LAPAROSCOPIC SLEEVE GASTRECTOMY VERSUS ROUX-EN-Y GASTRIC BYPASS IN THE REMISSION OF TYPE 2 DIABETES MELLITUS:
-EARLY RESULTS FROM A BARIATRIC CENTRE IN MALAYSIA-

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ABSTRACT

Background: Obesity is strongly associated with Type 2 diabetes mellitus (T2DM). Gastric bypass results in remission of T2DM. Sleeve gastrectomy has been shown to have comparable effects on T2DM resolution. We compared the outcomes of laparoscopic sleeve gastrectomy (LSG) with laparoscopic Roux-en-Y gastric bypass (LRYGB) on T2DM, dyslipidaemia, hypertension and body mass index (BMI) in obese patients with T2DM. Material and Methods: A retrospective chart review was performed on patients above 18years old with T2DM who underwent LSG or LRYGB in our university hospital from January 2012 to June 2017. Post-operative weight and metabolic parameters a year after surgery were collected and analyzed. Results: 167 (LSG:89, LRYGB:78) patients were included. At one year after surgery, 74.2% and 76.9% of patients in the LSG and LRYGB group had HbA1C < 6.1% respectively. Complete remission of T2DM was seen in 52.8% of patient after LSG and 58.9% after LRYGB (p=0.321). HbA1c decreased to 5.74% (±0.8) in LSG group and 5.67% (±0.8) in LRYGB group (p=0.559). Significant BMI reduction was seen in both groups [LSG: 35.2 (±7.6), LRYGB 31.2 (±7.2), p=0.001]. All patients experienced improvement in lipid profile post operatively. Conclusion: Bariatric surgery results not only in significant weight loss one year after surgery but also in improvement of metabolic disease in the Malaysian population. Longer follow-up is required to assess if this effect persists beyond a year.

Keywords: Metabolic surgery; Obesity; Asian population; Minimal access surgery; HbA1c.

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INTRODUCTION

Obesity, defined as having body mass index (BMI) of ≥30 kg/m² is a global health problem. The prevalence is steadily increasing due to sedentary lifestyles and consumption of high-calorie food. It is a risk factor for many diseases such as diabetes mellitus, hypertension, dyslipidaemia and even some malignancies. More than two third of obese individuals have type 2 diabetes mellitus (T2DM). Obesity is strongly associated with insulin resistance and beta cell dysfunction, hence development of T2DM even in younger population.[1] Treating the complications of T2DM is a burden for the healthcare system and involves a significant amount of resources. Therefore, an optimal glycaemic control is the best preventive strategy to avoid the morbidity and mortality associated with T2DM. Unfortunately, with current medical therapy, less than half of the patient are able to achieve therapeutic goal.[2]

Bariatric surgery has been proven to effectively induce weight reduction in obesity. An improvement of blood sugar control and even remission of T2DM is also seen following bariatric surgery.[3] Multiple studies have shown that obese people who had bariatric surgery lose a greater amount of excess weight as compared to medical treatment alone.[4] Bariatric surgery has profoundly evolved over the past 50 years. Since its first introduction, gastric bypass surgical techniques have
progressed into its current form of Roux-en-Y gastric bypass (RYGB). The application of laparoscopy in bariatric surgery has reduced perioperative complications. Sleeve gastrectomy was initially performed as a first stage procedure of RYGB. Subsequently, due to its comparable effectiveness in weight reduction and amelioration of obesity related co-morbidities, laparoscopic sleeve gastrectomy (LSG) is now being performed as a procedure on its own. The improvement of hyperglycaemia occurs within days after bariatric surgery, much earlier than weight loss. This finding suggests that mechanisms involved in the enhanced glucose metabolism are independent of weight loss.[5] The hindgut hypothesis postulated that following gastric bypass surgery, the accelerated transport of nutrients to the distal part of small bowel stimulates secretion of incretin hormones, such as glucagon-like peptide (GLP-1) and peptide YY (PYY) from the gut mucosa. These hormones improve glycaemic control by delaying gastric emptying, stimulation of pancreatic beta cell to increase insulin secretion and suppression of appetite.[6] However, a significant increase in GLP-1 level has been observed in obese diabetic patients after gastric bypass surgery ‘Anti-incretin’ hormones which are secreted by proximal small bowel are believed to cause insulin resistance in T2DM.[5][7]The foregut theory, on the other hand, proposed that the specialized neuroendocrine cells are not being stimulated to secrete ‘anti-incretin’ hormones as food bypasses duodenum and proximal small bowel.[7]

During sleeve gastrectomy, a major portion of the stomach is removed along the greater curvature, leaving a narrow ‘sleeve’ of gastric tube. Despite no gastrointestinal tract anatomical alteration, GLP-1 secretion is also remarkably enhanced following sleeve gastrectomy. [8] Reduction in gastric capacity expedites movement of ingested food through the gastrointestinal tract. Rapid delivery of nutrients to the distal ileum is believed to contribute to the enhanced secretion of GLP-1 and augmentation of glucose metabolism. A significant increase in postprandial GLP-1 has been observed as early as one week post sleeve gastrectomy. [9]

Gastric bypass surgery is regarded as the gold standard for weight loss. However, accumulating evidences are showing that sleeve gastrectomy has similar effects on weight loss, glycaemic control, and improvement of metabolic disorder as compared to gastric bypass. Studies worldwide have reported comparable effects on diabetes remission between both LSG and LRYGB. [10-13] Sleeve gastrectomy, being a relatively simpler surgery with fewer post-operative complications, is gaining more popularity among bariatric surgeons. Our bariatric surgeries annually in Malaysia. As there is scant local data on the metabolic effects of the two most commonly performed bariatric surgery, we performed a retrospective chart review on patients who underwent LSG and LRYGB in our teaching university hospital. The aim of the study was to assess the outcome of LSG and RYGB on T2DM, dyslipidaemia, hypertension, body weight in obese patients. We hypothesized that both LSG and RYGB will have bring about T2DM resolution in obese patients with T2DM.

METHODS

A retrospective study was performed on patients above 18years old with T2DM who underwent LSG or LRYGB in our university hospital from 1st of January 2012 to 30th of June 2017. Patients who underwent revisional bariatric surgery were excluded. The study was conducted in accordance with the principles of the Declaration of Helsinki. Study approval was obtained from our Institutional Review Board at the Universiti Kebangsaan Malaysia Medical Centre for a retrospective chart review (FF-2017-290). A review of patients' discharge summaries from the hospital’s Caring Hospital Enterprise System was done, along with patients’ medical record files. All data collected were kept confidential, and data presented do not identify individuals. Remission of T2DM is defined as having HbA1c <6.1% without any anti-diabetic medications.[14]

Definitions of glycemic outcomes after bariatric surgery [14]

<table>
<thead>
<tr>
<th>Remission</th>
<th>Normal measures of glucose metabolism (HbA1c&lt;6.1%, Fasting blood glucose &lt;5.56mmol/L) in the absence of anti-diabetic medications.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement</td>
<td>Reduction in HbA1c and fasting blood glucose not meeting criteria for remission or decrease in anti-diabetic medications requirement (by discontinuing insulin or one oral agent or reduction of previous dosage by half).</td>
</tr>
<tr>
<td>Unchanged</td>
<td>The absence of remission or improvement as described above.</td>
</tr>
</tbody>
</table>
Sample size estimation was calculated using two population means formulae. Existing data indicate that the mean HbA1c (%) of the LSG group was 7.28 (standard deviation = 1.74) and the mean of RYGB group was 8.11 (standard deviation = 1.80). Thus, a minimum sample size of 72 samples per group needed to be able to reject the null hypothesis with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. The independent t-test statistic will be used to evaluate this null hypothesis. The data analysis was carried out using SPSS version 25, IBM® (New York, United States). Student t-test, Fisher’s exact test and Chi-square test were used. Statistical significance was set at p<0.05.

Patient selection flowchart

<table>
<thead>
<tr>
<th>All patients who underwent bariatric surgery from 1st January 2012 to 30th June 2017</th>
<th>n=421</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with T2DM (inclusion criteria)</td>
<td></td>
</tr>
<tr>
<td>Pre-existing T2DM (n=102), Newly diagnosed T2DM (n=65)</td>
<td></td>
</tr>
<tr>
<td>Total included patients, n=167</td>
<td></td>
</tr>
</tbody>
</table>

SURGICAL TECHNIQUE

Laparoscopic Sleeve Gastrectomy.

The 5-port technique was used. By using an energy device (Harmonic Scalpel™ or Ligasure™), the greater omentum was dissected away from the greater curvature. The division was done close to stomach wall. Adhesions of stomach to retroperitoneal structures was carefully released. Dissection continued superiorly to expose the left crus and the cardia. Following placement of 36Fr gastric tube, sleeve of stomach was created. First firing with green cartridge linear stapler on the antrum was done 5 cm away from the pylorus, with subsequently blue cartridges. The stapler line was reinforced with a 2-0 absorbable suture. Finally, Methylene blue test was performed to check for a leak.

Laparoscopic Roux-En-Y Gastric Bypass

First, a stomach pouch was created by making a 4 cm horizontal division at lesser curve, followed by a vertical transection up to the angle of His. Next, small bowel was divided at approximately 40-60 cm from the ligament of Treitz. The alimentary limb (Roux limb) was then reconnected to the new stomach pouch using 21-mm circular stapler to create an end-to-side gastrojejunostomy. Then, jejunojunostomy anastomosis was performed by connecting the biliopancreatic limb to the alimentary limb at 75 -100 cm distal to the gastrojejunostomy site. The defect between the two transected mesentery edges was sutured closed to prevent internal herniation of bowel.

RESULTS

A total of 421 consecutive patients underwent bariatric surgery in our university hospital between 1st of January 2012 to 30th June 2017. 167 subjects met the inclusion criteria. 102 patients were known to have T2DM prior to surgery and another 65 patients were diagnosed with T2DM during preoperative screening. Amongst patients who met the inclusion criteria, 89 (male n=30, female n=59) underwent LSG and 78(male n=30, female n=48) underwent LRYGB. Female gender was predominant in both groups (59/89 in LSG and 48/78 in RYGB) respectively. The mean (±SD) age was 44.4±9.3 years old, mean BMI (±SD) was 46.4±10.4 kg/M², mean HbA1c level was 7.58%±1.53 (range 6.1% – 13.4 %). The baseline preoperative characteristics are shown in Table I.
Data are expressed as mean ± standard deviation of the mean.*p<0.05. BMI: body mass index, FBS: fasting blood sugar, TG: triglyceride, LDL: low density lipoprotein, HDL: high density lipoprotein, SBP: systolic blood pressure.

After surgery, all patients experienced significant improvement in glycaemic control. At 1 year, 74.2% of patients in LSG and 76.9% of patients in LRYGB group had HbA1c < 6.1%. 52.8% of patients who had LSG achieved complete remission of T2DM and 47.2% showed improvement in glycaemic control. Whereas in LRYGB group, complete remission was seen in 58.9% of the subjects and the remaining patients experienced significant improvement of T2DM. This is shown in Table II.

Table II: Glycaemic control outcomes at 12 months after surgery.

<table>
<thead>
<tr>
<th>Percentage patient with HbA1c &lt;6.1%</th>
<th>LSG (%)</th>
<th>LRYGB (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malay</td>
<td>55.1</td>
<td>62.8</td>
<td>0.553</td>
</tr>
<tr>
<td>Indian</td>
<td>14.6</td>
<td>10.3</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>3.4</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>1.1</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Complete remission</td>
<td>52.8</td>
<td>58.9</td>
<td>0.321</td>
</tr>
<tr>
<td>Improvement</td>
<td>47.2</td>
<td>41.1</td>
<td>0.422</td>
</tr>
</tbody>
</table>
Reduction in HbA1c occurred as early as 6 months after surgery (Figure 1).

Fig. 1. HbA1c (%) reduction over 12 months follow-up following LSG and LRYGB

At 12-month after surgery, mean HbA1c (±SD) decreased to 5.74% (±0.80) and 5.67% (±0.84) in LSG and LRYGB group respectively (p=0.559). Post-operative clinical and biochemical parameters in both groups are shown in Table III.

<p>| Table III. Mean value of patient’s clinical and biochemical parameters 12-months after surgery |
|-------------------------------------------------|-----------------|-----------------|------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>LSG (n=89)</th>
<th>LRYGB (n=78)</th>
<th>P-Value (Chi-square/ T-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>35.19 (±7.07)</td>
<td>31.20 (±7.19)</td>
<td>0.001*</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.74 (±0.80)</td>
<td>5.67 (±0.84)</td>
<td>0.559</td>
</tr>
<tr>
<td>FBS (mmol/L)</td>
<td>5.22 (±1.04)</td>
<td>5.29 (±1.14)</td>
<td>0.667</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.01 (±0.93)</td>
<td>5.01 (±1.02)</td>
<td>0.989</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.40 (±0.74)</td>
<td>1.36 (±0.91)</td>
<td>0.712</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>2.92 (±1.04)</td>
<td>3.01 (±1.05)</td>
<td>0.580</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.30 (±0.29)</td>
<td>1.28 (±0.38)</td>
<td>0.732</td>
</tr>
<tr>
<td>Cholesterol/HDL ratio</td>
<td>4.02 (±1.25)</td>
<td>4.38 (±2.32)</td>
<td>0.220</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>134.20 (±11.79)</td>
<td>134.22 (9.83)</td>
<td>0.992</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation of the mean.*p<0.05. BMI: body mass index, FBS: fasting blood sugar, TG: triglyceride, LDL: low density lipoprotein, HDL: high density lipoprotein, SBP: systolic blood pressure.

Mean fasting blood glucose was also optimally controlled at 12 months after surgery in both groups [LSG: 5.22 (±1.04) mmol/L, LRYGB: 5.29 (±1.14) mmol/L, p<0.667] (Figure 2).
All patients experienced significant weight loss. On average, patients who had LSG lost 25.8% (±7.6), whilst patients in LRYGB group lost 28.2% (±8.1) of their total body weight at 12 months after surgery. Mean BMI reduced to 35.2±7 and 31.2±7.2 in LSG and LRYGB group respectively (p=0.001). This is illustrated in Figure 3. Pearson correlation analysis demonstrated no significant relationships between change in HbA1c and change in BMI, with correlation co-efficient (r) close to zero. At 12 months follow-up, mean total cholesterol (TC) did not significantly improved in both groups, p=0.989. There was no significant changes in the systolic blood pressure (SBP) during follow up in both groups as well.

Figure 2. Fasting blood glucose level over 12months follow-up following LSG and LRYGB

Figure 3. BMI of patients over 12months follow-up following LSG and LRYGB
DISCUSSION

It has been well established that gastric bypass can effectively reduce weight, improve glycaemic control and dyslipidaemia. Meta-analysis by Cho et al reported T2DM remission rates after 1-year follow-up of 27% to 86% for LSG and 42% to 96% for LRYGB. [13] Our study demonstrated T2DM remission rates of 52.8% and 58.9% for LSG and LRYGB respectively at one year. The remaining patients all had improvement in their glycaemic control.

The proportion of patients who achieved T2DM remission in our cohort was encouraging, although not as high as other reported studies. However, a few explanation are identified. Firstly, we consider DM remission as having HbA1c levels below 6.1% without any anti-diabetic medication. Most of the literatures determined a cut-off HbA1c level of less than 6.5%, which provide greater probability of being accounted as accomplishing complete DM remission. Secondly, this is a short-term result as DM remission rates in our study were only recorded at 12 month post-operatively. Beyond this period, improvement in diabetic control should persist, resulting in more numbers of patient with diabetic resolution. The majority patients who did not achieved diabetic remission were those with higher HbA1c levels (>8%), patients with T2DM for more than 5 years, on multiple anti-diabetic medication or on insulin therapy. These individuals might have had a certain degree of pancreatic failure, therefore will be dependent on medication particularly insulin despite achieving optimal HbA1c. Some patients were found to be non-compliant to medication, diet and exercise regime, thus affecting improvement in diabetic control and slow reduction in HbA1C levels. Nevertheless, a significant number of subjects with established T2DM required decreased dosage of anti-diabetic medication, indicating the efficacy of LSG and LRYGB in the improving blood sugar control. There was no significant correlation between the change in HbA1c and the change in BMI. In other words, the improvement in blood sugar control, as evidence by the normalization of fasting blood sugar and reduction in HbA1c level involves mechanisms which are likely to be independent of weight loss. The alimentary tract anatomical and physiological changes that occurred following bariatric surgery have clearly played the major role in the improvement of insulin sensitivity. In addition, we believe that our dedicated post-operative clinic follow-up, diet counselling, and physical activity programs have also contributed significantly to diabetic control. Constant support provide awareness and motivation, leading to higher probability of success. The study population has similar baseline characteristics in both groups. Despite the retrospective nature of this study, the similarities have potentially reduced some bias. There were higher number of female subjects who underwent LSG and LRYGB. However, this is not unanticipated as women seek weight reduction surgery more readily. The fact that women have higher body fat composition might affect the rate of weight loss compared to men. Nevertheless, differences in gender and fat distribution should not affect weight loss-independent mechanisms of improvement in glucose metabolism. Zhang et al, in their meta-analysis of studies comparing LSG and LRYGB reported no significant difference in weight loss during the first 18-month follow-up but beyond that timeline, LRYGB achieved higher excess weight loss than LSG. [15] Our study also demonstrated no significant difference in percentage total body weight loss in both groups at 1 year, which is consistent with the above meta-analysis. SLEEVEPASS trial showed that the maximal weight loss occurred within one year after surgery.[16] Over their 5-year follow up, most of the subjects sustained their lowest weight but some had slight weight gain. Therefore, patients need to be continually encouraged to pursue non operative weight loss measures to achieve ideal weight goal. At 12 month after LSG and LRYGB, we observed a desirable decrease in TG and an increase in HDL. However, there was also a rise in LDL, but the total cholesterol level remained unchanged from baseline. These findings are consistent with studies by Meydan et al and Zhang et al, which reported little short-term effects on LDL and TC after sleeve gastrectomy.[17, 18] Reduction in TG levels was possibility due to the overall improvement in metabolic syndrome, which in turn induced amelioration of hepatic steatosis. Decreased accumulation of triglycerides in hepatocytes leads to reduction in serum TG levels. [17]

Meta-analysis of longer term follow up studies on lipid profiles reported a reduction in both TC and LDL.[19] We anticipate that our subjects will also experience improvement in dyslipidaemia in the long term. An important notion here is that some degree of worsening lipid profile maybe observed during the initial post-operative period after bariatric surgery but should improve later on. The mechanisms responsible for the initial increase in LDL and HDL are not yet fully understood but reduction in TG level is a positive indicator for impending enhancement of lipid profile. TC/HDL ratio is currently widely used as cardiovascular risk stratification tool [14]. According to the American Heart Association, TC/HDL of <3.3 halves the average risk while a ratio of >7.05 are associated with a double of the average risk of having a cardiovascular disease. Based upon TC/HDL ratio we observed that our subjects have an average risk of cardiovascular disease preoperatively, which further decreased to a lower value at 1 year after surgery (LSG: 4.02, LRYGB 4.38). Therefore, despite no apparent change in the absolute value of serum total cholesterol, the TC/HDL ratio is indicating a comparable benefit of LSG and LRYGB in reducing cardiovascular risks.
Assessment of blood pressure control following bariatric surgery in our cohort was rather suboptimal. Preoperative blood pressure in the subjects was within an acceptable range. Patients with established hypertension at baseline have already had a satisfactory blood pressure control with antihypertensive medications. After bariatric surgery, our retrospective analysis is unable to ascertain if the normalization of blood pressure was due to the effects of post-operative metabolic changes, of antihypertensive or a combination of both. Most of the patients continue to require antihypertensive despite significant weight reduction. Given the high prevalence of hypertension in our population, it would be reasonable to maintain patients on antihypertensive as long as good blood pressure control is achieved with tolerable side effects. Our study adds to the available literature that both RYGB and SG improves or resolves T2DM, although we were able to show that the T2DM remission rates were higher with RYGB. This is the first study assessing the metabolic effects of bariatric surgery in Malaysia. However, the limitations of our study are that it is a retrospective study. There could have been a selection bias as the choice of bariatric procedure was based upon patient’s condition and probably, surgeon’s preference. Apart from surgery, other factors such as compliance to medication, level of physical activity, diet and self-motivation might differ between individuals. This inevitably influence discrepancy in the degree of metabolic disorder resolution between patients. Furthermore, these are short term results but we are still following up on the patients to observe the longer term outcomes. A number of our patients defaulted follow up appointments and therefore we were unable to obtain post-operative parameters required. We could not completely retrieve information regarding the medication list in some patients as follow up and medication are taken from other healthcare centres. We realised that a more systematic data recording should be employed in our centre to improvise data collection in the future.

CONCLUSION

Bariatric surgery results not only in significant weight loss one year after surgery but also in improvement of metabolic disease in the Malaysian population. LSG has comparable effects to LRYGB at one year with regards to T2DM resolution. A longer follow-up is required to assess if this effect persists beyond a year.

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DISCLOSURE OF CONFLICTS OF INTEREST:

The authors declare that they have no conflict of interest.

INFORMED CONSENT:

Informed consent was obtained from all individual participants included in the study.

REFERENCES


