OBES SURG
DOI 10.1007/s11695-014-1460-2

REVIEW ARTICLE

The Long-Term Effects of Bariatric Surgery for Type 2 Diabetes: Systematic Review and Meta-analysis of Randomized and Non-randomized Evidence

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Abstract This study aims to assess the long-term effects of bariatric surgery on type 2 diabetic patients. We searched Cochrane Library, PubMed, and EMbase up to Dec 2013. Randomized controlled trials (RCTs) and cohort studies of bariatric surgery for diabetes patients that reported data with more than 2 years of follow-up were included. We used rigorous methods to screen studies for eligibility and collected data using standardized forms. Where applicable, we pooled data by meta-analyses. Twenty-six studies, including 2 RCTs and 24 cohort studies that enrolled 7883 patients, proved eligible. Despite the differences in the design, those studies consistently showed that bariatric surgery offered better treatment outcomes than non-surgical options. Pooling of cohort studies showed that BMI decreased by 13.4 kg/m^2 (95 % confidence interval (CI), −17.7 to −9.1), fasting blood glucose by 59.7 mg/dl (95 % CI, −74.6 to −44.9), and glycated hemoglobin by 1.8 % (95 % CI, −2.4 to −1.3). Diabetes was improved or in remission in 89.2 % of patients, and 64.7 % of patients was in remission. Weight loss and diabetes remission were greatest in patients undergoing biliopancreatic diversion/duodenal switch, followed by gastric bypass, sleeve gastrectomy, and adjustable gastric banding. Bariatric surgery may achieve sustained weight loss, glucose control, and diabetes remission. Large randomized trials with long-term follow-up are warranted to demonstrate the effect on outcomes important to patients (e.g., cardiovascular events).

Keywords Bariatric surgery · Type 2 diabetes mellitus · Systematic review · Meta-analysis

Introduction

Diabetes affects 7 % of adults worldwide [1]. More than 371 million people suffered from diabetes in 2012, leading to an estimated total cost of US$471 billion; the number may reach to 552 million by 2030 [2]. Overweight, particularly obesity, is an independent and significant risk factor for type 2 diabetes mellitus (T2DM) [3–5]. T2DM and obesity can decrease patient response to treatment and lead to serious micro- and macrovascular adverse outcomes.

Lifestyle modifications have shown effective in patients with T2DM [6]. Their effects are, however, modest and unsustainable, particularly in severely obese diabetes patients [7]. Anti-diabetes medications are used when lifestyle modifications fail to control blood glucose [8]. Nevertheless, decreased compliance to medications and the potential to gain weight have compromised the effective use of these treatment options in patients [9].

Due to the serious limitations of these care interventions, bariatric surgery has gained increasing interest and use in diabetic patients, particularly those who are obese. Compared with non-surgical treatment, bariatric surgery achieved greater and more sustained weight loss and higher remission rates of T2DM in a short term [10, 11]. The

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Published online: 30 October 2014

American Diabetes Association [12] and International Diabetes Federation [13] recommend that bariatric surgery should be considered in patients with T2DM and a body mass index (BMI) of 35 kg/m^2 or more; the surgery may also be considered as an alternative option in those patients with a BMI between 30 and 35 kg/m^2 when T2DM or co-morbidities cannot be adequately controlled with lifestyle and medical therapy, especially for patients with cardiovascular disease risk factors.

Several systematic reviews have demonstrated that bariatric surgery is effective for obese patients with T2DM [10, 11, 14–16]; these findings were, however, limited to short follow-up (most up to 2 years). In the past years, studies addressing the long-term effects of this treatment option are accumulating [19, 20]. This study aimed to conduct a rigorous systematic review of randomized and non-randomized evidence to offer a comprehensive overview of evidence regarding the long-term effects of bariatric surgery in diabetes patients.

Materials and Methods

Study Selection

We included studies if they were randomized controlled trials, non-randomized controlled clinical trials, cohort studies, or case-control studies; recruited participants with T2DM; assessed the effect of a bariatric surgery technique; and reported pre-defined outcomes with follow-up longer than 24 months. Pre-defined outcomes included BMI, glycated hemoglobin level (HbA1c), fasting blood glucose (FBG), diabetes remission, diabetes recurrence, mortality, and adverse events.

Data Sources and Searches

We searched PubMed, EMbase (via OVID), and the Cochrane Central Register of Controlled Trials (CENTRAL) up to Dec 2013, updated to June 2014. The search strategy was developed in collaboration with an information expert (Appendix 1). We restricted the publications to English language.

Study Procedures

One reviewer screened titles and abstracts for potential eligibility and full texts for final eligibility, and the other reviewer checked the study screening. They independently assessed risk of bias and extracted data from eligible studies, using pilot-tested forms. Discrepancies were resolved through discussion.

Risk of Bias Assessment

We assessed the risk of bias of randomized control trials using the Cochrane Risk of Bias tool [17]. We used a modified version of Newcastle-Ottawa Scale to assess the risk of bias in cohort studies [18]. We removed the item regarding "representativeness of the exposed cohort" and the item "was the follow-up long enough" as these items deal with applicability of results. We added one item "ascertainment of diabetes." For the cohort studies without comparison, the item "comparability of cohorts on the basis of the design or analysis" was not applicable.

Data Extraction

We extracted the following data from each of the eligible studies: study characteristics (simple size, country, study design, length of follow-up, and complete to follow-up), patient characteristic (gender, age, BMI, FBG, HbA1c, duration of diabetes, insulin, or oral hypoglycemic agents), comparisons (surgical procedures vs. non-surgical interventions; comparison of alternative surgical procedures; cohort studies without comparison), and outcomes (BMI, HbA1c, FBG, mortality, diabetes remission, diabetes recurrence, and adverse events).

Data Analyses

For the weight loss, glucose control, diabetes remission, and diabetes recurrence, we conducted the following two set of analyses: (1) long-term follow-up outcomes after bariatric surgeries on the basis of data reported in cohort studies and (2) comparison of the alternative bariatric surgeries or surgical vs. non-surgical interventions based on randomized trials and cohort studies.

For the first set of analyses, we pooled the follow-up data from cohort studies using random-effect model, and reported the pooled effects and their associated 95 % confidence intervals (CIs) by outcome. Heterogeneity among studies was assessed by Cochran's Q test and I^2 statistic. We used two pre-specified subgroup variables to explore if follow-up outcomes differed by type of surgical procedures (i.e., biliopancreatic diversion/duodenal switch (BPD/DS) vs. gastric bypass (GBP) vs. sleeve gastrectomy (SG) vs. adjustable gastric banding (AGB)) and length of follow-up (outcomes at $2<\text{year}<5$ vs. ≥ 5 years). We tested the subgroup difference using an interaction test.

For the second set of analyses, we analyzed randomized controlled trials and cohort studies with control separately. Because of variation in interventions of randomized trials, we qualitatively synthesized the results. For cohort studies, we used random-effect model to combine outcomes in the same intervention. Heterogeneity among studies was assessed by Cochran's Q test and I^2 statistic.

We also summarized the mortality and adverse events data from all studies, involving randomized trials and cohort studies. We collected the total deaths to calculate the mortality in surgical or non-surgical groups. For adverse events, we qualitatively described the data.

We assessed the publication bias by funnel plots and the Egger's test.

Results

The search of electronic databases yielded 3266 reports. After title and abstract screening, 106 were potentially eligible; after reading the full texts, 26 unique studies involving 7883 diabetic patients were finally included (Fig. 1) [19–43]. Of those 26 studies, 2 were randomized controlled trials; whereas 24 were cohort studies, among which 17 were studies without comparison. Four studies, 1 of which was RCT, compared surgical and non-surgical interventions (e.g., dietary, exercise, diabetes education, or medical therapy); five studies compared alternative surgical procedures. 26 studies reported 34 individual surgical procedures: 15 groups addressed GBP procedure, 10 SG procedure, 4 AGB procedure, and 3 BPD/DS procedure.

The mean age ranged from 41.4 to 51.9 years; mean baseline BMI ranged from 23.8 to 69.7 kg/m^2; HbA1c 5.6 to 10.0 %; fasting blood glucose 136.0 to 230.6 mg/dl; duration of diabetes 2.9 to 12.5 years, and length of follow-up 2.1 to 20 years (Table 1).

Results of the risk of bias assessment are reported in Appendix 2. The risk of bias was low for RCT, and cohort studies were considered to have moderate or high risk of bias. No publication bias was detected for BMI, percent of excess weight loss (%EWL), HbA1c, and T2DM remission.

Long-Term Outcomes of Surgical Procedures

Weight Loss

The mean changes in weight loss were available in 11 studies (n=1395) [22, 28, 31, 33, 34, 37, 38, 40, 42–44] (Table 2). Total BMI loss was 13.4 kg/m^2 (95 % confidence interval (CI), −17.7 to −9.1) and 50.5 % of EWL (95 % CI, 43.8 to 57.2 %) at the end of follow-up. Patients lost a mean weight of 14.3 kg/m^2 (95 % CI, −17.8 to −10.9) within 5 years and achieved 43.6 % EWL (95 % CI, 34.2 to 53.1 %). After 5 years, patients achieved a mean weight loss of 13.1 kg/m^2 (95 % CI, −18.8 to −7.3) and 54.9 % EWL (95 % CI, 48.7 to 61.1 %). Heterogeneity among studies was high (I^2=99 %, P<0.001). The subgroup analysis by the types of surgery suggested significant difference (interaction P<0.001). Mean BMI reduction in patients undergoing BPD/DS was 18.8 kg/m^2 (95 % CI, −18.9 to −18.7); GBP was 12.6 kg/m^2 (95 % CI, −20.1 to −5.1); AGB was 11.3 kg/m^2 (95 % CI, −13.4 to −9.2), and SG was 10.4 kg/m^2 (95 % CI, −15.0 to −5.7). However, no statistically significant differences were found in the subgroup analysis by length of follow-up (interaction P=0.71).

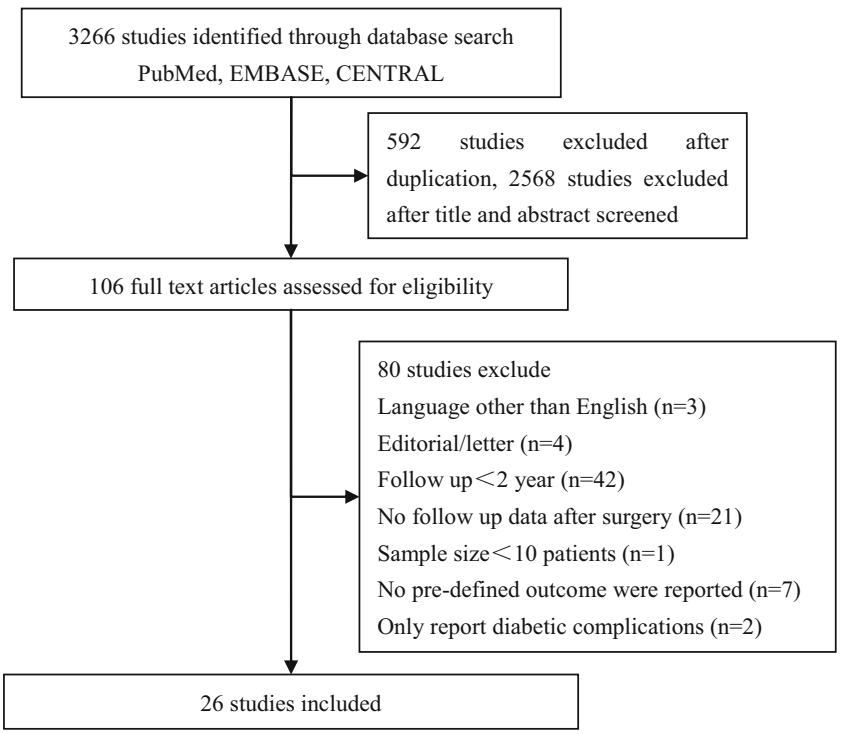

Fig. 1 Study selection

Table 1 Characteristics of included studies and patients

Study	Study design	Interventions	No of patients	Female	Age (years)	BMI	FBG (mg/dl)	HbA1c	Mean duration of diabetes (years)	Insulin/oral medication[a]	Follow-up (years)	Outcomes[b]
				N (%)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		*N* (%)		
Surgical treatments vs. surgical treatments												
Lee [20]	RCT	GBP	30	22 (73)	44.6 (8.6)	30.2 (2.2)	200.9 (76.6)	10.0 (1.8)	5.8	30 (100)	5	1; 2; 6; 7; 8; 9; 11
		SG	30	22 (73)	46.4 (8.1)	31.0 (2.8)	230.6 (85.3)	9.9 (1.8)	6.9	30 (100)		
Abbatini [21]	Cohort	AGB	24	19 (79)	49.3 (2.1)	43.7 (3.5)	152.4 (41.6)	7.2 (1.8)	NR	60 (100)	3	2; 7; 8; 9
		GBP	16	13 (81)	53.0 (8.3)	47.4 (8)	182.2 (45.2)	7.0 (1.5)				
		SG	20	12 (60)	46.6 (4.2)	51.6 (15.9)	158.7 (55.0)	7.7 (1.6)				
Alexandrides [22]	Cohort	GBP	26	106 (77)	41.4 (8.2)	46.1 (2.9)	173.0 (67.0)	NR	NR	43 (31.4)	2.5	1; 2; 7; 9
		BPD/DS	111			69.7 (10.6)	151.0 (42.0)				2.1	
Brethauer [23]	Cohort	AGB	32	22 (68)	49.4 (9.5)	48.8 (7.6)	139.0 (NR)	7.6 (1.6)	5.0	207 (95.4)	6	2; 3; 4; 5; 7; 8; 9
		GBP	162	120 (74)	57.3 (10.0)	47.5 (7.5)	137.0 (NR)	7.3 (1.3)	8.0			
		SG	23	17 (74)	57.7 (10.2)	50.7 (10.6)	136.0 (NR)	7.8 (1.6)	10.5			
Jimenez [25]	Cohort	GBP	98	67 (68)	49.6 (8.2)	44.8 (4.6)	NR	6.1 (5.6)	7.4	135 (88.2)	3	2; 3; 7; 8; 9
		SG	55	28 (51)	52.4 (9.1)	49.8 (7.2)	NR	5.6 (4.8)	7.7			
Surgical treatments vs. non-surgical treatments												
Schauer [19]	RCT	GBP	50	102/150	48 (8)	36±3.5	157 (115,199)	9.0 (1.4)	8.3	37 (74)	3	2; 4; 5; 6; 7; 8; 9; 11
		SG	50				193 (142,236)	9.3 (1.4)		40 (80)		
		Medical therapy	50				164 (132,224)	9.5 (1.7)		41 (82)		
Iaconelli [24]	Cohort	BPD/DS	22	12 (55)	43.8 (8.3)	50.5 (8.5)	156.0 (36.7)	8.0 (1.4)	NR	28 (100)	10	1; 2; 4; 5; 7
		conventional	28	16 (57)	43.7 (6.8)	51.5 (6.2)	156.4 (50.4)	8.0 (1.3)	NR	NR		
MacDonald [26]	Cohort	GBP	154	118	41.9 (NR)	50.6 (NR)	NR	NR	NR	NR	9	1; 4; 7; 9
		No intervention	78	57 (73)	43.5 (NR)	48.8 (NR)					6.2	
Sjostrom [27]	Cohort	GBP,gastroplasty, AGB	343	202 (59)	48.7 (5.9)	42.1 (4.7)	156 (48)	NR	2.9	163 (47.5)	15	1; 2; 4; 5
		conventional	260	156 (60)	50.4 (6.3)	40.0 (4.6)	156 (48)	NR	3.3	357 (52.3)	15	
Observational studies with single arm												
Abbatini [28]	Cohort	SG	33	23 (70)	49.3 (8.0)	52.1 (8.5)	143.2 (47.9)	7.3 (1.4)	7.0	33 (100)	5	2; 4; 7; 8; 9
Arterburn [29]	Cohort	GBP	4434	3349 (75)	49.6 (9.3)	NR	NR	NR	4.5	3432 (77.4)	3.1	1; 2; 3
Caiazzo [30]	Cohort	AGB	23	15 (65)	44.9 (6.7)	45.3 (6.4)	NR	NR	5.1	23 (100)	5	1; 2; 6; 8; 9; 10
Chikunguwo [31]	Cohort	GBP	177	147 (83)	47.3 (NR)	50.2 (8.1)	NR	NR	NR	123 (69.5)	8.6	2; 7
Cohen [32]	Cohort	GBP	66	26 (39)	47.0 (12.0)	32.5 (NR)	156.0 (11.0)	9.6 (NR)	12.5	66 (100)	5	1; 2; 4; 8; 9; 11
Cruz-Muñoz [33]	Cohort	GBP,AGB	377	236 (62)	48.2 (11.2)	47.2 (8.2)	149.0 (62.6)	8.1 (1.9)	NR	NR	3	7; 8; 9
DePaula [34]	Cohort	SG	125	59 (29)	53.0 (7.4)	30.3 (5.6)	NR	NR	10.1	202 (100)	3.2	1; 2; 4; 5; 7; 8;
		SG	77		50.9 (7.2)	29.6 (3.3)	NR	NR	9.1			9; 10; 11
DiGiorgi [35]	Cohort	GBP	42	16 (38)	45.4 (9.9)	51.4 (8.7)	168.0 (73.0)	7.6 (1.3)	7.6	37 (88.1)	5	2; 3; 8; 9
Heneghan [36]	Cohort	GBP, SG, AGB	52	39 (75)	51.2 (10.1)	49.0 (8.7)	147.2 (55.0)	7.7 (NR)	8.6	NR	5.5	2; 5; 7; 8; 9
Kim [37]	Cohort	GBP	219	174 (79)	46.8 (NR)	50.4 (8.7)	152.8 (56.4)	7.6 (1.5)	7.2	219 (100)	2.2	2; 7; 8; 9

Table 1 (continued)

Study	Study design	Interventions	No of patients	Female	Age (years)	BMI	FBG (mg/dl)	HbA1c	Mean duration of diabetes (years)	Insulin/oral medication[a]	Follow-up (years)	Outcomes[b]
				N (%)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		*N* (%)		
Kota [38]	Cohort	SG	43	18 (42)	47.2 (8.2)	33.2 (7.8)	NR	9.6 (2.1)	10.1	43 (100)	3	2; 5; 7; 8; 9
Lakdawala [39]	Cohort	GBP	52	25 (48)	49.0 (NR)	32.6 (NR)	NR	NR	8.4	52 (100)	5	1; 2; 7; 8; 9; 11
Marinari [40]	Cohort	BPD	268	166 (62)	42.1 (NR)	49.6 (0.5)	NR	NR	NR	268 (100)	5	1; 2; 7; 9
Nora [41]	Cohort	GBP	94	82 (87)	48.3 (0.8)	44.3 (0.7)	165.6 (6.3)	6.6 (0.2)	6.2	75 (79.8)	3	2; 7; 8; 9; 11
Sultan [42]	Cohort	AGB	95	50 (53)	49.3 (NR)	46.3 (7.3)	146 (NR)	7.5 (NR)	6.5	83 (88.3)	5	2; 7; 8; 9
Todkar [43]	Cohort	SG	23	NR	44.6 (11.9)	40.7 (6.6)	157.4 (48.5)	9.1 (1.2)	NR	NR	3	2; 6; 7; 8; 9; 10
Yang [44]	Cohort	GBP	21	6 (28)	57.9 (6.8)	23.8 (3.3)	244.1 (46.8)	9.2 (1.6)	4.6	21 (100)	5	2; 7; 8; 9; 10

AGB adjustable gastric banding, *BPD/DS* biliopancreatic diversion/duodenal switch, *GBP* gastric bypass, *SG* sleeve gastrectomy, *VBG* vertical-banded gastroplasty, *BMI* body mass index, *FBG* fasting blood glucose, *HbA1c* hemoglobin A1c, *NR* not reported

[a] The percentage of patients on oral medication or insulin preoperative

[b] Include the following: mortality (1), diabetes remission (2), diabetes recurrence (3), vascular events (4), nephropathy (5), quality of life (6), weight loss (7), HbA1c (8), FPG (9), 2-h plasma glucose (2hPG; 10), and adverse events (11)

Table 2 The outcome of weight loss: meta-analyses of cohort study

Outcomes	All procedures			Gastric bypass			Sleeve gastrectomy			Adjustable gastric banding			Biliopancreatic diversion/duodenal switch		
	N (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*
BMI (kg/m^2)	11 (1395)	−13.4 (−17.7,-9.1)	<0.001	4 (443)	−12.6 (−20.1, −5.1)	0.001	4 (301)	−10.4 (−15.0, −5.7)	<0.001	1 (95)	−11.3 (−13.4, −9.2)	–	2 (379)	−18.8 (−18.9, −18.7)	–
%EWL	10 (1340)	50.5 (43.8, 57.2)	<0.001	6 (625)	57.5 (41.2, 73.8)	<0.001	2 (43)	42.0 (29.2, 54.8)	0.015	3 (78)	38.2 (29.1, 47.3)	0.015	1 (12)	49.3 (38.7, 59.9)	–
Outcomes at 2<year<5															
BMI (kg/m^2)	4 (462)	−14.3 (−17.8, −10.9)	<0.001	1 (219)	−17.1 (−18.7, −15.6)	<0.001	2 (66)	−10.1 (−12.8, −7.5)	<0.001	–	–	–	–	–	–
%EWL	3 (656)	43.6 (34.2, 53.1)	<0.001	2 (235)	49.4 (10.8, 88.0)	<0.001	1 (20)	36.3 (33.1, 39.5)	–	1 (24)	43.5 (38.5, 48.5)	–	–	–	–
Outcomes at year≥5 years															
BMI (kg/m^2)	7 (933)	−13.1 (−18.8, −7.3)	<0.001	3 (224)	−11.1 (−22.4, 0.2)	0.05	2 (235)	−10.7 (−19.7, −1.6)	0.02	1 (95)	−11.31 (−13.4, −9.2)	–	2 (379)	−18.81 (−18.9, −18.7)	–
%EWL	7 (684)	54.9 (48.7, 61.1)	<0.001		61.3 (55.2, 67.4)	<0.001	1 (23)	49.5 (39.3, 59.7)	–	2 (54)	34.7 (23.5, 49.9)	0.09	1 (12)	49.3 (38.7, 59.9)	–

BMI body mass index, *%EWL* %excess weight lost, *N* number of treatment group, *n* number of patients, *CI* confidence interval, *P P* value for test of homogeneity of effects

Glucose Control

Changes in HbA1c were reported in 13 studies (n=1542) [23, 25, 28, 30, 32–38, 41, 44] (Table 3). Heterogeneity among studies was high (I^2=99 %, P<0.001). The overall mean change in HbA1c was −1.8 % (95 % CI, −2.4 to −1.3). HbA1c reduction was greatest after SG (−2.4 % (95 % CI, −2.8 to −1.9), followed by GBP (−1.8 %; 95 %, CI −2.8 to −0.9) and AGB (−1.7 %, (−2.4 to −0.9). However, the difference was not significant among those surgical procedures (interaction P=0.26) and length of follow-up (interaction P=0.73).

Fourteen studies (n=1794) reported the mean change in FBG [22, 23, 28, 30, 32–38, 40, 41, 44] (Table 3). Heterogeneity among studies was high (I^2=99 %, P<0.001). There was statistically significant reduction in FBG after surgery (−59.7 mg/dl; 95 % CI, −74.6 to −44.9). Patients after BPD/DS had a greatest reduction of FBG (−74.6 mg/dl; 95 % CI, −109.0 to −39.3) comparing with SG (−66.2 mg/dl; 95 % CI, −98.3 to −34.2), GBP (−60.4 mg/dl; 95 % CI, −75.0, −45.8), and AGB (−54.0 mg/dl; 95 % CI, −79.5, −28.5). The difference was not significant among those surgical procedures (interaction P=0.81) and length of follow-up (interaction P=0.92).

Diabetes Remission

The rate of diabetes remissions was available in 21 studies (n=6373) [21–25, 27–32, 35–44] (Table 4). Different definitions for diabetes remission were used among these studies. Pooled data showed that 64.7 % (4123/6373) of patients achieved complete or partial remission; diabetes was improved or in remission in 89.2 % (534/599) of patients. Heterogeneity among studies was high (I^2=99 %, P<0.001). The remission appeared greater in those receiving BPD/DS (99.2 %; 95 % CI, 97.0 to 99.8), followed by GBP (74.4 %; 95 % CI, 66.9 to 80.6), SG (61.3 %; 95 % CI, 45.9 to 74.8) and AGB (33.0 %; 95 % CI, 16.1 to 55.8). No significant difference was found in subgroup analysis by length of follow-up (interaction P=0.64).

Diabetes Recurrence

The rate of diabetes recurrences was available in 5 studies (n=2509) [23, 25, 29, 31, 35], among which 577 patients (577/2680; 21.5 %) recurred after initial partial or complete remission (three studies referred to GBP and the other two addressed more than one procedure). Of the three studies with GBP, the rate of diabetes recurrence was 43.3 % (68/157) at 8.6 years of follow-up, 25.9 % (7/27) at 5 year follow-up, and 20.6 % (464/2254) at 3 years.

Table 3 Changes in glucose and HbA1c levels: meta-analyses of cohort study

Outcomes	All procedures			Gastric bypass			Sleeve gastrectomy			Adjustable gastric banding			Biliopancreatic diversion/duodenal switch		
	N (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*
FPG (mg/dl)	14 (1794)	−59.7 (−74.6, −44.9)	<0.001	6 (468)	−60.4 (−75.0, −45.8)	<0.001	3(278)	−66.2 (−98.3, −34.2)	<0.001	1(23)	−54.0 (−79.5, −28.5)	–	2 (379)	−74.6 (−109.0, −39.3)	<0.001
HbA1c%	13 (1542)	−1.8 (−2.4, −1.3)	<0.001	6 (540)	−1.85 (−2.80, −0.91)	<0.001	4 (333)	−2.4 (−2.8, −1.9)	<0.001	1 (23)	−1.7 (−2.4, −0.9)	–	–	–	–
Outcomes at 2 <year<5															
FPG (mg/dl)	4 (733)	−58.8 (−77.7, −39.9)	<0.001	2 (313)	−61.5 (−89.5, −33.5)	<0.001	1 (43)	−65.2 (−89.2, −41.3)	<0.001	–	–	–	–	–	–
HbA1c%	4 (733)	−1.69 (−2.76, −0.62)	<0.001	2 (313)	−1.1 (−1.8, −0.5)	0.001	1 (43)	−2.4 (−3.9, −0.9)	–	–	–	–	–	–	–
Outcomes at year≥5 years															
FPG (mg/dl)	10 (1061)	−60.0 (−77.2, −42.9)	<0.001	4 (155)	−54.2 (−57.1, −51.3)	<0.001	2 (235)	−66.4 (−113.7, −19.1)	<0.001	1 (23)	−54.0 (−79.5, −28.5)	–	2 (379)	−74.6 (−109.0, −39.3)	<0.001
HbA1c%	9 (809)	−1.9 (−2.6, −1.2)	<0.001	4 (227)	−2.2 (−3.6, −0.8)	<0.001	3 (290)	−2.3 (−2.8, −1.8)	<0.001	1 (23)	−1.7 (−2.4, −0.9)	–	–	–	–

FPG fasting plasma glucose, *HbA1c* hemoglobin A1c, *N* number of treatment group, *n* number of patients, *CI* confidence interval, *P* *P* value for test of homogeneity of effects

Table 4 The outcome for improvement in diabetes: meta-analyses of cohort study

Outcomes	All procedures			Gastric bypass			Sleeve gastrectomy			Adjustable gastric banding			Biliopancreatic diversion/duodenal switch		
	N (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*	*N* (*n*)	Mean (95 % CI)	*P*
Diabetes remission	21 (6373)	64.7 (57.1, 71.7)	<0.001	12 (5283)	74.4 (66.9, 80.6)	<0.001	6 (177)	61.3 (45.9, 74.8)	0.004	4 (136)	33.0 (16.1, 55.8)	0.002	3 (400)	99.2 (97.0, 99.8)	0.312
Diabetes remission or improved	7 (599)	89.2 (81.9, 93.8)	0.003	6 (492)	92.6 (87.3, 95.7)	0.079	1 (23)	82.6 (61.8, 93.3)	–	1 (32)	43.8 (27.9, 61.0)	–	–	–	–
Diabetes unchanged	13 (1178)	16.3 (10.3, 24.8)	0.006	9 (767)	11.1 (7.6, 15.8)	0.015	5 (134)	27.4 (20.4, 35.7)	0.38	3 (114)	53.2 (40.4, 65.5)	0.147	1 (111)	0.9 (0.1, 6.1)	–
Outcomes at 2 <year<5															
Diabetes remission	6 (4749)	66.6 (57.8, 74.4)	<0.001	4 (4639)	71.6 (59.9, 81.0)	0.004	3 (86)	64.7 (42.2,82.1)	0.028	1 (24)	62.5 (42.2,79.2)	–	–	–	–
Diabetes remission or improved	–	–	–	1 (149)	90.6 (84.8, 94.4)	–	–	–	–	–	–	–	–	–	–
Diabetes unchanged	4 (254)	19.3 (10.2, 33.6)	0.006	2 (165)	11.2 (6.0, 19.7)	0.2	2 (43)	25.9 (14.9, 41.1)	0.3	1 (24)	37.5 (20.8, 57.8)		–	–	–
Outcomes at ≥5 years															
Diabetes remission	14 (1328)	68.7 (56.0, 79.2)	<0.001	8 (644)	75.0 (63.1, 84.0)	<0.001	3 (91)	58.2 (30.8, 81.3)	0.006	3 (112)	24.8 (10.9, 47.2)	0.001	3 (400)	99.2 (97.0, 99.8)	0.312
Diabetes remission or improved	6 (450)	89.4 (80.0, 94.7)	0.005	5 (343)	93.9 (86.4, 97.4)	0.052	1 (23)	82.6 (61.8, 93.3)	[	1 (32)	43.8 (27.9, 61.0)	–	–	–	–
Diabetes unchanged	9 (769)	15.3 (8.0, 27.3)	<0.001	7 (602)	10.6 (6.6, 16.7)	0.008	3 (91)	28.1 (19.7, 38.4)	0.268	2 (90)	58.9 (48.5, 68.5)	0.41	1 (111)	0.9(0.1,6.1)	–

N number of treatment group, *n* number of patients, *CI* confidence interval, *P P* value for test of homogeneity of effects

Comparison of Alternative Surgical Procedures or Surgical Procedures vs. Other Interventions

Evidence from Randomized Trials

Two randomized trials examined the long-term effects of bariatric surgery (Table 5). One trial randomized 150 obese patients with uncontrolled type 2 diabetes to receive either intensive medical therapy (lifestyle counseling, weight management, frequent home glucose monitor, and the use of newer drug therapy) alone or intensive medical therapy following GBP or SG [19]. Among those, 137 (91.3 %) completed 36 months of follow-up. The surgical group lost more body weight than medical therapy group at the end of follow-up (GBP: -26.2±10.6 kg vs. SG: -21.3±9.7 kg vs. medical therapy: -4.3±8.8 kg). The medical therapy group had lower HbA1c reduction (-0.6 %) at 3 years than among surgical patients (-2.5 % in GBP and SG group) ($P<0.001$). 5 % (2/40) of patients in the medical therapy group, 38 % (18/48) in GBP group, and 24 % (12/50) in SG group achieved target glycemic level (HbA1c≤6.0) ($P<0.001$).

The other trial randomized 60 patients with a BMI of 25 to 35 to GBP and SG group [20]. Of those, 48 (80 %) completed a 5-year follow-up. At 5 years, the mean weight lost 22.8 % of the starting weight after GBP, compared with 20.1 % reduction after SG; 60 % (18/30) of patients in GBP and 30 % (9/30) in SG group achieved an HbA1c≤6.5 % ($P=0.02$). The mean HbA1c reduction at 5-year follow-up was greater in GBP (−3.9 %) than SG (−2.8 %) ($P=0.36$).

Evidence from Cohort Studies

Weight Loss Seven cohort studies reported comparison of alternative treatment options [21–27]. Three studies compared surgical vs. non-surgical interventions ($n=885$) [24, 26, 27], of which two assessed surgical treatment vs. conventional medical therapy ($n=542$). However, these studies did not report usable data, instead of reporting figures [24, 26]; both consistently presented that surgical treatment achieved more loss of body weight than conventional treatment at the follow-up of 6.2 to 10 years. The third study showed a significant body weight reduction in surgical group ($n=343$, GBP, gastroplasty, and AGB, −22.5 kg) than control group ($n=260$, customary lifestyle and pharmacological treatment, −4.4 kg) after a 10-year follow-up ($P<0.001$) [27].

Four cohort studies compared alternative surgical interventions ($n=567$) [21–23, 25]. The first study showed a much greater reduction of mean BMI in BPD/DS group ($n=111$,

Table 5 Comparison of surgical vs. non-surgical interventions: randomized controlled trial (3-year outcomes)

Study	Intervention	No. of patients (baseline/ follow-up)	Baseline weight (kg) Mean (SD)	Baseline BMI (kg/m^2) Mean (SD)	Weight change (kg) Mean (SD)	BMI change (kg/m^2) Mean (SD)	Baseline HbA1c Mean (SD)	HbA1c change Mean (SD)	Baseline FBG Mean (IQR)	FBG change Mean (IQR)	Diabetes remission	No. of patients (%) with HbA1c ≤6 %	No. of patients (%) with HbA1c ≤6.5 %
Schauer [19]	Medical therapy	40/50	104.5 (14.2)		−4.3 (8.8)		9.0 (1.4)	−0.6 (2.5)	157 (115 to 199)	−6.0 (−68.5 to 56.0)	0	2 (5)	7 (18)
	GBP	48/50	106.8 (14.9)		−26.2 (10.6)		9.3 (1.4)	−2.5 (1.9)	193 (142 to 236)	−85.5 (−122.0 to −21.5)	18/48	18 (38)	23 (48)
	SG	49/50	100.6 (16.5)		−21.3 (9.7)		9.5 (1.7)	−2.5 (2.1)	164 (132 to 224)	−46.0 (−113.0 to −21.0)	12/49	12 (24)	23 (47)
P value					<0.001[a]			<0.001[a]		<0.001[a]		<0.05	<0.001[a]
					0.02[b]			0.99[b]		0.24[b]		0.17[b]	0.08[b]
Lee [20]	GBP	24/30		30.2 (2.2)		−6.9 (1.3)	10.0 (1.8)	−3.9 (1.3)	200.9 (76.6)	−93.7 (54.6)	18/30	NR	18/30
	SG	24/30		31 (2.8)		−5.9 (1.7)	9.9 (1.8)	−2.8 (1.1)	230.6 (85.3)	−108.2 (76.1)	9/30	NR	9/30
P value						0.007		<0.001		>0.2	<0.05		<0.05

BMI body mass index, *HbA1c* hemoglobin A1c, *SD* standard deviation, *IQR* interquartile range, *NR* not reported

[a] *P* value of surgical therapy vs. medical therapy

[b] *P* value of both gastric bypass vs. sleeve gastrectomy

19.8 kg/m^2) than GBP group (n=22, 13.5 kg/m^2) after 5 years of follow-up [22]. The second found that GBP was associated with a more significant reduction in weight comparing with SG and AGB (excess weight loss %: 60.5 vs. 49.5 vs. 29.5 %) [23]. The other two studies reported weight loss after surgery, but failed to report numerical data [21, 25].

Glucose Control Three cohort studies comparing alternative surgical procedures reported the mean change of HbA1c after surgery (n=407) [21, 23, 25]. The pooled data showed that the mean HbA1c change was higher in SG than GBP and AGB after 3 to 5 years of follow-up. Three studies (n=374) compared GBP with SG (MD, 0.3 %; 95 % CI, −0.5 to 1.2); two (n=234) compared GBP with AGB (MD, −0.1 %; 95 % CI, −2.3 to 2.1); two (n=99) compared SG with AGB (MD, −0.36 %; 95 % CI, −0.97 to 0.25). However, the difference was not statistically significant.

Diabetes Remission The relative risk of T2DM remission was pooled from six studies [21–25, 27]. Two studies compared surgical procedures with conventional treatment. The first one involving 50 patients found significant difference between BPD/DS and conventional therapy (blood pressure, lipid control, dietary, exercise, and diabetes education) after a 10-year follow-up (odds ratio (OR), 51.67; 95 % CI, 2.85 to 935.12) [24]. The second study also shows a favorable 10-year effect of surgical group (n=603; OR, 6.34; 95 % CI, 2.14 to 18.84).

Diabetes Recurrence Diabetes recurrence was reported in two cohort studies with alternative surgical procedures [23, 25]. One study with 6 years follow-up reported 17.4 % of patients (17/99) recurred after GBP, 33.3 % (1/3) after AGB, and 37.5 % (3/7) after SG; the beginning time to relapse was 3 years [23]. The second study comparing GBP and SG showed no significant difference (n=153; OR, 0.59; 95 % CI, 0.19 to 1.85) [25].

Mortality

Studies were included if they reported either the number of death or the lack of death. Thus, 14 studies reported mortality data, including one RCT (Table 6) [20, 22, 23, 25–27, 29–32, 34, 39, 41, 42]. The length of follow-up ranged from 2.6 to 10 years. One hundred eighty-two patients (182/6479, 2.8 %) died at the end of follow-up (including four perioperative deaths).

Of 182 deaths, 159 (159/6141, 2.6 %) occurred in surgical group and 23 (23/338, 6.8 %) in non-surgical group. These included 123 deaths (123/5019, 2.4 %) in the GBP group, 6 (6/117, 5.1 %) in AGB, 3 (3/133, 2.2 %) in BPD/DS, and 4 (4/232, 1.7 %) in SG.

Table 6 Mortality of including studies

Study	Follow-up (year)	Intervention	Deaths	Total
Lee [20]	5	GBP	1	30
		SG	0	30
Alexandrides [22]	5	GBP	0	26
		BPD	3	111
Brethauer [23]	6	AGB, SG, GBP	21	297
Iaconelli [24]	10	BPD	0	22
MacDonald [26]	9	GBP	14	154
	6.2	Conventional	22	78
Sjostrom [27]	15	AGB; GBP, gastroplasty	2	343
		Conventional	1	260
Arterburn [29]	3.1	GBP	108	4434
Caiazzo [30]	5	AGB	1	23
Chikunguwo [31]	8.6	GBP	0	177
Cohen [32]	5	GBP	0	66
DePaula [34]	4	SG	4	202
Lakdawala [39]	5	GBP	0	52
Nora [41]	2.6	GBP	0	80
Sultan [42]	5	AGB	5	94
Total			178	5816

GBP gastric bypass, *AGB* adjustable gastric banding, *SG* sleeve gastrectomy

Adverse Events

The adverse events were reported in 9 studies [19, 20, 25, 26, 28, 32–34, 38] (Appendix 3). The length of follow-up ranged from 3 to 5 years. The definition of adverse events varied significantly across studies. The information about adverse events (e.g., when the adverse events took place and how to treat them) were rare in these studies. The major adverse events in RCT were hypoglycemic (32 patients in GBP (32/50, 64 %); 40 in SG (40/48, 82 %); 39 in medical therapy (39/43, 91 %)) and anemia (8 in GBP (8/50, 16 %); 15 in SG (15/48, 31 %); 6 in medical therapy (6/43, 14 %)). Moreover, in the surgical procedures, the adverse events with highest incidences were gallstones (24/202, 12 %) and urinary lithiasis (10/202, 4.9 %) in SG and port-site hematomas (8/66, 12 %) and leaks of the gastrojejunal anastomosis (6/94, 6.4 %) in GBP.

Discussion

This study systematically reviewed global evidence investigating long-term effects of bariatric surgery in obese individuals with type 2 diabetes. Up to now, there was limited long-term follow-up data from RCT; we identified two only. Existing cohort studies—at moderate to high risk of bias—suggested that bariatric surgery is likely to achieve sustained weight loss and glycemic benefits (e.g., blood glucose and HbA1c reduction, diabetes remission, or improvement). We also found that some surgical procedures such as BPD/DS may achieve greater weight loss and higher diabetes remission rate than others like GBP, SG, and AGB. Notably, the small simple size and limited study may affect the power of test to detect the difference among these surgical procedures.

Evidence showed intensive glycemic control can reduce the incidence of diabetic complications [45, 46]. They showed bariatric surgery had a significant reduction on the incident of macrovascular (e.g., brain, heart) and microvascular (e.g., eye, kidneys and peripheral nerves) diabetic complications with follow-up longer than 10 years. Although the primary outcomes in our review did not involve diabetic complications, we also found favorable 15-year effects of surgery on macrovascular and microvascular diabetic complications in one study [27]. Additionally, we observed a higher mortality than data published in other reports, likely because the participants in these studies were obese and diabetic [47–49] and that the length of follow-up is longer than other studies.

This study has several limitations. First, an appreciable proportion of studies addressing long-term effects of bariatric surgeries suffered from important methodological limitations, which made the findings compromised. The existing evidence has, however, consistently suggested potential long-term benefits of bariatric surgeries. Second, the diagnostic criteria and definitions for diabetes remission varied considerably across studies; such variations may make the comparison of results less compelling. Third, due to the limited randomized evidence, we were unable to make robust inference on the effects of bariatric surgery.

Our findings are consistent with a previously published systematic review and meta-analysis that included 621 studies involving 135,246 patients [14]. In that study, those with follow-up longer than 2 years reported a weight reduction in diabetes patients of 12.9 kg/m^2 and 58.0 % of excess weight loss at 2 years of follow-up or longer; the remission rate was 62.1 %, and diabetes resolved or improved in 100 % of patients. However, the purpose of this meta-analysis was not to explore the long-term effect, and only 48 diabetic patients achieved more than 2 years follow-up. Moreover, compared with this meta-analysis, our study conducted analysis about comparison between different surgical procedures or surgical intervention vs. non-surgical intervention.

Conclusions

Our study has systematically assessed the long-term effects of bariatric surgery in patients with T2DM. The findings suggest that bariatric surgery had effects on sustained weight loss and zglucose control. The included studies, however, suffer from important methodological limitations. More carefully designed studies, particularly adequately powered, well-conducted randomized trials are warranted.

Acknowledgments We thank Xun Yao for his generous support in performing the database search. XS is supported by Young Investigator Award, Sichuan University (project no. 2013SCU04A37).

Author Contributions JY conceived and designed this study, searched the literature, extracted data, synthesized data, and developed the first draft of the manuscript. XZ carefully checked studies and extracted data. LL contributed substantially to the update of the study and analyses. XS provided critical methodological guidance. All authors critically revised the manuscript

Conflict of Interest Authors reported no potential conflicts of interest

Appendix 1: Search Strategy

PubMed:
#1 “Bariatric Surgery” [Mesh]
#2 “Biliopancreatic Diversion” [Mesh]
#3 “Gastrectomy” [Mesh]
#4 Bariatric Surger*[tw]
#5 obesity surger*[tw]
#6 metabolic surger*[tw]
#7 Gastric Bypass*[tw]
#8 stomach bypass*[tw]
#9 gastric banding*[tw]
#10 gastric band [tw] or gastric bands [tw]
#11 Gastroplast*[tw]
#12 “Gastrectomy” [Mesh]
#13 gastrectom*[tw]
#14 “Biliopancreatic Diversion” [Mesh]
#15 Biliopancreatic Diversion*[tw]
#16 Biliopancreatic Bypass*[tw]
#17 Bilio pancreatic Diversion*[tw]
#18 Bilio pancreatic Bypass*[tw]
#19 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR No. 15 OR 16 OR 17 OR 18
#20 Randomized controlled trial [pt]
#21 Controlled clinical trial [pt]
#22 Randomized [tiab]
#23 Placebo [tiab]
#24 Clinical trials as topic [Mesh]
#25 randomly [tiab]
#26 Trials [ti]
#27 “case-control studies” [Mesh]
#28 “Cohort studies” [Mesh]
#29 “Longitudinal studies” [Mesh]
#30 “retrospective studies” [Mesh]
#31 “Follow-Up Studies” [Mesh]
#32 “prospective studies” [Mesh]
#33 Cohort analys*[ti,ab]
#34 Cohort stud*[ti,ab]
#35 Follow-up stud*[ti,ab]
#36 Follow-up stud*[ti,ab]
#37 Follow-up stud*[ti,ab]
#38 Longitudinal stud*[ti,ab]
#39 Longitudinal survey*[ti,ab]
#40 Prospective stud*[ti,ab]
#41 Retrospective stud*[ti,ab]
#42 incidence stud*[ti,ab]
#43 concurrent stud*[ti,ab]
#44 comparison group*[ti,ab]
#45 nonrandom*[ti,ab]
#46 control group*[ti,ab]
#47 database*[ti,ab]
#48 population*[ti,ab]
#49 "Registries"[Mesh]
#50 registr*[ti,ab]
51 case-control stud*[ti,ab]
#52 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51
#53 19 AND 52
#54 animals [mh] NOT humans [mh]
#55 and 53 NOT 54
EMbase (OVID)
1 exp bariatric surgery/
2 exp biliopancreatic diversion/
3 exp Gastrectomy/
4 exp sleeve gastrectomy/
5 bariatric surger*.af.
6 metabolic surger*.af.
7 obesity surger*.af.
8 gastric bypass*.af.
9 stomach bypass*.ti, ab.
10 Jejunoileal Bypass*.af.
11 Biliopancreatic Bypass*.af.
12 Bilio pancreatic Bypass*.af.
13 BilioPancreatic Diversion*.af.
14 Bilio Pancreatic Diversion*.af.
15 Gastrectom*.af.
16 Gastric banding*.af.
17 Gastric band or gastric bands.af.
18 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

19 (clinical trial or controlled clinical trial or randomized controlled trial).pt.

20 Clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/

21 Random*.ti,ab.

22 Clinical trial*.ti,ab.

23 Controlled trial*.ti,ab.

24 Case-control studies/

25 Retrospective studies/

26 Cohort studies/

27 Longitudinal studies/

28 Follow-up studies/

29 Prospective studies/

30 Cohort.ti,ab.

31 Longitudinal.ti,ab.

32 Follow-up.ti,ab.

33 Follow-up.ti,ab.

34 Prospective*.ti,ab.

35 Retrospective*.ti,ab.

36 Non-random*.ti,ab.

37 Comparison group*.ti,ab.

38 Control group*.ti,ab.

39 Database*.ti,ab.

40 Population*.ti,ab.

41 registries/

42 Registr*.ti,ab.

43 Case-control stud*.ti,ab

44 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43

45 18 and 44

46 Limit 45 to humans

CENTRAL

1 exp bariatric surgery/

2 exp biliopancreatic diversion/

3 exp Gastrectomy/

4 exp sleeve gastrectomy/

5 bariatric surger*.af.

6 metabolic surger*.af.

7 obesity surger*.af.

8 gastric bypass*.af.

9 stomach bypass*.ti, ab.

10 Jejunoileal Bypass*.af.

11 Biliopancreatic Bypass*.af.

12 Bilio pancreatic Bypass*.af.

13 BilioPancreatic Diversion*.af.

14 Bilio Pancreatic Diversion*.af.

15 gastrectom*.af.

16 gastric banding*.af.

17 gastric band or gastric bands.af.

18 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

Appendix 2: Assessment of the Risk of Bias

Table 7 Risk of bias of randomized controlled trial

	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of clinicians	Blinding of outcome assessor	Incomplete outcome data	Selective reporting
Schauer [19]	Block-randomization method with a 1:1:1 ratio. The randomization scheme was developed by a statistician	Sealed and sequentially numbered envelopes were used	Patients and study personnel will not be blinded to treatment assignment	Patients and study personnel will not be blinded to treatment assignment	Patients and study personnel will not be blinded to treatment assignment	137 patients (91.3 %) completed the follow-up	Free of selective reporting
Lee [20]	The randomization schedule used permuted blocks for every ten patients	Unclear. The randomization assignment was double-blinded until 1 month after surgery	Patients and study personnel will not be blinded to treatment assignment	Patients and study personnel will not be blinded to treatment assignment	The investigators, data collectors, and outcome adjudicators were blinded to aggregate outcomes	24 patients (80 %) completed the follow-up	Free of selective reporting

Table 8 Risk of bias of cohort studies (with control)

Study	Ascertain of exposure	Ascertain of diabetes	Demonstration that outcome of interest was not present at start of study	Comparability of study controls for important factors	Assessment of outcome	Completeness of outcome data
Abbatini [21]	Not reported	Unclear. Only reported the diagnostic criteria	Yes, all subjects are diabetic patients before surgery	No, the type of surgery was determined according to ASBS and EAES criteria	Not reported	Not reported
Alexandrides [22]	Unclear; only described the procedure of surgery	Unclear; data collected from electronic database in their institution	Yes; patients with a diagnosis of T2DM were collected	Unclear, only reported the difference of BMI	Not reported	21 patients (80.8 %) completed the follow-up in RYGB group; 83 patients (74.8 %) in BPD-RYGB group
Brethauer [23]	Not reported	Not reported	Yes; subjects had the diagnosis of T2DM preoperatively	Yes, logistic analyses used to control for the influence of age and T2DM duration	Unclear, Medical records form clinical visit	217 patients (73.1 %) completed the follow-up (217/297)
Iaconelli [24]	Not reported	Not reported	Yes, subjects with cardiovascular events ,congestive heart failure, severe angina, internal malignancy, or portal hypertension were excluded	Yes, no significant differences were found in baseline characteristics	Not reported	50 patients (100 %) completed the follow-up
Jimenez [25]	Not reported	Not reported	Yes, the including patients with a diagnosis of T2DM for at least 6 months	Yes, logistic analyses used to control for the influence of age, gender, HbA1c,T2DM duration, insulin use	Not reported	147 patients (96 %) completed the follow-up
MacDonald [26]	Unclear; only described the procedure of surgery	Not reported	Yes, the patients were diagnosis with T2DM were included	Yes, no significant differences were found in baseline characteristics	Unclear; data on the surgery group were from chart in obesity research program; data on control group were from clinical records	All patients (100 %) complete the follow-up
Sjostrom [27]	Unclear; only described the procedure of surgery	Unclear; Only reported the diagnostic criteria	Yes, the patients were diagnosis with T2DM were included	Yes, no significant differences were found in baseline characteristics	yes; all sample were assessed at the central library	Participants rates at 15-year examination were 41 % and 47 % in control and surgical group

Appendix 3

Table 9 Risk of bias of cohort studies (without control)

Study	Ascertain of exposure	Ascertain of diabetes	Demonstration that outcome of interest was not present at start of study	Assessment of outcome	Completeness of outcome data
Abbatini [28]	Not reported	Unclear, only reported the diagnostic criteria	Yes, patients were diagnosis with T2DM were included	Not reported	33 patients (100 %) completed the follow-up
Arterburn [29]	Yes, identified by ICD-9 and CPT-4 procedure codes	Unclear, only reported the defines of diabetes	Yes, uncontrolled or medication-controlled diabetes were included	Unclear, extracted the data from administrative and clinical databases, and state death indices.	3462 patients (78.1 %) completed 3-year follow-up; 3006 patients (67.8 %) completed 5-years follow-up
Caiazzo [30]	Unclear, only described the procedure of surgery	Unclear, only reported the diagnostic criteria	Yes, patients with diabetes were included	Yes, date were collected by multidisciplinary team in the outpatient clinic	22 patients (95.6 %) completed the follow-up
Chikunguwo [31]	Unclear, only described the procedure of surgery	Unclear; diabetes patients were identified from the medical records or took diabetic medication.	Yes, patients were diagnosis with T2DM were included	Unclear, data were collected by annual clinic visit or telephoned patients without follow-up visits	All patients (100 %) completed the follow-up
Cohen [32]	Not reported	Unclear, only reported the diagnostic criteria	Yes, all patients met ADA criteria for diabetes	Unclear, all date collected in person, rather than nurses or telephone interviews.	All patients (100 %) completed the follow-up
Cruz-Munoz [33]	Unclear, only described the procedure of surgery	Unclear, determined by previous diagnosis and/or medication usage	Yes, all patients met ADA criteria for diabetes	Yes, data from medical chart with routine clinical visit	Not reported
DePaula [34]	Unclear, only described the procedure of surgery	Unclear, only reported the diagnostic criteria	Yes, patient had T2DM for at least 3 years or HbA1c>7.5 % for at least 3 months were included	Unclear, date were determined by interview or special tests	Not reported
DiGiorgi [35]	Not reported	Not reported	Unclear, only described the subjects were T2DM.	Unclear, likely date from medical records	No reported
Heneghan [36]	Not reported	Not reported	Yes, all patients with a biochemically confirmed diagnosis of T2DM	Unclear; likely assessment was performed by annual clinical visit	52 patients (50.5 %) completed the follow-up
Kim [37]	Unclear, only described the procedure of surgery	Unclear, Only reported the diagnostic criteria	Yes, patients met the criteria of diagnosis of T2DM were included	Data was measured at each clinic visit	149 patients (68 %) completes the follow-up than 24 months
Kota [38]	Unclear, only described the procedure of surgery	Unclear, only reported the diagnostic criteria	Yes, patients having T2DM of more than 1 year duration were included	Not reported	14 (39 %) completed 2 years follow-up, 5 (36 %) completed 3 years follow-up.
Lakdawala [39]	Unclear, only described the procedure of surgery	Unclear, only reported the diagnostic criteria	Yes, patients with T2DM that was uncontrolled with medical management and lifestyle modifications were enrolled	Unclear, only reported to take follow-up examine	Not reported
Marinari [40]	Not reported	Unclear, only reported the diagnostic criteria	Yes, patients with a diagnosis of T2DM were included	Not reported	190 patients (71 %) completed the follow-up
Nora [41]		Unclear, only reported the diagnostic criteria	Yes, patients met the criteria of diagnosis of T2DM were included	Not reported	All patients completed the follow-up

Table 9 (continued)

Study	Ascertain of exposure	Ascertain of diabetes	Demonstration that outcome of interest was not present at start of study	Assessment of outcome	Completeness of outcome data
	Unclear, only described the procedure of surgery				
Sultan [42]	Not reported	Unclear, only reported the diagnostic criteria	Yes, all patients met ADA criteria for diabetes	Unclear, data collected at the encounter by the patients' primary care physician or endocrinologist	80 patients (85.1 %) completed the follow-up
Todkar [43]	Unclear, only described the procedure of surgery	Not reported	Not reported	Not reported	All patients completed the follow-up
Yang [44]	Unclear, only described the procedure of surgery	Unclear, only referred to T2DM were confirmed in all patients before surgery and diagnostic criteria	Yes, patients with a diagnosis of T2DM were included	Not reported	87.5 % of subjects completed 5 years follow-up

Table 10 Adverse events following bariatric surgery

Study	Intervention	*n* (%)	Adverse events	Treatment
Schauer [19]	GBP	1 (2)	Bowel obstruction	NR
		1 (2)	Stricture	NR
		4	Ulcer	NR
		2 (4)	Intra-abdominal bleeding	NR
		4 (8)	Dumping syndrome	NR
		1 (2)	Gallstone	NR
		1 (2)	Retinopathy	NR
		7 (14)	Nephropathy	NR
		2 (4)	Foot ulcer	NR
		8 (16)	Anemia	NR
		7 (14)	Intravenous treatment for dehydration	NR
		32 (64)	Hypoglycemic episode	NR
		1 (2)	Severe hypoglycemia requiring intervention	NR
		1 (2)	Wound infection	NR
		3 (6)	Hernia	NR
		2 (4)	Pneumonia	NR
		5 (10)	Renal calculus	NR
		2 (4)	Cancer	NR
	SG	1 (2)	Bowel obstruction	NR
		1 (2)	Stricture	NR
		1 (2)	Leak	NR
		1 (2)	Dumping syndrome	NR
		1 (2)	gallstone	NR
		1 (2)	stroke	NR
		2 (4)	Retinopathy	NR
		5 (10)	Nephropathy	NR
		1 (2)	Foot ulcer	NR
		15 (31)	Anemia	NR
		4 (8)	Intravenous treatment for dehydration	NR
		40 (82)	Hypoglycemic episode	NR
		1 (2)	Hernia	NR
		1 (2)	Pneumonia	NR
		4 (8)	Renal calculus	NR
		2 (4)	Cancer	NR
	Medical therapy	1 (2)	Bowel obstruction	NR
		1 (2)	Ulcer	NR
		4 (9)	Nephropathy	NR
		6 (14)	Anemia	NR
		3 (7)	Intravenous treatment for dehydration	NR
		39 (91)	Hypoglycemic episode	NR
		1 (2)	Hernia	NR
		6 (14)	Renal calculus	NR
		2 (5)	Cancer	NR
Lee [20]	GBP	1 (3.3)	Acute myocardial ischemia	Stent treatment

Table 10 (continued)

Study	Intervention	*n* (%)	Adverse events	Treatment
		1 (3.3)	Marginal ulcer	NR
	SG	1 (3.3)	End stage kidney disease	Hemodialysis
		1 (3.3)	Mini stroke	NR
Iaconeli [23]	BPD/DS	1 (4.5)	Pulmonary	NR
		1 (4.5)	Wound infection	NR
		3 (13.6)	Incisional hernias	NR
		2 (9.1)	Peptic ulcer	Medical treatment
MacDonald [26]	GBP	1 (0.6)	Pulmonary embolism	NR
		1 (0.6)	Non-gastric bypass-related sepsis	NR
		1 (0.6)	Anemia	NR
		1 (0.6)	Asphyxia	NR
		2 (1.2)	Cardiovascular	NR
		1 (0.6)	Malnutrition	NR
Abbatini [28]	SG	1 (8)	Retinopathy	NR
		9 (34)	Reoperation	NR
Cohen [32]	GBP	8 (12)	Port-site hematomas	NR
		1 (1.5)	Anatomic ulcer	NR
		1 (1.5)	Urinary tract infection	NR
Cruz-Munoz [33]	GBP, AGB, SG	NR	Iron deficiency anemia	Blood transfusion for severe anemia; intravenous or oral replenishment of iron stores
			Post-operative gastrointestinal bleeding	Withdrawal prophylactic anticoagulation
			Internal hernias	NR
DaPaula [34]	SG	4 (2)	Pneumonia	NR
		5 (2.5)	Ileus	NR
		2 (1)	Gastrointestinal bleeding	NR
		1 (0.5)	Acute renal failure	NR
		1 (0.5)	Myocardial infarction	NR
		1 (0.5)	Cardiac arrhythmia	NR
		1 (0.5)	Urinary tract infection	NR
		1 (0.5)	Intra-abdominal abscess	NR
		2 (1)	Gastric leak	NR
		1 (0.5)	Abdominal wall infection	NR
		1 (0.5)	Intra-abdominal bleeding	NR
		2 (1)	Intestinal obstruction	NR
		1 (0.5)	Gastric tube stricture	NR
		1 (0.5)	Early myocardial infection	NR
		2 (1)	Angina	NR
		1 (0.5)	Stroke	NR
		1 (0.5)	Pericardial effusion	NR
Kota [38]	SG	7 (16)	Difficult in swallowing	NR
		12 (28)	Nausea	NR

GBP gastric bypass, *SG* sleeve gastrectomy, *BPD/DS* biliopancreatic diversion/duodenal switch, *AGB* adjustable gastric banding

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