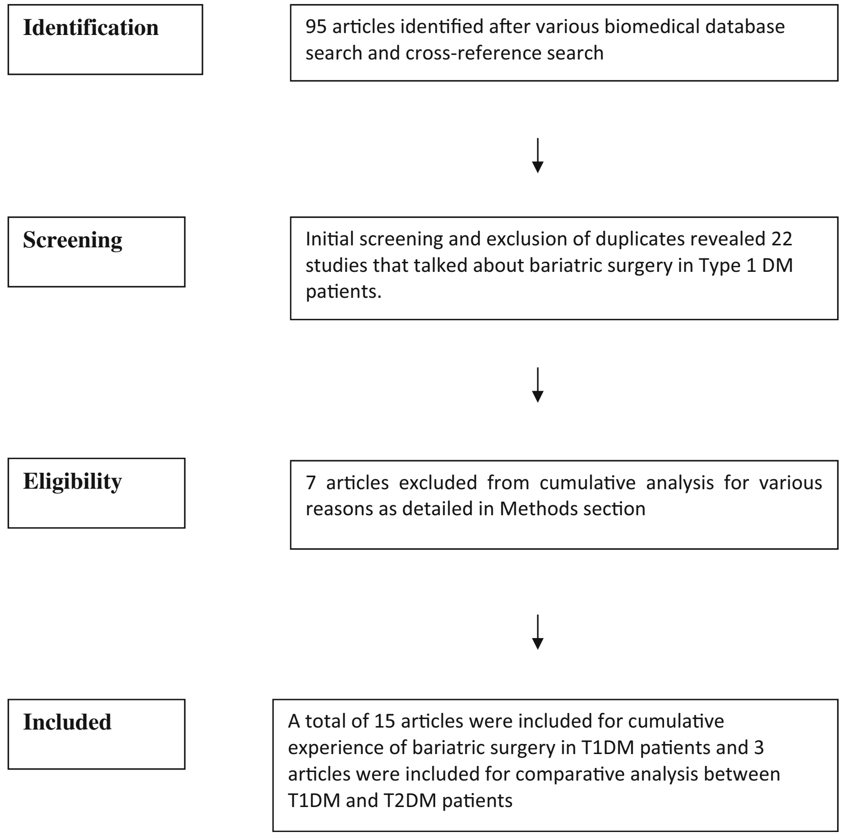

Fig. 1 PRISMA flow chart for article selection

Given that bariatric surgery can bring about real improvements in the lives of obese patients suffering with T1DM, it becomes important to understand the results with bariatric surgery in these patients. Over the last decade, a number of authors have reported on their experience with this group of patients. However, lack of a systematic review has made interpretation of data from small studies difficult. This prompted us to carry out the current review.

This review shows that total insulin requirement decreases in the majority of T1DM patients after bariatric surgery. Most studies also reported a significant reduction in insulin requirement expressed as units/kilogram but a few did not [3, 17]. These results are significant as the main problem in T1DM patients is impaired secretory capacity of beta cells and differences in pathogenesis compared to the commoner T2DM are widely recognised. Improved understanding of mechanisms underlying reduction in insulin requirement could open up newer areas for research into pathogenesis and management of diabetes mellitus (Reviewer 2, Comment 2, and Comment 4). Some of the potential factors responsible for this could be reduction in insulin resistance, improvement in function of remaining beta cell, preservation of beta cell mass, and increased hepatic insulin sensitivity. It is probable that just like patients with T2DM [27], there are multiple underlying mechanisms at play including weight loss [1], altered hormonal milieu, reduction in calorie intake, and reduction in pancreatic and liver triacylglycerol. Preservation of beta cell mass and function may be more important in those with LADA, which was seen in three patients (n=3/89, 3.3 %) in this review [1, 28, 29]. Moreover, it is possible that some of these patients have “Double Diabetes” on the basis of recent findings that that some T1DM patients actually suffer with both T2DM and T1DM [30, 31]. These individual have both insulin resistance (due to obesity) and evidence of autoimmunity against beta cells. It is suggested that obesity may “accelerate” beta cell destruction in such genetically susceptible individuals.

Dirksen et al. [32] noticed significant improvement in insulin requirement within a week of surgery, which was associated with marked increases in postprandial glucagon-like peptide 1 (GLP-1) and peptide YY (PYY) secretions. Same authors also noticed a brisk rise in glucose reaching maximal concentration 1-h postprandial indicating faster glucose absorption. Authors suggested that treatment with a faster acting insulin analogue before meals may be better than regular human insulin to control postprandial hyperglycaemia. Authors wondered if GLP-1 response could even lead to regeneration of some beta cells in the long term. Though there is some basis [33–35] for such a theory, convincing evidence is lacking. Blanco et al. [3] found in their comparative study of the effect of RYGB on T1DM and T2DM patients that despite statistically “not different” effect on GLP-1 and glucagon response between the two groups, glycaemic control in T1DM group

Table 1 Experience with bariatric surgery in T1DM patients

Authors	Mean age	Weight (kg)	BMI (kg/m^2)	Procedures	Weight loss	Mortality	Morbidity	Comorbidity remission	Alteration in insulin requirements	HbA1c levels	Duration of diabetes (years)
Robert [1] Retrospective Comparative study Level III Number=10, M:F=2:8 Time period 2004 to May 2013	39.2	NA	46.9	SG =3 BPD=7	Mean EWL of 70.17 % (mean FU of 55 months)	0	NA	Hypertension in 66.7 % and dyslipidaemia in 88.9 %	Decreased from 1.09 to 0.44 units/kg/day	7.1 % postop vs to 7.5 % preop (NS)	23.1
Chuang [17] Case series Level IV Number=2, M:F=1:! Time period: NA	16	142	50.6	RYGB=1 SG=1	BMI came down to 30.2 (FU 12 months) and to 34.9 (FU 28 months), respectively	0	NA	Patient 1 does not require treatment for dyslipidaemia and sleep apnoea. Patient 2 with PCOS has regular menses and does not need OCP anymore	Decreased, but insulin requirement/kilogram/day did not change much	HbA1c unchanged	5.5
Fuertes-Zamorano [45] Case series Level IV Number=2, M:F=0:2 Time period: NA	32.5	117	46.9	BPD=2	BMI came down to 24.5 at 5 years in first patient and to 23.3 in second patient	0	0	Resolution of dyslipidaemia in first patients and both hypertension and dyslipidaemia in second	Decreased in first patient from 1.21 to 0.98 units/kg/day and in second patient to 0.45 units/kg/day from 0.74 units/kg/day	7.6 % postop vs 6.2 % preop at 5 years	29.5
Raab [28] Case series Level IV Number=6, M:F=0:6 Time period: NA	43	NA	41.7	RYGB=2 SG=1 BPD=3	Mean BMI 30 at 6 months and 27.8 at 12 months	0	NA	NA	Decreased from 0.86 to 0.38 units/kg at 6 months (n=5) and 0.4 units/kg at 12 months (n=4)	6.9 % postop vs 8.2 % preop	17.1
Manning [29] Case report Level IV Number=1, M:F=0:1 Time period: NA	43	106	35	RYGB=1	38 % total body weight loss at 1 year	0	NA	NA	Insulin was discontinued initially as patient was mistakenly presumed to be T2DM. Later diagnosed as LADA	NA	7
Lannoo [38] Case series Level IV Number=1, M:F=NA Time period: NA	NA	NA	39.7	RYGB=16 SG=6	BMI decreased to 31.4	3	4	NA	Decreased from 0.8 to 0.5 units/kg	8.2 % postop vs 8.4 % preop	NA
Brethauer [46] Case series	45.6		41.6	RYGB=7 AGB=2	EWL of >60 %, mean BMI 27.0	0	5	Hypertension in 71 % (n=5/7). albuminuria	Decreased from 0.74 to 0.40 units/kg	8.9 % postop vs 10.0 % preop	22

Table 1 (continued)

Authors	Mean age	Weight (kg)	BMI (kg/m^2)	Procedures	Weight loss	Mortality	Morbidity	Comorbidity remission	Alteration in insulin requirements	HbA1c levels	Duration of diabetes (years)
Level IV Number=10, M:F=1:9 Time period: January 2005 to December 2012				SG=1	(mean FU 36.8 months)			resolved in one of the two patients. Lipid profile improved significantly			
Reyes Garcia [47] Case report Level IV Number=1, M:F=0:1 Time period: June 2009	43	121	43.3	RYGB=1	Weight came down to 80 kg with a BMI of 28.7 at 10 months	0	NA	NA	"Significant reduction in insulin dose" but clear numbers NA	7.2 % post vs 8.5 % preop at 10 months FU	24
Czupryniak [11] Case series Level IV Number=3, M:F=1:2 Time period: August 2000 to March 2004	23.3	125	42.2	RYGB=3	First patient: 89 kg (BMI 30.5) at 8 years Second patient: 108 kg and BMI of 39.7 at >6 years. Her lowest weight was 89.5 kg at 18 months Third patient: 99.5 kg (BMI 30.4) at 5 years	0	0	100 % remission of hypertension and dyslip idaemia (n=2/3)	Insulin requirements came down from a mean of 0.75 units/kg to 0.55 units/kg. Absolute insulin requirement came down from a mean of 94.6 to 47.6 units	First patient: 6.9 % post op vs 9.5 % Second patient: 7.5 % vs 10.4 % Third patient: 6.8 % vs 10.5 %	11.6
Dirksen [32] Case report Level IV Number=1, M:F=0:1 Time period: NA	35	126.9	48.4	RYGB=1	Weight and BMI came down to 84.8 kg and 32.3 respectively at 1 year	0	0	Significant improvement in hypertension and dyslipidaemia	Decreased from 1.37 to 0.71 units/kg at 1 year	8.8 % postop vs 8.6 % preop	15
Maraka [2] Retrospective comparative study Level III Number=10, M:F=3:7 Time period: May 2008 to April 2013	50.6	NA	44.3	RYGB=9 SG=1	At 2 years, BMI came down to 31.2	0	0	Reduction in medications for dyslipidaemia but not hypertension	NA	7.8 % at 2 years vs 8.2 % preop	20.6
Mendez [48] Case series Level IV Number=3, M:F=0:3 Time period: NA	42.3	130.7	45.9	RYGB=3	At 1 year, the mean weight and BMI were 83.1 kg and 29.4, respectively	0	0		Mean postoperative insulin requirement at 1 year was 0.52 units/kg compared to 0.70 units/kg preoperatively	Unchanged	25

Table 1 (continued)

Authors	Mean age	Weight (kg)	BMI (kg/m^2)	Procedures	Weight loss	Mortality	Morbidity	Comorbidity remission	Alteration in insulin requirements	HbA1c levels	Duration of diabetes (years)
Blanco [3] Retrospective comparative study Level III Number=7, M:F=0:7 Time period: July 2005 to October 2011	38.2	NA	39.4	RYGB=7	Mean BMI of 27.3 and EWL of 82.6 % at 24 months	0	NA	NA	Insulin requirement at 24 months was 0.62 units/kg compared to 0.61 units/kg	8.2 % postop vs 8.3 % preop	NA
Middlebeek [13] Case series Level IV Number=10, M:F=0:10 Time period: NA	39.6	121.9	43.5	RYGB=10	BMI decreased by 33 % from 43.5 to 29.3	0	0	Significant improvements in dyslipidaemia and hypertension at 1 year but changes were not sustained at 5 years	Decreased from 0.42 units/kg preoperatively to 0.27 units/kg at 1 year and 0.37 units/kg at 5 years	8.3 % at 1 year and 9.8 % at 5 years vs 8.1 % preop	24.6
Ziemiański [49] Case report Level IV Number=1, M:F=0:1 Time period: NA	40	139.8	46.2	RYGB=1	At 18 months, BMI came down to 25.8	0	0	Improvement in renal graft function (post-transplant patient)	Decreased from 74 to 40 units/day	NA	NA

NA not applicable, *EWL* excess weight loss, *BMI* body mass index, *NS* not significant, *HbA1c* glycosylated haemoglobin, *FU* follow-up

Table 2 Comparison of cumulative quantitative data from studies comparing bariatric surgery in type 1 and type 2 diabetes mellitus patients

Characteristic	T1DM patients	T2DM patients
Number of patients	27	145
Mean age	43.1	53.1
Mean BMI	44	46.8
Females	22 (81.4 %)	100 (68.9 %)
Procedures	RYGB=16	RYGB=95
	SG=4	SG=19
	BPD=7	BPD=31
Duration of diabetes	21.8 years (*n*=20)[a]	12 years (*n*=138)
Alteration in insulin requirement	Robert [1]: In T1DM, patients came down to 0.44 units/kg/day from 1.09 units/kg/day preoperatively and to 0.03 units/kg/day from 0.9 units/kg/day preoperatively in T2DM group.	
	Maraka [2]: NA	
	Blanco [3]: Remained unaltered at 0.62 units/kg postop in T1DM group compared to 0.64 units/kg preop. Corresponding values in T2DM group were 0.32 and 0.46 units/kg.	
HbA1c at 24 months	7.96 (*n*=17)	6.74 (*n*=125)
Glycaemic control	Robert [1]: In T1DM patients, no statistical difference between preop and last HbA1c (7.5 % vs 7.1 %). However, in T2DM patients, last HbA1c was significantly lower postop HbA1c (5.5 % vs 8.1 %)	
	Maraka [2]: Patients with T2DM had better glycaemic control. At 2 years, HbA1c was 7.8 % (preop 8.2 %) in T1DM patients (*p*=NS) and 6.8 % (preop 7.8 %) in T2DM patients (*p*=0.04).	
	Blanco [3]: Patients with T2DM achieved an HbA1c of 5.9 % (9.4 % preop) at 24 months compared to 8.2 % (8.3 % preop) in T1DM patients.	
Weight loss	Robert [1]: Mean excess BMI loss was 77.1 % in T1DM patients compared to 68.3 % in T2DM. *p*=0.14 (mean FU 55 months)	
	Maraka [2]: At 2 years post surgery, T1DM patients achieved a BMI of 31.2 compared to 33.3 achieved by T2DM patients. (No significant difference)	
	Blanco [3]: At 2 years, T1DM patients achieved a mean BMI and EWL of 27.0 and 82.6 % respectively compared to 30.4 and 87.4 % achieved by T2DM patients.	
Comorbidity resolution	Robert [1]: Remission rates of hypertension (66.7 % vs 62.5 %) and dyslipidaemia (88.9 % vs 75 %) were similar in two groups	
	Maraka [2]: There was no significant difference in need of medications for hypertension and dyslipidaemia between the two groups.	
	Blanco [3]: NA	

NA not applicable, *HbA1c* glycosylated haemoglobin, *EWL* excess weight loss, *BMI* body mass index, *FU* follow-up

[a] Duration of diabetes was statistically longer in T1DM group in both studies that reported on it

was significantly poorer than that in T2DM patients. At the same time, studies have shown that T1DM patients treated with GLP-1 analogues achieve better glycaemic control at lesser insulin dosages [36, 37]. These finding could indirectly support a role for hormonal factors.

Hypoglycaemic episodes have been seen after bariatric surgery by a number of authors in this review [2, 17]. Altered glucose kinetics and difficulty in insulin dosing are probable contributory factors [17]. Some authors believe that sleeve gastrectomy may be a more attractive procedure for patients with T1DM because of more predictable carbohydrate absorption [38]. However, it is worth remembering that hypoglycaemic episodes are also seen with intensive insulin management of T1DM [4].

Weight loss seen in these patients seems to be on expected lines. Even though these patients continue to need some insulin, it does not seem to have a significant impact on weight loss. This was further evident from the three studies [1–3] that compared results in these patients with those seen in T2DM patients. The same is true of comorbidity resolution. Most of the studies in this review have shown satisfactory resolution/improvement of comorbidities.

There are voices [14] suggesting that we might even consider undertaking "clinical studies that address the safety, tolerability, efficacy, and durability of such surgical procedures in non-obese patients with T1DM." Others [22] feel bariatric surgery should be considered early in the course of T1DM to decrease pancreatic beta cell damage. This may have some appeal as intensive insulin treatment typically results in weight gain with consequent worsening of Insulin resistance, dyslipidaemia, and hypertension. Given the fact that a large number of T1DM patients are now obese, it has been suggested that strategies for weight control, including bariatric surgery, should form part of management strategy for these patients much like those with T2DM or even general population [4]. However, these patients will need close, perhaps lifelong, monitoring by an endocrinologist postoperatively because of the continued need for insulin treatment and the need for close titration of insulin regime to decrease the frequency of severe hypoglycaemic episodes.

Much has happened in the field of surgical management of diabetes since Pories first reported on the effect of bariatric surgery in patients with T2DM [39]. Progress has been somewhat slower in T1DM patients. Many authors argue that it is more common in bariatric surgery cohorts than has been appreciated thus far accounting for some of the failure of remissions [9]. In this review, we found many patients [38] were diagnosed with T1DM postoperatively as they were suffering with undiagnosed LADA at the time of surgery. LADA accounts for 2–12 % of cases of diabetes [40] and 3.3 % ($n-3$) patients in this review. Prevalence of LADA in adults presenting with non-insulin-dependent diabetes is approximately 10 % [41].

It is currently unclear if this should prompt more routine investigations for evidence of autoimmunity and c-reactive peptide levels in patients considering bariatric surgery. Though the additional cost implications may not be justified for patients who would benefit from bariatric surgery as such on the grounds of their weight or comorbidities, screening for LADA and Double Diabetes may be appropriate for type 2 diabetics seeking pure metabolic surgery. This will help us target metabolic surgery for T2DM and improve its accuracy and chances of success, some of the biggest challenges facing metabolic surgeons. For all other insulin-dependent patients, it may make more sense to simply monitor diabetic status more closely in the earlier postoperative period with a lower threshold for investigations in patients with difficulties.

This review only includes obese patients with T1DM, who would as such qualify for bariatric surgery on the grounds of their weight and associated comorbidities. Our systematic review sheds light on what these patients can expect in terms of weight loss, comorbidity resolution, and diabetic control. As we can see, this review shows satisfactory weight loss and comorbidity resolution in obese type 1 diabetics undergoing bariatric surgery. In studies comparing outcomes in these patients with those seen with type 2 diabetics, weight loss and comorbidity resolution were similar in two groups. Glycaemic control however did not improve to the extent seen with type 2 diabetics. Bariatric or metabolic surgery is increasingly being recognised for even patients with BMI<35 kg/m^2 and patients with T2DM [42–44] (Reviewer 2, Comment 4). This review is not qualified to comment on the role of surgery for non-obese type 1 diabetics but one suspects it will offer limited advantages.

A number of surgical procedures have been used by surgeons in this group of patients but RYGB accounts for the majority of the procedure. This review cannot make any recommendation on the ideal bariatric procedure for obese patients with T1DM. There are other obvious weaknesses of this review that need to be recognised. There is no level 1 or 2 data available in scientific literature on this topic comprising the strength of the data in this review. Most of the studies describe retrospective experience with a small cohort of patients. Time is now ripe for a well-designed randomised controlled trial assessing the efficacy of adding bariatric surgery to intensive insulin management for selected obese patients with T1DM.

Conclusion

Obese T1DM patients can expect significant weight loss, comorbidity resolution, and reduction in insulin doses with bariatric surgery. Surgery does not however result in improved glycaemic control in a significant proportion of patients.

Authors' Contribution KM conceived the idea for the topic. KM and ND independently collected information and analysed it. All authors participated in departmental discussion on the topic and manuscript writing. All authors have seen the final version and approve of it.

Compliance with Ethical Standards

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

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