ELSEVIER

Surgery for Obesity and Related Diseases 9 (2013) 370–378

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Roux-en-Y gastric bypass stands the test of time: 5-year results in low body mass index (30–35 kg/m^2) Indian patients with type 2 diabetes mellitus

Muffazal Lakdawala, M.S.[a,b,c], Shehla Shaikh, M.D., D.M. (Endocrinology)[a,b,d], Saifee Bandukwala, M.D.[a,b,c], Carlyne Remedios, M.Diet., A.P.D.[a], Miloni Shah, R.D.[a], Aparna Govil Bhasker, M.S.[a,b,*]

[a]*Center for Obesity and Diabetes Surgery, Mumbai, India*
[b]*Department of Minimal Access and Bariatric Surgery, Saifee Hospital, Mumbai, India*
[c]*Lilavati Hospital and Research Center, Mumbai, India*
[d]*Prince Aly Khan Hospital, Mumbai, India*

Received March 27, 2012; accepted July 23, 2012

Abstract

Background: Our objective was to evaluate the long-term results of laparoscopic Roux-en-Y gastric bypass on excess weight loss, remission of the metabolic syndrome, and complications in Indian patients with uncontrolled type 2 diabetes mellitus (T2DM) with a body mass index of 30–35 kg/m^2. The setting was a corporate hospital in Mumbai, India.

Methods: The present prospective observational study was begun in January 2006. A total of 52 patients with uncontrolled T2DM and a body mass index of 30–35 kg/m^2 elected to undergo laparoscopic Roux-en-Y gastric bypass. The duration of T2DM was 3.5–14.5 years (median 8.4). Of the 52 patients, 61.5% had hypertension and 59.6% had dyslipidemia. Remission of T2DM and other components of the metabolic syndrome were assessed. All patients were followed up for 5 years.

Results: The median percentage of excess weight loss was 72.2% at 1 year and 67.8% at 5 years. Of the 52 patients, 84.6% had achieved euglycemia and 73.1% had achieved complete remission, 23.1% partial remission, and 3.84% no remission at 1 year. Weight regain occurred in 8 patients. They required antihypertensive drugs and statins, decreasing the complete remission rate to 57.7% and partial remission rate to 38.5% at 5 years. However, 96.2% improvement in metabolic status was found at the end of 5 years.

Conclusion: Laparoscopic Roux-en-Y gastric bypass is a safe, efficacious, and cost-effective treatment for uncontrolled T2DM in patients with a body mass index of 30–35 kg/m^2. Early-onset T2DM, better weight loss, and greater C-peptide levels were predictors of success after surgery. The improvement after surgery in hyperglycemia, hypertension, and dyslipidemia could help in controlling the occurrence of micro- and macrovascular complications and decrease the morbidity and mortality associated with T2DM. (Surg Obes Relat Dis 2013;9:370–378.)

Keywords: Type 2 diabetes mellitus; Low body mass index diabetic; BMI; 5-Year results; Roux-en-Y gastric bypass; Asia; C-peptide; Metabolic syndrome; Thrifty gene

*Correspondence: Aparna Govil Bhasker, M.S., Department of Minimal Access and Bariatric Surgery, Saifee Hospital, Mumbai, India and Center for Obesity and Diabetes Surgery, Ground Floor, Shiv Tapi Building, H. Goregaonkar Marg, Opposite Motor House, Opera House, Mumbai 400007 India.

E-mail: aparna@codsindia.com

1550-7289/13/$ – see front matter
http://dx.doi.org/10.1016/j.soard.2012.07.017

India is the second most populous country in the world after China. Its large labor force has been principally responsible for realizing the great Indian dream and sustaining its growth, even during 1 of the greatest economic slowdowns in human history. With the newfound affluence, increasing urbanization, and a population that has crossed the 1 billion mark, the greatest challenge that India faces today is the steep increase in noncommunicable diseases, especially type 2 diabetes mellitus (T2DM) and obesity.

The high incidence of T2DM among Asians can be attributed to greater adiposity levels and presence of the "thrifty" gene that has become a curse in these times of surplus [1]. Some aspects of maternal nutritional intake during pregnancy, along with low birth weights of the newborns, can lead to an increased predisposition for developing insulin resistance, even as early as 8 years of age [2]. It is widely known that the risk of the metabolic syndrome in Asians starts at relatively lower body mass index (BMI) levels (22–23 kg/m^2) [3]. Hence, one can deduce that Asians develop T2DM with a lesser degrees of obesity, at younger ages, and experience complications longer.

Recent results from Screening India's Twin Epidemic study revealed that 34.7% of all patients screened had T2DM and 20% had both T2DM and hypertension [4]. It has also been projected that by 2030, one third of the world's diabetic burden will be living in India and China [5]. When we include the numbers of those who are prediabetic and those with hitherto undiagnosed diabetes, it is obvious that the Asian growth story is bound to be greatly affected by this looming epidemic of T2DM.

Does Asia have the resources to tackle this epidemic?

The current treatment modalities for T2DM are ineffective in achieving good glycemic control in most patients. The American Diabetes Association (ADA) has recommended that the goal of therapy should be a glycosylated hemoglobin (HbA1c) level of $<$7%. Levels consistently $>$7% warrant re-evaluation and a change in the treatment regimen [6].

Lifestyle modification and medication remain the mainstays of therapy for the control of T2DM; however, the goals of T2DM remission or control are difficult to achieve. A review of data from the Third National Health and Nutrition Examination Survey and 1999–2000 National Health and Nutrition Examination Survey conducted on the U.S. population revealed that of all the patients reviewed, only 7.3% of adults with T2DM could achieve the ADA recommended goal of HbA1c $<$7% [7].

There has been a great impetus in research for a cure of T2DM. Despite the infusion of millions of dollars worldwide, researchers have failed to find the answer that could stall the progression of this disease and decrease the burden of the micro and macrovascular complications associated with T2DM.

Over the years, strong evidence of improvement in T2DM and impaired glucose tolerance in obese patients with diabetes (BMI $>$35 kg/m^2) has been achieved with all types of bariatric surgery [8]. In the long term, all-cause mortality has been shown to decrease by 40% and disease-specific mortality by 92% after surgery [9]. Bariatric surgery was recognized as an effective treatment option for obese patients with T2DM by the ADA as recently as 2009 [10]. Even a recent position statement by the International Diabetes Federation has endorsed the use of bariatric surgery as a treatment option for obese patients with T2DM uncontrolled by medication [11].

During the past few years, some expert consensus summits have been held, including the Diabetes Surgery Summit, the Asian Consensus Meeting on Metabolic Surgery, and the Asian Diabetes Surgery Summit. All these meetings were held with the aim of discussing whether the National Institutes of Health guidelines for bariatric surgery were relevant for patients with T2DM and a lower BMI. It is well known that the BMI alone is an imperfect measure of obesity, especially amongst Asians. In 2008, the Asian Consensus Meeting on Metabolic Surgery guidelines included waist circumference and the other features of the metabolic syndrome in conjunction with BMI as the qualifying criteria for surgery for Asian patients with T2DM and lower BMIs [12,13]. The recent International Diabetes Federation guidelines have also decreased the cutoff for BMI by 2.5 for Asians with T2DM [11].

Our study included Indian patients with uncontrolled T2DM and a BMI of 30–35 kg/m^2. These patients underwent laparoscopic Roux-en-Y gastric bypass (LRYGB) with the aim of evaluating the long-term results in terms of excess weight loss (EWL), remission rates of T2DM, and complication rates. The main objective was to assess whether the results seen in those with a BMI $>$35 kg/m^2 would be equally promising in those in the lower BMI range of 30–35 kg/m^2, and whether these results would be sustained during a 5-year period.

Methods

The present study was a prospective observational study. It was performed at the Centre for Obesity and Diabetes Surgery, Saifee Hospital (Mumbai, India). The hospital review board approved the study, which was conducted in conformance with the Helsinki Declaration.

The study began January 2006. Fifty-two patients with a BMI of 30–35 kg/m^2 and T2DM that was uncontrolled with the best medical management and lifestyle modifications available at that point were enrolled. These patients elected to undergo LRYGB. All patients provided written informed consent before surgery.

Demographic features

The study group included 27 male and 25 female patients, with a median weight of 85.6 kg (range 75–115) and a median BMI of 32.6 kg/m^2 (range 30–35). The median

waist circumference was 102 cm (range 86–126). The median hip circumference was 110 cm (range 90–140). The median age was 49 years (range 20–65). The T2DM duration was 3.5–14.5 years (median 8.4). Of the 52 patients, 46 required insulin (20–240 U/d, median 84). These 46 patients were also taking ≥1 oral hypoglycemic agent; 6 patients were taking only oral hypoglycemic agents (1–3 drugs).

Of the 52 patients, 61.5% had hypertension and required 1–3 antihypertensive drugs; 59.6% had dyslipidemia and were taking statins. The other associated co-morbidities were hyperuricemia in 34.6%, cholelithiasis in 3.8%, obstructive sleep apnea in 5.76%, gastroesophageal reflux disease in 3.8%, joint pain in 9.6%, and depression in 3.8%.

All patients underwent a series of consultations with the surgeon, endocrinologist, and nutritionist and a mandatory consultation with a clinical psychologist. The procedure was discussed extensively with all patients, and eligibility for inclusion in the study was determined by the following criteria: uncontrolled T2DM despite currently accepted diet, exercise, and pharmacologic interventions and a HbA1c persistently >7%; a history of T2DM for a minimum of 2 years; age 18–65 years; and BMI 30–35 kg/m^2. The exclusion criteria were as follows: type 1 DM; T2DM duration >15 years; fasting C-peptide level <1; the presence of end organ damage, such as diabetic retinopathy, diabetic nephropathy, neuropathy, peripheral gangrene; chronic smoking; and an inability to take lifelong nutritional supplements.

An extensive preoperative evaluation was done for all patients. This included fasting and postprandial blood glucose levels, fasting and postprandial serum insulin levels, HbA1c levels, fasting C-peptide levels, glutamic acid decarboxylase autoantibodies, lipid profile, and urine for microalbuminuria, in addition to other routine tests. In patients with signs of early nephropathy, additional evaluation was done using 24-hour urinary albumin levels and urine creatinine clearance. All patients underwent routine preoperative blood pressure monitoring and a fundoscopic examination of the retina. Preoperative nutritional parameters such as iron, folic acid, vitamin B_{12}, and calcium were also assessed. All patients were instructed to consume a strict low-calorie liquid diet for 7 days preoperatively and were given low-molecular-weight heparin 12 hours before surgery. Stockings and sequential compression devices were used for all patients intraoperatively for prophylaxis against deep vein thrombosis.

The diagnosis of T2DM was according to the ADA criteria. Hypertension was diagnosed if the patient had a history of hypertension or was taking medications for the same or had a resting recumbent blood pressure of >130/80 mm Hg on 2 separate occasions.

The ADA criteria for T2DM remission were used. These included fasting blood glucose <120 mg/dL, postprandial blood glucose <140 mg/dL, HbA1c <7%, low-density lipoprotein <100 mg/dL, high-density lipoprotein >40 mg/dL in men and >50 mg/dL in women, triglycerides <150 mg/dL, and blood pressure of 130/80 mm Hg.

Normoglycemia was defined as the achievement of normal fasting and postprandial blood glucose levels with HbA1c <7%. Complete remission after surgery was defined as the achievement of the ADA criteria without any medication for a continuous minimum period of 6 months. Partial remission was defined as the achievement of these results but with some medication required. No remission was defined as the nonachievement or the worsening of these parameters of control despite medication. The %EWL was used as a measure of EWL. Weight regain was defined as the percentage of weight regained from the nadir of the %EWL.

A complication was defined as the occurrence of an unexpected medical event that deviated from the standard pathway. Immediate complications were defined as those within 3 days of surgery, early complications were defined as those within 3 weeks, and late complications as those occurring after 3 weeks. A major complication was identified as an event that required hospitalization and interventional management and a minor complication as one that did not.

Surgical technique

Standard-limb anticolic and antigastric LRYGB was performed for all patients using a 6-port technique. The biliopancreatic limb length was taken as 50 cm from the duodenojejunal junction. The alimentary limb length was 250 cm. A side-to-side jejunojejunostomy was performed. The mesenteric defect was sutured in all cases. A 30–50-cm^3 vertical gastric pouch was created, followed by an end-to-side gastrojejunal anastomosis using a 25-mm circular stapler with an Orvil (Covidien). Underwater gastroscopy was performed on the operating table in all cases.

Postoperative course

All patients were kept nil per oral for the day of the surgery. An oral contrast study was performed the day after surgery, after which the patients began to consume clear liquids and were subsequently discharged from the hospital that evening. Patients were instructed to continue oral liquids for the first 15 days postoperatively, followed by semisolids for the next 15 days. A solid diet was begun 1 month after surgery. All patients were given low-molecular-weight heparin for 5 days after surgery and were prescribed iron, multivitamin, and calcium supplements beginning 15 days postoperatively. Follow-up examinations were done by our multidisciplinary team at 7 days, 1, 3, 6, and 12 months postoperatively, and annually thereafter. The medications for T2DM, hypertension, and dyslipidemia were maintained and tapered off as required.

Statistical analysis

The median was preferred over the mean for statistical analysis in the present study because of a few outliers. To depict the effect across the study period, some quantitative laboratory variables, such as the fasting blood glucose and postprandial blood glucose, required log transformation before parametric analysis. The Pearson product-moment correlation was used as a measure of correlation. $P \leq .05$ was considered statistically significant.

Results

All the procedures were completed laparoscopically. The median operating time was 75.6 minutes (range 55–125). The median intraoperative blood loss was 52.5 mL (range 34–85). No intraoperative complications were seen. The median hospital stay was 48 hours (range 36–72).

Complications

Early complications occurred in 3.8% of patients and mainly consisted of seromas and nausea. No major surgical complications developed in the postoperative period. No delayed complications, such as anastomotic stricture, ulcer, internal herniation, or nutritional deficiencies, were seen in our study group during the 5-year period. No significant dumping was reported by any patient. There was no mortality in the study group.

Excess weight loss

A median %EWL of 72.2% (range 66–92%) was reported at the end of 1 year. However, 8 of these 52 patients had some degree of weight regain, to a maximum of 20% of the %EWL. Thus, the median %EWL was 67.8% (range 48–88%) at the end of 5 years.

Remission of co-morbidities

The fasting and postprandial blood glucose levels showed a steep downward trend and were reported near normal at the end of the first month. The percentage of reduction increased exponentially during the initial evaluation points and then plateaued to lie within the normal range. To depict the effect across the study period, the log of the period in days was chosen as the x axis against the number of days (Figure 1).

At the end of 1 year, 84.6% of the patients had achieved euglycemia without medication. Using the ADA criteria, 73.1% had achieved complete remission and no longer required medication for T2DM, hypertension, or dyslipidemia; 23.1% of patients had achieved partial remission. These patients continued to require statins, antihypertensive drugs, insulin, or oral hypoglycemic agents, as needed, albeit at lower doses. Finally, 2 (3.8%) of the 52 patients showed no remission and continued to require medication with poor control. As seen in Figure 1, the blood glucose levels were stable, even at the end of 5 years. No patient had episodes of hypoglycemia in the postoperative period. No hyperglycemia recurred in any of the patients with remission, despite weight regain; however, they did require medication, either antihypertensive agents or statins, or both, to achieve the ADA acceptable levels for remission. Thus, the rate of complete remission decreased to 57.7% and the partial remission rate increased to 38.5% at the end of 5 years, with a similar overall improvement rate of 96.2% in their metabolic status.

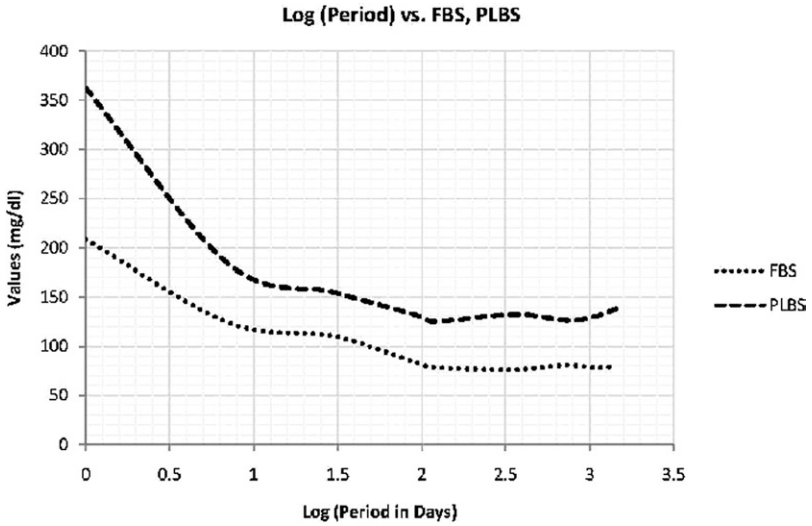

Fig. 1. Fasting blood glucose and postprandial blood glucose cumulative percentage of reduction from preoperative observation levels. A statistically significant correlation was found between elapsed period and fasting blood glucose/postprandial blood glucose cumulative percentage of reduction [fasting blood glucose, $r(7) = .88$, postprandial blood glucose, $r(7) = .81$; $P < .05$].

Table 1
Depicts the reduction in biochemical parameters from the preoperative levels for the first 5 years after LRYGB

Biochemistry	Preoperatively	7 d	1 mo	3 mo	6 mo	1 yr	2 yr	3 yr	4 yr	5 yr
Average blood glucose (mg/dL)	286.4	145.6	132.6	121.7	102.4	108.6	104.2	106.1	110.4	108
Fasting serum insulin (μIU/mL)	68.2	28.4	26.3	16.4	12.5	14.3	12.5	13.8	11.6	11.9
Postprandial serum insulin (μIU/mL)	114.4	42.6	36	26.7	16.5	17.5	18.4	19.2	18.7	19.4
Fasting C-peptide (ng/mL)	3.2	—	—	2.6	2.4	1.8	2.2	2.1	1.9	1.8
HbA1c (%)	8.8	—	7.5	6.2	5.8	5.3	5.6	5.9	5.6	5.8
Serum creatinine (mg/dL)	1.1	—	—	0.9	0.8	0.9	0.9	0.9	1	0.9
Total cholesterol (mg/dL)	206.3	—	174.7	152.6	138	135.7	134.6	136.1	142.5	140

LRYGB = laparoscopic Roux-en-Y gastric bypass; HbA1c = glycosylated hemoglobin.

The reduction in biochemical parameters from the preoperative levels for the first 5 years after LRYGB is listed in Table 1.

Patients with a shorter T2DM duration of <5 years achieved the best results (100% complete remission), and those with a duration of 5–10 years achieved complete remission in 36.3% and partial remission in 63.6%. Those with a T2DM duration >10 years had no remission in 40% and partial remission in 60%.

Patients with the best %EWL had the best chance of complete remission. Patients with >75% EWL had statistically significant greater remission rates than those with a %EWL of <50% (Fig. 2).

In terms of fasting C-peptide levels, those with levels >6 exhibited 100% complete remission, those with C-peptide levels of 3–6 exhibited 73.8% remission, and those with levels <3 had 31% remission after surgery. The remission rate in relation to the preoperative fasting C- peptide levels is shown in Figure 3.

Hypertension was seen in 61.5% of these patients preoperatively, 25% of them continued to require antihypertensive drugs, albeit at lower dosages at the end of 1 year, and 34.3% did so at the end of 5 years. This could also be explained because some patients were >50 years and might have had some component of age-related hypertension. Also, 59.6% of patients were taking statins in the preoperative period for dyslipidemia, and 26.6% of these patients continued to need statins at 1 year postoperatively and 46.6% required statins after 5 years. Hyperuricemia, gastroesophageal reflux disease, sleep apnea, and joint pain had resolved in all patients.

The change in low-density lipoprotein and high-density lipoprotein levels from the preoperative observation levels are shown in Figure 4. Low-density lipoprotein reached

%EWL	Complete Remission	Partial Remission	No Remission	Number of patients	p-value
Less than 25%	0	0	0	0	
25 to 50%	0	75	25	8	0.00253
50 to 75%	61.76	38.24	0	34	< 0.0001
More than 75%	90	10	0	10	< 0.0001

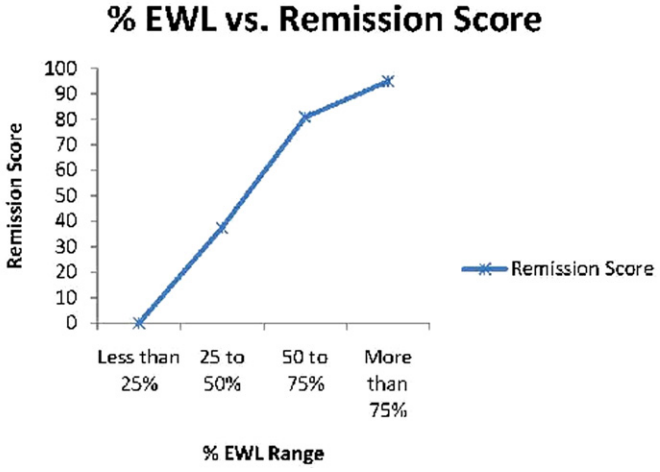

Fig. 2. Remission of T2DM with relation to percentage of excess weight loss (%EWL).

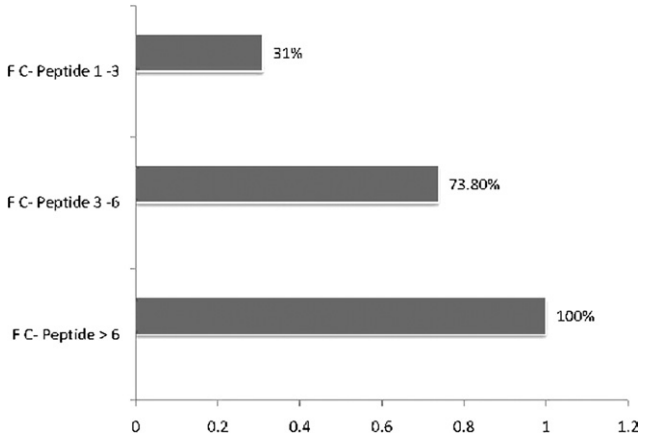

Fig. 3. Remission of T2DM with relation to preoperative fasting C (FC)-peptide levels.

normal levels within (10^2) 100 days. High-density lipoprotein took about ($10^{1.7}$) 50 days to increase to normal levels. To depict the effect across the period, the log of period in days was chosen as the x axis against the number of days.

Discussion

The prevalence of T2DM is reaching epidemic proportions in Asia. Unlike the west, Asians are affected by T2DM at a younger age and a lower BMI [14]. Asian patients experience the disease longer and have a greater propensity to develop long-term complications of T2DM, such as retinopathy, nephropathy, peripheral neuropathy, gangrene, and cardiovascular events such as stroke or myocardial infarction. Compounding the problem is the cost-effectiveness and compliance with long-term medical therapy. With >50% of patients with T2DM having poor glycemic control (HbA1c >8%), uncontrolled hypertension, and dyslipidemia, T2DM care in India has a long way to go [15].

The total annual cost of the treatment of T2DM in India has been estimated to be 14,517.42 Indian rupees (US$290.3) per person [16]. The cost increases progressively, in accordance with the increase in disease duration and the development of complications. Endpoints, such as end-stage renal disease necessitating hemodialysis or renal transplantation, can lead to an 11-fold increase in the treatment cost. In a country in which the government's share of healthcare expenditure is declining and the annual per capita income is as low as US$1000, this definitely requires novel therapeutic options with better compliance rates, that are cost-effective in the long run, and have better remission rates.

Bariatric surgery has proved to be the more effective and long-lasting option compared to medical therapy for the treatment of morbid obesity (BMI ≥35 kg/m^2) with related co-morbidities, especially T2DM [17–20]. Cause-specific mortality from T2DM has been reported to decrease after bariatric surgery in the long term [8]. The Swedish Obese Subject study in 2007 showed a lower mortality rate in the operated group than in the control group. It also showed that the remission of T2DM was 32 times better in the surgical group [20]. Surgery, with a 1-time cost of US$7000–10,000 in India, has been found to be the more economic option in

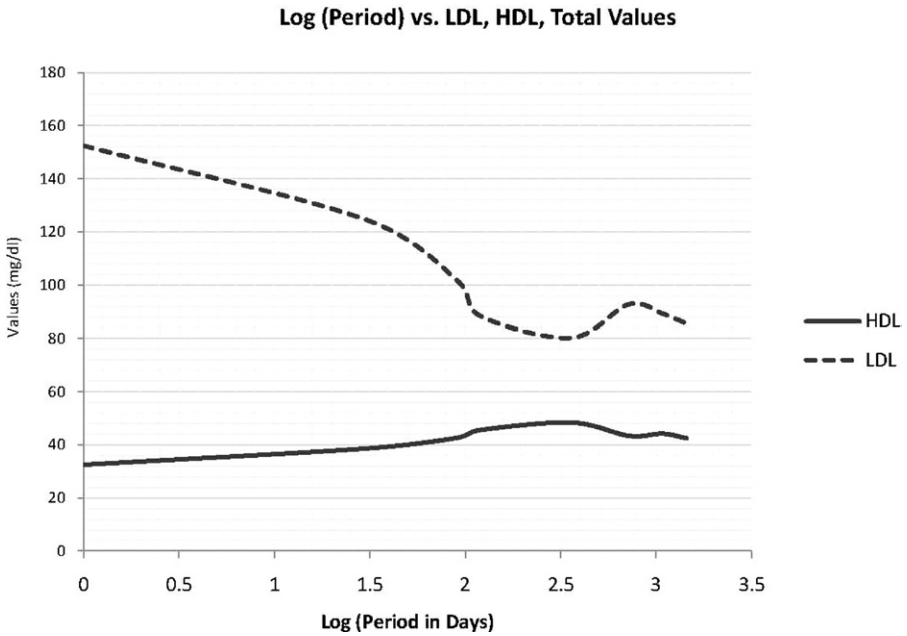

Fig. 4. Change in low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels from preoperative observation. Statistically significant negative correlation seen between elapsed period and HDL cumulative percentage of reduction [gain; r(7) = .80, $P < .05$]. Statistically significant correlation demonstrated between elapsed period and LDL cumulative percentage of reduction [r(7) = .92, $P < .05$].

the long term compared with the recurring annual cost of medical treatment. The projected long-term expenditure, including the expense of possible complications of T2DM, has made surgery an economical option, even with the recurring cost of supplements.

Another advantage of surgery is that it diminishes the "compliance" factor to a very large extent. Nonadherence to treatment regimes is the greatest problem with medical treatment. Studies have shown that only about 53–67% patients adhere to medical treatment [21,22]. Compliance decreases further with an increasing pill count [23]. Noncompliance is not only frustrating to the healthcare providers, but also proves to be a guaranteed harbinger of long-term complications. Surgery, in turn, is not entirely dependent on factors such as patient adherence to medical treatment or compliance with diet and exercise regimens and hence has had better outcomes in the long term.

The present study was begun in January 2006. LRYGB was our choice of procedure because it had proven long-term results in terms of T2DM remission (83.7%) in the obese population with a BMI >35 kg/m^2 that were better than those with adjustable gastric banding [8]. Although better remission rates of $\leq$98% have been reported for T2DM after biliopancreatic diversion and duodenal switch, we did not offer these procedures to our patients with a lower BMI. Indians are predominantly a vegetarian population and fail to meet the nutritional demands of severely malabsorptive surgeries such as these. Sleeve gastrectomy, which has become popular in Asia, was considered a novel procedure back in 2006, and the long-term results were lacking at that point in time.

Fasting C-peptide levels were used as a surrogate marker of pancreatic function in the present study. Although type 1 DM is associated with markedly decreased β-cell function, T2DM is also associated with deterioration of pancreatic function over a prolonged period. Fasting C-peptide screening combined with glutamic acid decarboxylase autoantibody screening has been proposed to identify those patients who have compromised β-cell function secondary to a protracted disease process [24]. We acknowledge that clamp studies that measure the acute insulin response are better in this regard, but these are too cumbersome and expensive to use routinely.

We believe that the duration of T2DM, percentage of excess weight loss, and status of pancreatic function as judged by the C-peptide levels are the main indicators for predicting outcomes after surgery. In our study, patients with a shorter duration of T2DM (<5 yr), percentage of excess weight loss >75%, and fasting C-peptide level >6, showed the best results in terms of complete remission of T2DM. Patients with a longer history of T2DM, percentage of excess weight loss <50%, and with a compromised pancreatic reserve, as indicated by a lower fasting C-peptide level experienced partial or no remission. This is in accordance with the existing evidence for patients with a BMI >35 kg/m^2 suggesting that patients with recent-onset T2DM experience greater remission rates [18]. Therefore, surgery as a treatment option for uncontrolled T2DM must not be deemed as a last resort and should be introduced early in the disease spectrum to achieve the best outcomes.

In our study, 84.6% patients had achieved euglycemic levels by the end of 1 year without any medications. As per the ADA criteria, complete remission was reported in 73.1% patients, and 23.1% experienced partial remission with decrease in drug dosages. In all, 96.2% of patients showed marked improvement in their diabetic status at 1 year. Cohen et al. [25] reported 97% remission at 2 years in 37 patients with a mean baseline BMI of 32.5 kg/m^2. Among the Asian studies, Shah et al. [26] performed LRYGB on a group of 15 patients with a BMI of 22–35 kg/m^2. They reported 100% remission of T2DM at a follow-up of 9 months. Lee et al. [27] demonstrated the efficacy of mini-gastric bypass in a Taiwanese population in 2008. At the end of 1 year, 76.5% of their patients had experienced remission of T2DM [27]. In a recent review of studies of diabetic patients with a BMI <35 kg/m^2, 97.7% remission of T2DM was reported in 5 studies that had treated T2DM with malabsorptive/restrictive procedures [28].

Hypoglycemia and weight gain are known concerns after intensive medical management, as shown by the UK Prospective Diabetes Study [29] and the Action to Control Cardiovascular Risk in Diabetes Study Group trial [30]. The Action to Control Cardiovascular Risk in Diabetes Study Group trial showed that escalating intensive medical therapy targeted at lowering the HbA1c levels to normal values led to increased mortality. Because of these findings, the trial was terminated 17 months early [30]. In our study, none of the patients reported hypoglycemia during the 5-year postoperative period. During the 5-year period, weight regain, which was reported by 8 patients, did not alter the overall remission rates of T2DM, although it did alter the complete remission rate. Re-emergence of T2DM has been reported by DiGiorgi et al. [31] at the end of 3 years in 24% of patients who underwent LRYGB for morbid obesity. Interestingly, despite the marginal weight regain, this phenomenon did not affect the control of the glucose levels in our patients at the end of 5 years in this BMI group. This implies that the results of surgery in the lower BMI (30–35 kg/m^2) group might not be an exact replica of those with morbid obesity, necessitating an obvious need for more research trials.

Because all these patients had uncontrolled T2DM before surgery, an improvement of 96.2% was significant. We believe that in the treatment of T2DM, it is not sufficient to achieve euglycemia alone as a measure of success after surgery. Improvement in the total metabolic state (blood glucose, lipid profile, and blood pressure) is imperative for reducing the potential micro and macrovascular complications and cardiovascular risk.

It is important to realize that complete remission, if achieved, is ideal, but the morbidity and mortality associated with T2DM and its micro and macrovascular complications would also decrease significantly even if the patient has partial remission as a result of LYRGB. ADA acceptable levels of control can be maintained with just an oral hypoglycemic agent, a statin, or an antihypertensive drug.

In our study, no major complications or mortality occurred. At the end of 5 years, none of the patients reported late complications secondary to surgery. The potential to develop iron, vitamin, and calcium deficiencies remains a concern. In our study, most patients presented with vitamin B_{12}, vitamin D_3, and iron deficiencies preoperatively. These deficiencies were corrected by our nutritionists and did not worsen as a result of the surgery in the postoperative period. This could be attributed to the stringent follow-up and support provided by the nutritionists.

Evidence for the results of surgery in the group with a BMI <35 kg/m^2 has been slow to materialize. To date 16 studies with a total of 343 diabetic patients have been reported in the low-BMI group, with a mean follow-up of 26 months [28]. Procedures including gastric banding, sleeve gastrectomy, minigastric bypass, roux-en-Y gastric bypass, biliopancreatic diversion, ileal transposition, and duodenojejunal bypass have been tried in this group of diabetic patients. However, only 1 randomized controlled trial has been reported in this BMI group that compared the outcomes of T2DM remission between adjustable gastric banding and best medical management (24-mo follow-up period) [32]. However, most patients in that study had a very short T2DM duration <2 years, that was the greatest limitation of this otherwise excellent study. The strength of our study was the demonstration of favorable results that were sustained for a 5-year period in patients with longstanding T2DM.

Never before in the history of surgery has a procedure led to so much debate and deliberation in the medical fraternity. Currently, multiple randomized trials comparing surgery and best medical treatment are ongoing.

It is imperative that we move beyond surgical one-upmanship and dispense with terminologies, such as “cure” after surgery. There is a lot of room for circumspection, and the ultimate goal must be to extend the real benefit of good glycemic control to these patients. In the interest of patients with T2DM, it is important to decrease long-term morbidity and mortality associated with the disease. For this, we need a combined approach in which surgery and medical treatment work together to achieve the best outcome. We require pragmatic clinical studies with an integrated management approach, rather than illogically trying to advocate for one form of therapy over another, to decide which diabetic patient will benefit from surgery and when it would be optimum to refer the patient for surgery.

Conclusion

LRYGB is a safe, efficacious, and cost-effective method for remission or improvement of T2DM in patients with a BMI of 30–35 kg/m^2 that are uncontrolled with current medical therapy. The determinants for success could be classified as clinical (a shorter duration of T2DM and better weight loss after surgery) and biochemical (greater C-peptide levels).

Surgery leads to an overall improvement of the metabolic status of the patient. It not only achieves euglycemia, but also controls blood pressure and lipid levels, decreasing the overall risk of micro and macrovascular complications. It also decreases the morbidity associated with T2DM, which will eventually lead to lower cardiovascular risk and decreased mortality rates long term.

An integrated management approach amongst endocrinologists, diabetologists, and surgeons would be the most prudent method of treating this emerging epidemic of T2DM in the developing world.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

References

[1] Neel JV. Diabetes mellitus: a “thrifty” genotype rendered detrimental by “progress”? Am J Hum Genet 1962;14:353–62.
[2] Bavdekar A, Yajnik CS, Fall CHD, et al. The insulin resistance syndrome (IRS) in eight-year old Indian children: small at birth, big at 8 years or both? Diabetes 2000;48:2422–9.
[3] Ko GTC, Tang JSF. Waist circumference and BMI cut-off based on 10-year cardiovascular risk: evidence for central pre-obesity. Obesity 2007;15:2832–40.
[4] Joshi SR, Saboo B, Vadivale M, et al. Prevalence of diagnosed and undiagnosed diabetes and hypertension in India-results from the Screening India’s Twin Epidemic (SITE) study. Diabetes Technol Ther 2012;14:8–15.
[5] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047–53.
[6] Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan DM, Peterson CM, et al. Tests of glycemia in diabetes. Diabetes Care 2004;27: S91–93.
[7] Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA 2004;21:335–42.
[8] Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and metaanalysis. JAMA 2004;292:1724–37.
[9] Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med 2007;357:753–61.
[10] Summary of revisions for the 2009 Clinical Practice recommendations. Diabetes Care 2009;32(Suppl 1):S3–5.
[11] Dixon JB, Zimmet P, Alberti KG, Rubino F, for the International Diabetes Federation Taskforce on Epidemiology and Prevention. Bariatric surgery: an IDF statement for obese type 2 diabetes. Diabet Med 2011;28:628–42.

[12] Lakdawala M, Bhasker A; Asian Consensus Meeting on Metabolic Surgery (ACMOMS). Report: recommendations for the use of bariatric and gastrointestinal metabolic surgery for treatment of obesity and type II diabetes mellitus in the Asian population. Obes Surg 2010;20:929–36.
[13] Rubino F, Kaplan LM, Schauer PR, Cummings DE, for the Diabetes Surgery Summit Delegates. The Diabetes Surgery Summit Consensus conference: recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus. Ann Surg 2010;251:399–405.
[14] Ramachandran A, Wan Ma RC, Snehalatha C. Diabetes in Asia. Lancet 2010;375:408–18.
[15] Raheja BS, Kapur A, Bhoraskar A, et al. DiabCare Asia—India study: diabetes care in India—current status. J Assoc Physicians India 2001;49:717–22.
[16] Grover S, Avasthi A, Bhansali A, Chakrabarti S, Kulhara P. Cost of ambulatory care of diabetes mellitus: a study from north India. Postgrad Med J 2005;81:391–5.
[17] Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? an operation proves to be the most effective therapy for adult-onset diabetes mellitus. Ann Surg 1995;222:339–52.
[18] Schauer PR, Burguera B, Ikramuddin S, et al. Effect of laparoscopic Roux-en-Y gastric bypass on type 2 diabetes mellitus. Ann Surg 2003;238:467–84.
[19] Sugerman HJ, Wolfe LG, Sica DA, Clore JN. Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. Ann Surg 2003;237:751–6.
[20] Sjöström CD, Lissner L, Wedel H, Sjöström L. Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS intervention study. Obes Res 1999;7:477–84.
[21] Mason BJ, Matsuyama JR, Jue SG. Assessment of sulfonylurea adherence and metabolic control. Diabetes Educ 1995;21:52–7.
[22] Ahp P, Bakker A, Soe-Agnie CJ. Impact of dosage frequency on patient compliance. Diabetes Care 1997;20:1512–7.
[23] Winkler A, Teuscher AU, Mueller B, Diem P. Monitoring adherence to prescribed medication in type 2 diabetic patients treated with sulfonylureas. Swiss Med Wkly 2002;132:379–85.
[24] Kim CS, Nam JH, Nam JS, et al. Clinical and biochemical characteristics of non obese type 2 diabetic patients with glutamic acid decarboxylase antibody in Korea. Metabolism 2006;55:1107–12.
[25] Cohen R, Pinheiro JS, Correa JL, Schiavon CA. Laparoscopic Roux-en-Y gastric bypass for BMI <35 kg/m^2: a tailored approach. Surg Obes Relat Dis 2006;2:401–4.
[26] Shah SS, Todkar JS, Shah PS, Cummings DE. Diabetes remission and reduced cardiovascular risk after gastric bypass in Asian Indians with body mass index <35 kg/m^2. Surg Obes Relat Dis 2010;6:332–8.
[27] Lee WJ, Wang W, Lee YC, Huang MT, Ser KH, Chen JC. Effect of laparoscopic mini-gastric bypass for type 2 diabetes mellitus: comparison of BMI>35 and <35 kg/m^2. J Gastrointest Surg 2008;12:945–52.
[28] Fried M, Ribaric G, Buchwald JN, Svacina S, Dolezalova K, Scopinaro N. Metabolic surgery for the treatment of type 2 diabetes in patients with BMI <35 kg/m: an integrative review of early studies. Obes Surg 2010;20:776–90.
[29] UK Prospective Diabetes Study (UKPDS) Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837–53.
[30] Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008;358:2545–59.
[31] DiGiorgi M, Rosen DJ, Choi JJ, et al. Re-emergence of diabetes after gastric bypass in patients with mid- to long-term follow-up. Surg Obes Relat Dis 2010;6:249–53.
[32] Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA 2008;299:316–23.