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Review

Role of Bariatric-Metabolic Surgery in the Treatment of Obese Type 2 Diabetes with Body Mass Index <35 kg/m^2: A Literature Review

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Abstract

Bariatric surgery has been used to treat type 2 diabetes mellitus (T2DM); however, its efficacy is still debatable. This literature review analyzed articles that evaluated the effects of bariatric surgery in treatment of T2DM in obese patients with a body mass index (BMI) of <35 kg/m^2. A paired t test was applied for the analysis of pre- and postintervention mean BMI, fasting plasma glucose (FPG), and glycosylated hemoglobin (A1c) values. A significant ($P<0.001$) reduction in BMI (from 29.95±0.51 kg/m^2 to 24.83±0.44 kg/m^2), FPG (from 207.86±8.51 mg/dL to 113.54±4.93 mg/dL), and A1c (from 8.89±0.15% to 6.35±0.18%) was observed in 29 articles ($n=675$). T2DM resolution (A1c <7% without antidiabetes medication) was achieved in 84.0% ($n=567$) of the subjects. T2DM remission, control, and improvement were observed in 55.41%, 28.59%, and 14.37%, respectively. Only 1.63% ($n=11$) of the subjects presented similar or worse glycemic control after the surgery. T2DM remission (A1c <6% without antidiabetes medication) was higher after mini-gastric bypass (72.22%) and laparoscopic/Roux-en-Y gastric bypass (70.43%). According to the Foregut and Hindgut Hypotheses, T2DM results from the imbalance between the incretins and diabetogenic signals. The procedures that remove the proximal intestine and do ileal transposition contribute to the increase of glucagon-like peptide-1 levels and improvement of insulin sensitivity. These findings provide preliminary evidence of the benefits of bariatric-metabolic surgery on glycemic control of T2DM obese subjects with a BMI of <35 kg/m^2. However, more clinical trials are needed to investigate the metabolic effects of bariatric surgery in T2DM remission on pre-obese and obese class I patients.

Introduction

The prevalence of obesity and type 2 diabetes mellitus (T2DM) has increased dramatically worldwide, becoming a serious global public health problem. These diseases increase the risk of cardiovascular diseases and favor the increase in morbidity and mortality.[1] Bariatric surgery is currently the most efficient method for treating obesity, and significant improvement in glycemic control has been observed in individuals with diabetes subjected to this surgery.[2]

Bariatric surgery should be considered as an alternative treatment in patients with a body mass index (BMI) of 30–35 kg/m^2 when diabetes cannot be controlled by medical regimen, especially in the presence of other major cardiovascular disease risk factors. The surgery must be performed within accepted international and national guidelines. It requires appropriate assessment for the procedure, ongoing multidisciplinary care, and patient education, as well as safe and effective surgical procedures.[3] However, the efficacy and safety of bariatric surgery to treat T2DM are still debatable, especially in obese individuals with a BMI of <35 kg/m^2.

Considering the significant metabolic improvement resulting from bariatric-metabolic surgery in T2DM obese patients, the purpose of this review is to analyze the results of investigations that evaluated the effects of bariatric surgery in the treatment of obese T2DM patients with a BMI of <35 kg/m^2.

Methodology

Data sources

An extensive English-language literature review was conducted to investigate articles published between January 1990

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and August 2011 on the electronic databases MEDLINE, ISI Web of Knowledge, and Science Citation Index. The search and cross-referenced terms used were "Obesity," "Bariatric surgery," "Metabolic surgery," "Diabetes surgery," "Type 2 diabetes mellitus," "T2DM," "BMI <35," "Biliopancreatic diversion," "Gastric bypass," "Laparoscopic adjustable gastric banding," "Ileal interposition," "Duodenal jejunal bypass," "Gastric banding," "Sleeve gastrectomy," and "Mini gastric bypass."

Prior to 1990, the literature offered no clinical data on the impact of bariatric surgery on T2DM obese patients with a BMI of <35 kg/m^2. Original articles with a protocol approved by a human ethics committee and that also contained data about T2DM treatment by any form of bariatric surgery in obese humans with diabetes having a BMI <35 kg/m^2 were selected. In order to broaden the search, additional articles were sought from the references cited in the selected articles. The inclusion criteria were assessed by reading the summary and methodology of the articles. When necessary, additional data were requested from the corresponding author. The following information was explored in each article and is presented here: country and year of publication, study design, surgical procedure, sample size, characteristics of the subjects, statistical analyses, study outcomes, and proposed mechanisms discussed. T2DM remission was considered when the subjects presented fasting plasma glucose (FPG) <100 mg/dL or glycosylated hemoglobin (A1c) <6% without the use of any antidiabetes medication at the end of the study. T2DM control was identified when FPG was between 100 and 125 mg/dL or A1c varied from 6.0% to 7.0% without antidiabetes medication, and T2DM improvement occurred when there was improved FPG, improved A1c, and/or reduced use of antidiabetes medications.[3] T2DM resolution (remission + control) was considered when subjects presented an A1c of <7% without antidiabetes medication. Complication and mortality rates were difficult to categorize because they were not always reported and dependent on duration of follow-up and the type of the procedure; thus they are not included here.

Statistical analysis

The FPG reported in SI units (mmol/L) was multiplied by the conversion factor 18 to provide the conventional units (mg/dL) reported in most studies. Study, patient, and outcome data were summarized using basic descriptive statistics. Mean BMI, FPG, and A1c pre- and postintervention were calculated from the data available in the articles. The data presented before and after the surgery were compared using paired-sample *t* tests. All statistical analysis was calculated from the data available in the articles using the

Table 1. Description of Studies Involving Obese Type 2 Diabetes Patients with a Body Mass Index of <35 kg/m^2 After Bariatric Surgery

Reference (year)	*Country*	*Technique*	*Design, mean follow-up time*
Angrisani et al.[4] (2004)	Italy	Lap-Band	Prospective multicenter, 12 months
Parikh et al.[5] (2006)	Australia	Lap-Band	Prospective, 36 months
Sultan et al.[6] (2009)	United States	Lap-Band	Prospective, 24 months
Noya et al.[7] (1998)	Italy	BPD	Prospective, 3–12 months
Scopinaro et al.[8] (2007)	Italy	BPD	Prospective, 36 months
Chiellini et al.[9] (2009)	Italy	BPD	Prospective, 18 months
Scopinaro et al.[10] (2011)	Italy	BPD	Prospective, 24 months
Cohen et al.[11] (2006)	Brazil	LRYGB	Prospective, 6–48 months
Shah et al.[12] (2010)	India	LRYGB	Prospective, 9 months
Navarrete et al.[13] (2011)	Venezuela	LRYGB	Prospective, 12 months
Lanzarini et al.[14] (2010)	Chile	RYGB	Retrospective, 22 months
Boza et al.[15] (2011)	Chile	RYGB	Prospective, 12–24 months
Lee et al.[16] (2008)	China	MGB	Prospective, 60 months
Kim et al.[17] (2011)	Korea	MGB	Prospective, 6 months
Lee et al.[18] (2010)	China	LSG	Prospective, 12 months
Cohen et al.[19] (2007)	Brazil	LDJB	Prospective, 9 months
Ferzli et al.[20] (2009)	U.S	LDJB	Prospective, 12 months
Ramos et al.[21] (2009)	Brazil	LDJB	Prospective, 6 months
Geloneze et al.[22] (2009)	Brazil	DJB	Prospective, 6 months
Lee et al.[23] (2010)	Korea	DJB	Prospective, 6 months
DePaula et al.[24] (2008)	Brazil	LII	Prospective, 4–16 months
DePaula et al.[25] (2008)	Brazil	LII	Prospective, 3–19 months
Depaula et al.[26] (2009)	Brazil	LII	Prospective, 14–22 months
Depaula et al.[27] (2009)	Brazil	LII	Prospective, 7–42 months
De Paula et al.[28] (2010)	Brazil	LII	Prospective, 24 months
DePaula et al.[29] (2010)	Brazil	LII	Prospective, 12–38 months
Depaula et al.[30] (2011)	Brazil	LII	Prospective, 1 month
De Paula et al.[31] (2011)	Brazil	LII	Prospective, 2–33 months
Kumar et al.[32] (2009)	India	LII	Prospective, 2–16 months

BPD, biliopancreatic derivation; DJB, duodenal–jejunal bypass; Lap-Band, laparoscopic adjustable gastric banding; LDJB, laparoscopic duodenal–jejunal bypass; LII, laparoscopic ileal interposition; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; MGB, mini-gastric bypass; RYGB, Roux-en-Y gastric bypass.

SPSS® software package, version 17.0 for Windows (SPSS Inc., Chicago, IL). The criterion for statistical significance was $P < 0.05$. Data are presented as mean ± SE values.

Results

Characteristics of the studies

From a total of 29 articles selected,[4–32] 41.38% were from Brazil ($n = 12$), 17.24% from Italy ($n = 5$), 6.90% from the United States ($n = 2$), 6.90% from China ($n = 2$), 6.90% from India ($n = 2$), 6.90% from Korea ($n = 2$), 6.90% from Chile ($n = 2$), 3.44% from Australia ($n = 1$), and 3.44% from Venezuela ($n = 1$). The effects of laparoscopic ileal interposition (LII) were evaluated in 31.03% ($n = 9$) of the studies, laparoscopic/duodenal–jejunal bypass (L/DJB) in 17.24% ($n = 5$), laparoscopic/Roux-en-Y gastric bypass (L/RYGB) in 17.24% ($n = 5$), biliopancreatic derivation (BPD) in 13.80% ($n = 4$), laparoscopic adjustable gastric banding (Lap-Band) in 10.35% ($n = 3$), mini-gastric bypass (MGB) in 6.90% ($n = 2$), and laparoscopic sleeve gastrectomy (LSG) in 3.44% ($n = 1$) (Table 1). A total of 1,209 pre-obese and obese class I patients with T2DM underwent bariatric surgery; 62.30% were male, and the mean age was 48.46 years at baseline (Table 2). Data for 675 subjects were available in the articles.

Metabolic implications

After intervention, reductions were noted in mean BMI from $29.95 \pm 0.51\ \text{kg/m}^2$ to $24.83 \pm 0.44\ \text{kg/m}^2$ ($\Delta = -5.12\ \text{kg/m}^2$) ($P < 0.001$), in FPG from 207.86 ± 8.51 mg/dL to 113.54 ± 4.93 mg/dL ($\Delta = -94.32$ mg/dL) ($P < 0.001$), and in A1c from $8.89 \pm 0.15\%$ to $6.35 \pm 0.18\%$ ($\Delta = -2.54\%$) ($P < 0.001$) (Table 3).

All available subject data from the articles ($n = 675$) were used in descriptive statistics for describing the rate of T2DM remission, control, and improvement. The analyses of the data presented by the selected articles indicated that T2DM resolution (A1c <7% without antidiabetes medication) was achieved in 84.0% ($n = 567$) of the subjects. T2DM remission was observed in 55.41% ($n = 374$), the disease was controlled in 28.59% ($n = 193$), diabetes improvement was verified in 14.37% ($n = 97$), and only 1.63% ($n = 11$) presented similar or worse glycemic control (FPG and/or A1c) after the surgery. The best procedures for T2DM remission were MGB (72.22%), L/RYGB (70.43%), and Lap-Band (70.37%). T2DM resolution (A1c <7% without antidiabetes medication) was high (>85%) in most of the procedures: L/RYGB, 89.56%; MGB, 88.89%; LII, 87.71%; and BPD, 86.54%. Similar or worse glycemic control was verified in LSG (10.00%, $n = 3$), L/DJB (4.26%, $n = 2$), L/RYGB (1.74%, $n = 2$), and LII (1.14%, $n = 4$) (Table 4).

Table 2. Sample Characterization Studies Involving Obese Type 2 Diabetes Patients with a Body Mass Index of $<35\ \text{kg/m}^2$ After Bariatric Surgery

Reference (year)	n	Gender		Mean age (years) (minimum–maximum)
		Male (%)	Female (%)	
Angrisani et al.[4] (2004)	4	—	—	38.2 (17–66)
Parikh et al.[5] (2006)	8	—	—	44.6 (16–76)
Sultan et al.[6] (2009)	15	—	—	46.9 (16–68)
Noya et al.[7] (1998)	10	5 (50)	5 (50)	52.1 (40–62)
Scopinaro et al.[8] (2007)	7	5 (71)	2 (29)	49.0 (39–60)
Chiellini et al.[9] (2009)	5	3 (60)	2 (40)	48.3
Scopinaro et al.[10] (2011)	30	19 (63)	11 (37)	56.4 (43–69)
Cohen et al.[11] (2006)	37	7 (19)	30 (81)	34.0 (28–45)
Shah et al.[12] (2010)	15	8 (53)	7 (47)	45.6 (33–57)
Navarrete et al.[13] (2011)	10	5 (50)	5 (50)	46.5 (29–75)
Lanzarini et al.[14] (2010)	23	14 (61)	9 (39)	62.9 (43–77)
Boza et al.[15] (2011)	30	13 (43)	17 (57)	48.0 (28–65)
Lee et al.[16] (2008)	44	6 (14)	38 (86)	39.0
Kim et al.[17] (2011)	10	2 (20)	8 (80)	46.9 (29–59)
Lee et al.[18] (2010)	20	6 (30)	14 (70)	46.3
Cohen et al.[19] (2007)	2	2 (100)	0 (0)	47.0 (43–51)
Ferzli et al.[20] (2009)	7	—	—	43.3 (33–52)
Ramos et al.[21] (2009)	20	11 (55)	9 (45)	43.0 (29–60)
Geloneze et al.[22] (2009)	12	9 (75)	3 (25)	50.0
Lee et al.[23] (2010)	6	6 (100)	0 (0)	50.2 (38–64)
DePaula et al.[24] (2008)	39	23 (59)	16 (41)	50.3 (36–66)
DePaula et al.[25] (2008)	60	36 (60)	24 (40)	51.7 (27–66)
Depaula et al.[26] (2009)	58	40 (69)	18 (31)	51.4 (40–66)
Depaula et al.[27] (2009)	69	47 (68)	22 (32)	51.4 (41–63)
De Paula et al.[28] (2010)	38	27 (71)	11 (29)	53.6 (27–66)
DePaula et al.[29] (2010)	72	51 (71)	21 (29)	53.1 (38–66)
Depaula et al.[30] (2011)	454	322 (71)	132 (29)	53.6 (27–75)
De Paula et al.[31] (2011)	94	61 (65)	33 (35)	54.0
Kumar et al.[32] (2009)	10	4 (40)	6 (60)	48.2 (34–62)
Total	1,209	732 (62)	443 (38)	48.46

A dash indicates data not supplied.

Table 3. Clinical Results of Studies Involving Obese Type 2 Diabetes Patients with a Body Mass Index of <35 kg/m² After Bariatric Surgery

	BMI (kg/m²)		FPG (mg/dL)		A1c (%)	
Reference (year)	Before	After	Before	After	Before	After
Angrisani et al.[4] (2004)	33.9	28.2	—	—	—	—
Parikh et al.[5] (2006)	32.7	27.6	—	—	—	—
Sultan et al.[6] (2009)	33.1	25.8	—	—	—	—
Noya et al.[7] (1998)	33.3	27.5	—	—	—	—
Scopinaro et al.[8] (2007)	33.4	27.0	252.7	92.1	—	—
Chiellini et al.[9] (2009)	30.9	25.1[a]	—	—	8.48	5.7[a]
Scopinaro et al.[10] (2011)	33.1	27.4[a]	234	134[a]	9.5	5.9[a]
Cohen et al.[11] (2006)	32.5	—	146	88[b]	—	≤6
Shah et al.[12] (2010)	28.9	23.0[c]	233	89.2[c]	10.1	6.1[c]
Navarrete et al.[13] (2011)	27.2	23.9	206.4	103.1[b]	9.0	6.3[b]
Lanzarini et al.[14] (2010)	29.1	—	151.4	—	—	—
Boza et al.[15] (2011)	33.5	24.4	145	94.4[a]	8.1	5.9[a]
Lee et al.[16] (2008)	31.7	23.2	168.7	80.1[c]	7.3	5.6[c]
Kim et al.[17] (2011)	27.2	23.4	222	144	9.7	6.7
Lee et al.[18] (2010)	31.0	24.6[a]	240.1	132.9[a]	10.1	7.1[a]
Cohen et al.[19] (2007)	29.6	28.2	163	83	8.3	5.3
Ferzli et al.[20] (2009)	27.5	27.3	208.8	154.8[NS]	9.4	8.5[NS]
Ramos et al.[21] (2009)	27.1	24.4[c]	171.3	96.3[c]	8.8	6.8[c]
Geloneze et al.[22] (2009)	26.1	25.6[NS]	185.4	158.2[b]	8.9	7.8[b]
Lee et al.[23] (2010)	25.25	20.45[NS]	322.2	—	8.1	7.4[NS]
DePaula et al.[24] (2008)	30.1	24.9	210.7	116.7[c]	8.8	6.3[c]
DePaula et al.[25] (2008)	30.1	23.8	209.8	106.3[c]	9.0	5.8[c]
Depaula et al.[26] (2009)	28.2	—	215.3	105.4[c]	8.9	5.4[a]
Depaula et al.[27] (2009)	25.7	21.8[c]	218.1	102[c]	8.7	5.9[c]
De Paula et al.[28] (2010)	28.9	22.2[a]	206.9	114.6[c]	8.5	5.88[c]
DePaula et al.[29] (2010)	27.0	21.3[c]	282.1	142.2[c]	8.5	6.1[c]
Depaula et al.[30] (2011)	29.7	25.8	198.3	125.8[c]	8.8	—
De Paula et al.[31] (2011)	28.1	22.4[a]	195	118.8[a]	8.7	6.1[a]
Kumar et al.[32] (2009)	33.8	26.3[a]	202.5	116[a]	10.0	6.7[a]
Mean ± SE	29.95 ± 0.51	24.83 ± 0.44[c]	207.86 ± 8.51	113.54 ± 4.93[c]	8.89 ± 0.15	6.35 ± 0.18[c]

A dash indicates data not supplied.
Difference from before value was significant: [a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.001$.
BMI, body mass index; FPG, fasting plasma glucose; A1c, glycosylated hemoglobin; NS, not significant.

Discussion

Metabolic mechanisms

The metabolic mechanisms leading to improved glycemic control after bariatric surgery have been partly elucidated. Restrictive procedures decrease the food intake, leading to a reduction in glycemic load of the diet, causing an improvement on glucose control. Furthermore, the caloric restriction contributes to weight loss, leading an improvement on insulin sensitivity and on glycemic levels. In addition, the duodenal bypass increases glucagon-like peptide-1 (GLP-1) levels, leading an increase in insulin secretion, causing amelioration in glycemic control.[33]

Bariatric surgery leads to glycemic control improvement by increasing insulin sensitivity.[34–36] GLP-1 has been considered the main hormone responsible for the increase of insulin secretion and insulin sensitivity, leading its effect on glycemic control.[37]

It was demonstrated that L/RYGB led to improved glucose and insulin levels and increased GLP-1 and peptide YY (PYY) release a few months after surgery.[36,38,39] Improvements in glucose levels, insulin resistance measured by homeostasis model of assessment, and GLP-1 levels were observed after the first week following BPD, which was not necessarily associated with weight loss,[40–43] with restoration of the first phase of insulin secretion 1 month after the surgery.[44] These metabolic changes may be responsible for the high T2DM resolution occurrence.

When Goto-Kakizaki rats were subjected to DJB, although no improvement of glucose tolerance was observed, there was a significant increase in GLP-1 levels and restoration of the first phase of insulin secretion, regardless of the intestinal bypass.[45–49] These data may explain the early beneficial effects of this procedure on glycemic control in humans.

The Lap-Band metabolic improvement proves to be effective and enduring.[50,51] Jiang et al.[52] observed significantly reduced insulin resistance measured by homeostasis model of assessment and increased GLP-1 levels. However, more studies involving T2DM obese patients with a BMI of <35 kg/m² should be conducted, and the mechanisms responsible for the glucose metabolism improvement should be investigated.

The results of experimental ileal transposition studies revealed that the interposition of a segment of the distal ileum into the proximal jejunum leads to increased production and secretion of GLP-1. It has been hypothesized that the

Table 4. Type 2 Diabetes Mellitus Resolution According to the Technique

	% (n)			
Technique	*Remission*[a]	*Control*[b]	*Improvement*[c]	*Same or worse*
MGB	72.22 (39)	16.67 (9)	11.11 (6)	0.00 (0)
L/RYGB	70.43 (81)	19.13 (22)	8.70 (10)	1.74% (2)
Lap-Band	70.37 (19)	0.00 (0)	29.63 (8)	0.00 (0)
LII	58.00 (203)	29.71 (104)	11.14 (39)	1.14 (4)
BPD	48.08 (25)	38.46 (20)	13.46 (7)	0.00 (0)
LSG	13.33 (4)	33.33 (10)	43.33 (13)	10.00 (3)
L/DJB	06.39 (3)	59.57 (28)	29.78 (14)	4.26 (2)
Total	55.41 (374)	28.59 (193)	14.37 (97)	1.63 (11)

[a]Fasting plasma glucose < 100 mg/dL or glycosylated hemoglobin < 6.0% without antidiabetes medication.
[b]Fasting plasma glucose 100–125 mg/dL or glycosylated hemoglobin < 7.0% without antidiabetes medication.
[c]Improvement in glycosylated hemoglobin and/or reduction in antidiabetes medication.
BPD, biliopancreatic derivation; Lap-Band, laparoscopic adjustable gastric banding; L/DJB, laparoscopic/duodenal–jejunal bypass; LII, laparoscopic ileal interposition; L/RYGB, laparoscopic/Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; MGB, mini-gastric bypass.

presence of a greater amount of partially digested nutrients in the interposed ileum segment leads to increased production and secretion of PYY and GLP-1, thus improving glucose metabolism.[53,54]

Foregut and Hindgut Hypotheses

Several diabetogenic signals (anti-incretin factors) produced by the proximal intestine have been associated with T2DM development. It has been suggested that the surgical removal of the proximal duodenum and jejunum may reduce the level of these substances, increasing glycemic control in T2DM.[55] The Foregut Hypothesis was created after Rubino and Marescaux[45] verified a significant improvement in glucose tolerance but with no effect on body weight in non-obese Goto-Kakizaki rats subjected to a duodenum–jejunal bypass. In a similar study, these same investigators confirmed that proximal duodenum and jejunum removals are the main components involved in the improvement on glycemic control.[56] It has been suggested that the removal of the proximal intestine leads to an increase in incretin levels and a reduction of the anti-incretin factors, supporting the glycemic control improvement.

According to the Hindgut Hypothesis the early arrival of food bolus on the interposed ileum causes an increase of incretins, especially GLP-1 and PYY production and secretion, contributing to the observed glycemic control. A significant increase of GLP-1 levels in rats subjected to glucose tolerance test was observed 3 weeks after the ileal transposition.[53] In another study involving Goto-Kakizaki rats there was a significant improvement in glucose tolerance 45 days after the ileal transposition.[54]

In summary, the intestine seems to be an important endocrine organ involved in glucose level regulation, and therefore on T2DM physiopathology. GLP-1 is considered a key hormone in this process due to its positive effects on β cells and on insulin secretion and action. Two hypotheses can explain the rapid effects of bariatric surgery on T2DM control—the Foregut and Hindgut Hypotheses. According to these hypotheses, insulin resistance and hyperglycemia result from the imbalance between the incretin levels and the anti-incretin factors. The effects of the surgeries that remove the proximal duodenum and the jejunum and that do the ileal transposition anticipate the arrival of food contributing to the increase in GLP-1 levels and the consequent improvement on insulin sensitivity.[53–56]

Limitations

Despite the beneficial effects of bariatric surgery on diabetes control, the articles presented in this review have several methodological limitations that pose difficulties for data interpretation and generalization of results. None of the studies was a randomized controlled trial, to specifically analyze the optimal medical treatment of diabetes versus bariatric surgery. Moreover, the articles do not show diabetes therapy before the surgery; thus it is not possible to assess the effectiveness of treatments on the patients.

All available data of subjects from the articles were used in our research, and pre- and postintervention analysis and descriptive statistics ($n = 675$) for describing the rate of T2DM remission, control, and improvement are reported (Table 4). Unfortunately not all necessary data were available in the articles, resulting in decreased power of statistical analysis, interpretation, and generalization of results. These limitations worsen the comparison of results of the bariatric procedures.

Because of the short time of follow-up in these studies it is not possible to evaluate the late metabolic effects of these surgeries. Some studies have evaluated the long-term weight loss and show high rates of weight regain and surgical failure. Magro et al.[57] analyzed the weight loss after gastric bypass for 5 years; they observed weight regain within 24 months after surgery in approximately 50% of patients, with the percentage of surgical failure reaching 18.8% at 48 months after surgery. Capella and Capella[58] and MacLean et al.[59] reported an excess weight loss of less than 50% in 7% of the patients after 5 and 3 years of follow-up, respectively. Higa et al.[60] observed 33.2% excess weight loss in less than 50%, and 26% of patients demonstrated sustainable weight loss and resolution of comorbidities. Articles with follow-up periods ranging from 3 to 10 years demonstrated failure rates in superobese patients ranging from 26% to 43%.[61–63] A long-term follow-up of more than 10 years is necessary to precisely determine the extent of weight loss/regain and sustained benefits on T2DM.

Unfortunately, bariatric surgery also has the potential to cause various health complications. Follow-up research observed gastrointestinal complications, the most common of which were hernia, anastomotic stenosis, hemorrhage, dumping, epigastric pain, vomiting, esophagitis, pouch dilation, esophageal dilation, port problems, and band migration.[64] In addition, nutritional complications are associated with bariatric surgery because of malabsorption and decreased intake of specific nutrients. Macronutrient deficiencies can include severe protein–calorie malnutrition and fat malabsorption. The most common micronutrient deficiencies are vitamin B12, iron, calcium, vitamin D, thiamine, folate, and the fat-soluble vitamins. Counseling, monitoring, and nutrient and mineral supplementation are essential for the treatment and prevention of nutritional and metabolic complications after bariatric surgery.[65]

Future studies

Research studies on bariatric-metabolic surgery have produced new perspectives for the treatment of T2DM. However, this therapeutic approach still requires adjustments to further increase its effectiveness. The establishment of well-defined recommendations and guidelines for clinical use and the definition of specific criteria for consideration of T2DM remission and control are also needed. Careful, well-designed multicenter studies are needed to investigate the benefits of the surgery in different populations, by analyzing the procedures used and investigating the mechanisms involved, in order to propose a model for the creation of a safe and effective surgical procedure for T2DM remission in obese patients with a BMI of $<35\,kg/m^2$.

Despite the favorable results of bariatric-metabolic surgery, some questions still need to be answered: Which procedure is most appropriate for each condition presented by the patients? What are the surgical risks and benefits of each procedure? Can these surgical procedures be used safely in nonobese T2DM patients? What are the long-term results of these surgical treatments? What are the physiological and molecular mechanisms of the metabolic improvements observed? What are the safety and cost-effectiveness of each of the surgical treatments? There is no doubt that these and other questions need to be answered for a complete understanding of the efficacy and safety of bariatric surgery in T2DM remission. Uncertainties remain, and further research is required to provide detailed data of the impact of the type of surgery on outcome, duration of comorbidity remission, and late complications and mortality. Good-quality randomized controlled trials will provide evidence about bariatric-metabolic surgery for remission of the T2DM.

Conclusions

The analyses of the 29 studies involving 675 T2DM obese patients with BMI $<35\,kg/m^2$ subjected to a bariatric surgery shows a significant ($P<0.001$) reduction in BMI, FPG, and A1c after the procedure. Eighty-four percent of the subjects achieved a T2DM resolution (A1c $<7\%$ without antidiabetes medication), and the glycemic control was not reached in 1.63% of the diabetes patients. The L/RYGB, MGB, and LII procedures showed high ($>85\%$) efficiency for T2DM resolution. The Foregut and Hindgut Hypotheses show that procedures that remove the proximal intestine and interposition of an ileum section lead to earlier arrival of food at the ileum, contributing to the increase in GLP-1 levels and improvement in glucose metabolism.

These data provide preliminary evidence the benefits of bariatric-metabolic surgery on the glycemic control of T2DM obese subjects with a BMI of $<35\,kg/m^2$. However, more randomized controlled trials are needed to investigate the effects of bariatric surgery in T2DM remission in pre-obese and obese class I patients. It is prudent to compare surgical interventions with other medical interventions in more robust studies. A combination of surgical, medical, and behavioral interventions should be considered for treating obese patients with T2DM.

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