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Review Article

Recent advances in bariatric/metabolic surgery: appraisal of clinical evidence

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Abstract

Obesity and associated type 2 diabetes mellitus (T2DM) are becoming a serious medical issue worldwide. Bariatric surgery has been shown to be the most effective and durable therapy for the treatment of morbid obese patients. Increasing data indicates bariatric surgery as metabolic surgery is an effective and novel therapy for not well controlled obese T2DM patients. The review of recent developments in bariatric/metabolic surgery covers 4 major fields. 1) Improvement of safety: recent advances in laparoscopic/metabolic surgery has made this minimal invasive surgery more than ten times safer than a decade ago. The safety profile of laparoscopic/metabolic surgery is compatible with that of laparoscopic cholecystectomy now. 2) New bariatric/metabolic surgery: laparoscopic sleeve gastrectomy (LSG) is becoming the leading bariatric surgery because of its simplicity and efficacy. Other new procedures, such as gastric plication, banded plication, single anastomosis (mini) gastric bypass and Duodeno-jejunal bypass with sleeve gastrectomy have all been accepted as treatment modalities for bariatric/metabolic surgery. 3) Mechanism of bariatric/metabolic surgery: Restriction is the most important mechanism for bariatric surgery. Weight regain after bariatric surgery is usually associated with loss of restriction. Recent studies demonstrated that gut hormone, microbiota and bile acid changes after bariatric surgery may play an important role in durable weight loss as well as in T2DM remission. However, weight loss is still the cornerstone of T2DM remission after metabolic surgery. 4) Patient selection: patients who may benefit most from bariatric surgery was found to be patients with insulin resistance. For Asian T2DM patients, the indication of metabolic surgery has been set to those with not well controlled (HbA1c $>$ 7.5%) disease and with their BMI $>$ 27.5 Kg/m^2. A novel diabetes surgical score, ABCD score, is a simple system for predicting the success of surgical therapy for T2DM.

Keywords: bariatric surgery, metabolic surgery, type 2 diabetes mellitus, advances

Introduction

Obesity and type 2 diabetes mellitus (T2DM) are becoming epidemic diseases worldwide[1,2]. These two diseases are closely related and both are very difficult to treat[3,4]. Bariatric surgery, aimed at weight reduction, has been proven to be a viable option for the treatment of severe obesity in comparison to conservative methods, resulting in long-lasting weight loss, improved quality-of-life, and the resolution of obesity-related co-morbidities[5]. Among all of the obesity-related co-morbidities, bariatric surgery has been proven especially successful in treating T2DM[6–8] in morbidly obese patients (BMI $>$ 35 Kg/m^2) as well as preventing the development of T2DM[9]. Recently, gastrointestinal metabolic surgery has been proposed as a new treatment

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modality for T2DM in patients with body mass index (BMI) < 35 Kg/m^2[10]. Several randomized trials have proven that metabolic surgery resulted in better glycemic control compared with medical treatment in T2DM patients with BMI < 35 Kg/m^2[11–17]. Therefore, it is not surprising that the number of bariatric/metabolic surgeries worldwide has grown rapidly over the past decade, including Asia[18–22]. The increasing acceptance of bariatric/metabolic surgery deserves a detailed review and discussion. Therefore, we summarize the currently available randomized controlled trials and review articles on bariatric/metabolic surgery over the past decade. The review will allow current and future bariatric/metabolic surgeons to build a foundation of bariatric/metabolic surgery and development of further clinical trials to provide more powerful evidence in bariatric/metabolic surgery.

Improved safety

The most important technique change in bariatric/metabolic surgery is from open surgery to laparoscopic surgery. Many randomized trials had proven the superity of laparoscopic bariatric surgery in reducing the impairment of post-operative pulmonary function, intra-operative blood loss, hospital stay, wound infection and incisional hernia rate, and quick return to work[22–24]. An additional benefit of laparoscopic surgery over open surgery is the decrease of postoperative venous thrombo-embolism[25]. However, some adverse effects have been found, such as that laparoscopic gastric bypass resulted in decreased intra-operative urine output[26], transient postoperative elevation of liver enzymes[27], and decreased femoral venous flow[28]. These biologic changes may result from the effect of intra-abdominal hypertension caused by pneumo-peritoneum which may influence the respiratory and abdominal organ function[29]. These findings highlight the importance avoiding prolonged operative time in older, more obese patients, and patients with unstable hemodynamic or chronic kidney disease.

A decade ago, the 30 day operation mortality for bariatric/metabolic surgery was up to 2% and 1-year mortality was up to 5% in USA[30]. The operative risk was found to be closely related to surgeon′s experience and hospital volume. Improvement in technology and experience has dramatically improved the safety of this procedure. Recent reports have confirmed that bariatric/metabolic surgery can be performed as safe as laparoscopic cholecystectomy with operation mortality around 0.1%[31,32]. However, although the major complication rate was similar between the bariatric and metabolic surgery, patients who already had metabolic syndrome tended to develop more severe complications that resulted in higher mortality rates. A recent report from Inabet et al. had found that bariatric surgery carried a three times higher risk in patients with metabolic syndrome compared with patients without metabolic syndrome[32]. The reason for the more severe complication in T2DM patients might be related to the compromised cardiovascular system and depressed immunity in patients with poorly controlled diabetes[33,34].

New bariatric/metabolic procedures

Laparoscopic gastric banding and gastric bypass are the two most commonly performed bariatric surgeries currently[18]. The major obstacle to laparoscopic adjustable gastric banding (LAGB) is the requirement of patient compliance and a high revision rate, resulting in a rapid decrease in the acceptance of LAGB worldwide[19]. Laparoscopic sleeve gastrectomy (LSG), a vertical gastrectomy that leaves a narrow gastric tube along the lesser curvature of the stomach, has been accepted as a primary procedure for morbid obese patients recently because of its simplicity and effectiveness. The American College of Surgeons Bariatric Surgery Center Network has put it in the intermediate position between laparoscopic gastric banding and laparoscopic gastric bypass in term of reduction of BMI, complication rates and resolution of obesity related illness[35]. Several randomized trials also demonstrated that LSG has a similar efficacy of weight reduction comparing to Roux-en-Y gastric bypass (RYGB) at short- to mid-term[36–38]. The acceptance of LSG is especially high in Asia because of the concern of remnant gastric cancer[39]. LSG has now consisted more than 50% of the bariatric surgery in Asia and more than 70% in Japan where gastric cancer is the leading cancer death[20,40]. However, the main long-term drawback of LSG is the development of gastro-esophageal reflux disease (GERD) in around 15% of the patients [41]. This remains to be an important issue of LSG[42].

Laparoscopic gastric greater curvature side plication (LGGCP) is a new restrictive technique that was first reported in 1981 by Wilkinson[43] and more recently by Talepour and Amoi[44]. Currently, LGGCP has been investigated as a novel bariatric surgery[45–48] and adopted for the salvage of failed bariatric surgery, such as a dilated sleeve gastrectomy, pouch dilatation after gastric bypass or inadequate weight loss after LAGB[49]. Combination of LAGB with LGGCP (LAGB-P) has recently been reported to increase weight loss after LAGB[50,51]. However, long-term data is indicated before accept these restrictive novel procedures as standard bariatric/metabolic surgery.

Another important change of technique is from two anastomosis Roux-en-Y reconstruction to single loop anstomosis technique. The elimination of one anasto–mosis may reduce operative time and decrease the possibility of surgically related complication. Laparoscopic single anastomosis (mini-) gastric bypass (SAGB), a sleeve gastric tube with a Billroth II loop bypass, had been proven to have a shorter operative time and lower complication rate comparing to RYGB in a randomized trial[52]. At longer follow-up, SAGB still had the advantage of less revision surgery for intestinal obstruction comparing to RYGB[53,54]. At the same time, another modified duodenal switch (DS) was proposed by Sanchez-Pernaute et al. by doing a single anastomosis DS, called single anasto–mosis duodeno-ileal bypass with sleeve gastrectomy (SADI-SG)[55,56]. However, the major obstacles of DS are technical difficulty and the possibility of long-term nutritional problems. A modified short DS has been proposed by Kasama et al. from Asia with a procedure called duodeno-jejunal bypass with sleeve gastrectomy (DJB-SG)[57]. This procedure is specifically designed for metabolic surgery and was especially welcomed in Asia[58]. A simplified DJB-SG by single anastomo–sis, SADJB-SG has also been reported recently[59].

Mechanisms of effect

The most important mechanism for weight reduction is believed to be restriction and the accompanying reduced daily calories intake. A recent study has esti–mated that the most important mechanism for the gold standard bariatric surgery, RYGB, is the reduced intake due to restriction and satiety and contributes about 75% of the effect[60]. The restriction effect of RYGB is provided by a tiny gastric pouch and small outlet. In SAGB, the restriction is provided by the long sleeve tube, very similar in sleeve gastrectomy. The reason why LSG had a similar result to RYGB is that LSG may provide a better restriction than RYGB[35–37]. Therefore, the reason for weight regain after bariatric surgery is mainly contributed to lost restriction and the goal of revision surgery is to rebuild the restriction.

The second important mechanism of RYGB is from the duodeno-jejunal bypass which was estimated to contribute less than 25% of the efficacy[60]. Exclusion of the duodenum from food stream may eliminate the physiologic response of duodenal gut hormone and related enzyme secretion (glucagon, cholecystokinin and bilio-pancreatic enzymes). The rapid food transit to distal gut induces a surge of distal gut hormone (GLP-1 and PYY) release[37,61,62]. These two gut hor–mone responses were also called ''fore gut theory'' and ''hint gut theory'' which help in weight loss as well T2DM remission[63].

Another mechanism involved is the gut microbiota. Recent studies have shown that the gut microbiota of obese human beings is distinct from that of healthy-weight individuals[64,65]. Changes in the gut microbiota might be responsible for the development of non-alcoholic fatty liver disease (NAFLD) and gastroin–testinal symptoms[66]. Probiotic agents were found to be helpful in treating irritable bowel syndrome and improving outcomes after gastric bypass surgery[67,68].

The mechanism of LSG is also intriguing. LSG was found not a pure restrictive bariatric procedure because some complex gut hormone changes were involved with LSG. The first one is the markedly reduced ghre–lin level after complete removal of gastric fundus, site of production of hormone ghrelin, will help in the weight loss[60,62,63]. Another one is the quickly elevated of post-meal GLP-1 and PYY response induced by the rapid bowel transit time after LSG which may help in weight reduction and metabolic control[37,60,63]. However, a recent study by Randy has shown that neither ghrelin nor GLP-1 played an essential role in LSG. They found that bile acid is the key player in weight loss after LSG[69]. Further studies are indicated to elucidate this intrigue question about the mechanism of LSG.

Table 1 **Randomized controlled trials for metabolic surgery in T2DM with BMI < 35 Kg/m^2**

Author	*n*	BMI Mean (range)	HbA1C Mean	LAGB	LSG	RYGB	SAGB	Medicine
Dixon[11]	60	36 (30–40)	7.7%	-1.8%	—	—	—	-0.4%
Lee[12]	60	30 (25–35)	10.0%	—	-2.8%	—	-3.3%	
Shauer[13,17]	150	36 (28–42)	9.3%	—	-2.5%	-2.6%		-0.6%
Ikramuddin[14]	120	36 (30–40)	9.6%	—	—	3.3%		-1.8%
Liang[15]	120	30 (>28)+	10.5%	—	—	-4.4%		2.4%
Wentworth[16]	51	29 (25–30)	7.0%	-08%	—	—	—	+0.2%

LAGB: Laparoscopic adjustable gastric banding; LSG: laparoscopic sleeve gastrectomy; RYGB: Roux-en-Y gastric bypass; SAGB: single anastomosis gastric bypass; SAGB: single anastomosis gastric bypass.

Although LSG had a similar weight loss comparing to gastric bypass, several randomized trials have shown that procedure with duodenal exclusion had a higher rate in diabetes remission or off medication than those without duodenal exclusion, especially in lower BMI diabetics[12,13,17]. The reason is that duodenal exclusion may have a significant role in diabetes treatment other than weight reduction. The recent study has identified some possible duodenal factor related to duodenal exclusion[70]. Therefore, although LSG may be the first choice for bariatric surgery, gastric bypass may be a preferred metabolic surgery for the treatment of T2DM in patients with BMI < 35 Kg/m^2. Further stu–dies are indicated to elucidate the mechanism of duo–denum exclusion and develop possible new treatments for T2DM.

Studies have illustrated some patients whose T2DM remission after surgery experienced a recurrence of their disease over time[71–73]. DiGiorgi et al. have shown that beyond 3 years after gastric bypass, 24% of patients with initial remission of their T2DM had re-emergence of diabetes[72]. The recurrence of T2DM was usually associated with weight regain and longer duration of T2DM[73]. Other studies also showed that weight reduction is the most important predictor of T2DM remission after bariatric/metabolic surgery[74]. Even in low BMI T2DM patients, weight reduction is still the most important deciding factor of T2DM remission[75,76]. Therefore, patients receiving metabolic surgery for their T2DM required long-term follow-up and education for life style modification in order to prevent weight regain.

Patient selection

Although not a perfect one, the BMI, surrogate of obesity, is now the most important indicator of bariatric surgery as well as metabolic surgery for diabetes treat–ment. Indication for bariatric surgery was universally accepted for BMI > 35 Kg/m^2 with co-morbidities and BMI may be lowered to 32 in Asian because of the tendency of central obesity for Asian[20]. However, recent study has shown that BMI did not predict the effect of bariatric surgery on mortality or cardiovascular disease and patients who may benefit from bariatric sur–gery are those with insulin resistance[7,71,77]. These find–ings are very important in patient selection and may be incorporated into indication for bariatric/metabolic sur–gery in the future. We shall select those patients who are most likely to benefit from bariatric surgery, and more importance should be given to metabolic variables and less to BMI.

Recently, gastrointestinal metabolic surgery has been proposed as a new treatment modality for T2DM in patients with BMI < 35 Kg/m^2[78]. Several randomized trials have proven that metabolic surgery resulted in a better glycemic control compared with medical treatment in T2DM patients with BMI < 35 Kg/m^2[11–17]. ***Table 1*** disclosed the magnitude of HbA1c reduction in various treatment arms of these randomized trials. International Diabetes Federation (IDF) guideline has recommended that surgery is an eligible treatment for Asian patients with not well con–trolled T2DM (HbA1c > 7.5%) and BMI > 27.5 kg/m^2[10]. However, previous study also disclosed that T2DM remission after bariatric surgery was progres–sively decreased associated with the lower of BMI[79]. Therefore, it is mandatory to select patients who are best suited to the surgery and those who will predictably have a poor result are excluded to avoid the unnecessary

Table 2 **Variables and point values used for the computation of the age, body-mass index, c-peptide, duration of diabetes (ABCD) score.***

Variable	Points on ABCD index Gastric bypass *P* value			
	0	1	2	3
Age	⩾40	< 40		
BMI (kg/m^2)	< 27	27–34.9	35–41.9	⩾ 42
C-peptide (mmol/L)	< 2	2–2.9	3–4.9	⩾ 5
Duration of DM (years)	> 8	4–8	1–3.9	< 1

*The cutoff values for the assignment of points are shown for each variable.

The total possible values range from 0 to 10. BMI denotes body mass index.

Table 3 **Remission rate of T2DM according to ABCD score**

ABCD score	Complete remission (HbA1C < 6%)	Partial remission (HbA1C < 6.5%)
0	5.9%	5.9%
1	5.0%	20.0%
2	26.3%	38.6%
3	31.9%	42.0%
4	52.5%	67.8%
5	55.4%	75.0%
6	61.7%	78.3%
7	77.0%	92.3%
8	85.2%	96.3%
9	87.1%	87.1%
10	93.3%	93.3%
Overall	52.2%	64.7%

According to the analysis of 510 cases of Asian Diabetes Surgery Study (ADSS).

exposure to the surgical risk. To be able to make such decisions, we need preoperative information on the association between possible predictors and outcome. A simple scoring system consisted of four variables – the age, BMI, C-peptide and duration of diabetes- was developed for predicting the success of T2DM treatment after metabolic surgery; the ABCD Diabetes Surgery Score was previously reported[80]. This simple multidimensional grading system can predict the success of T2DM treatment and is clinically recommended (***Table 2*** and ***3***).

Conclusion

Laparoscopic bariatric/metabolic surgery is becoming a safe and effective treatment for morbid obesity and obese T2DM. LSG and many new procedures have been developed and adapted into the treatment modalities of bariatric/metabolic surgery. Good patient selection and durable weight loss remain the cornerstones of the success of bariatric/metabolic surgery.

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