

Metabolic and bariatric surgery for Type 2 diabetics with BMI <35: the time is now



“We believe obese patients with Type 2 diabetes would benefit from metabolic surgery and that metabolic surgery should be included in an algorithm for those patients who fail intensive medical management.”

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Summary

Diabetes and obesity are twin epidemics that we are currently facing in the USA. More than 25 million adults in the USA are Type 2 diabetic and 79 million are pre-diabetic. This number continues to grow and has almost tripled in the past 20 years. Obesity is a major independent risk factor for developing Type 2 diabetes. More than a third of adults are obese and 90% of Type 2 diabetics are overweight or obese [1,2]. Current treatment for Type 2 diabetics with class I obesity is intensive medical management, which has shown poor to mixed results. There have been several randomized control trials and systemic reviews looking at nonsurgical treatment of class I obesity. These studies incorporate diet, exercise, behavioral and pharmacological treatment. These studies show moderate weight loss at 1 year (2–8 kg) and 95–97% of patients regain their weight within 2–5 years [3–5]. The look AHEAD research group recently published their results of cardiovascular effects of intensive

lifestyle intervention in Type 2 diabetes. The trial was stopped early at mean follow-up of 9.6 years when futility analysis showed an intensive lifestyle intervention focusing on weight loss did not reduce the rate of cardiovascular events in overweight or obese adults with Type 2 diabetes [6]. We now have several randomized control trials and multiple observational studies showing the safety and efficacy of bariatric surgery on Type 2 diabetic patients with class I obesity. These studies have shown an overwhelming superiority for weight loss and resolution of comorbidities in the surgical group versus the medical group with good safety outcomes.

Efficacy of bariatric surgery for obese patients with BMI<35

We now have five randomized control trials that include patients with a BMI 30–35 kg/m² [7–11]. O'Brien *et al.* randomized 80 patients to laparoscopic adjustable gastric band (LAGB) versus optimal nonsurgical therapy. He recently published

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“...current studies show that metabolic surgery can provide durable short-term remission and improvement of Type 2 diabetes in BMI <35.”

his 10-year follow-up of his original randomized control trial in 2002. Weight loss was superior in the LAGB at 63% EWL versus 22% EWL for the nonsurgical group. Sustained reduction in metabolic syndrome was also higher in the LAGB group at 10 years [7].

Dixon *et al.* randomized 60 patients with new-onset Type 2 diabetes to LAGB versus conventional therapy for Type 2 diabetes and weight management. Main outcome measures were diabetes remission (a fasting glucose level <126, HbA1c <6.2 while not taking any glyce-mic therapy). Remission of Type 2 diabetes at 2 years was seen in 73% of the surgical group versus 13% in the conventional therapy group. No serious adverse events were reported [8].

Schauer *et al.* published their randomized control trial of bariatric surgery versus intensive medical therapy for obese patients with diabetes. They randomly assigned 150 patients to receive either intensive medical therapy versus bariatric surgery. In this study 34% of the subjects had a BMI <35. The primary end point was a HgbA1c <6% at 1 year. They reported statistically significant remission rates for diabetes in the gastric bypass group versus the medical therapy group at 1 year (42 and 12%, respectively) [9].

Ikramuddin *et al.* published the Diabetes Surgery Study Randomized Clinical Trial comparing gastric bypass to intensive medical management for control of Type 2 diabetes, hyperlipidemia and hypertension in obese patients. They had 120 patients followed for 12 months. Primary American Diabetes Association end points were HgbA1c <7%, LDL <100 mg/dl and systolic blood pressure <130. In total, 60% of the patients in the gastric bypass group and 58% in the medical group had a BMI <35. Primary end points were achieved in 49% of the gastric bypass patients versus 19% of the medically managed patients. HgbA1c <7% was achieved in 75% of the gastric bypass patients at 1 year compared with 32% from the medical group. HgbA1c <6% was achieved in 44% of the gastric bypass patients compared with 9% in the medical group [10].

Lee *et al.* published a randomized controlled trial of 60 patients with BMI 25–35 with poorly controlled Type 2 diabetes to sleeve gastrectomy versus minigastric bypass. Primary outcome was diabetes remission (fasting blood glucose <126 mg/dl and HbA1c <6.5% without glyce-mic therapy). There was no medical therapy control group. At 1 year overall, 70% of patients

achieved diabetes remission. Diabetes remission was achieved in 93% of the gastric bypass group versus 47% in the sleeve gastrectomy group [11].

There are over 16 observational studies and at least two meta-analyses showing superiority of bariatric surgery versus medical management for diabetic patients with class 1 obesity, with good safety outcomes [12]. Shimizu *et al.* reviewed 18 clinical studies with 477 patients that described surgical treatment for patients with BMI <35 and Type 2 diabetes. Overall, surgical patients were able to achieve a 64.7% remission rate of Type 2 diabetes (fasting plasma glucose: <126 mg/dl, HgbA1c <6.5%, off medications) and 86.8% of patients had their anti-diabetic medications discontinued. Follow-up ranged from 6 to 216 months [13]. Blue Cross and Blue Shield technology evaluation center (TEC) published their review of bariatric surgery in Type 2 diabetic patients with BMI <35. Their goal was to determine if bariatric surgery improved outcomes for patients with BMI <35 and Type 2 diabetes. Their review of the literature showed remission rates ranging from 48 to 100% at 1 year. The Blue Cross and Blue Shield Advisory Medical Panel recommended gastric bypass for Type 2 diabetics with BMI <35 as the evidence met TEC criteria [14].

Safety of bariatric surgery for obese patients with BMI <35

Safety is always a concern when discussing treatment options for patients. Medical therapy is not without inherent adverse events. In the paper published by Schauer there was a 9% adverse event observed in the medical therapy group, which was equivalent to the sleeve gastrectomy group with an observed adverse event of 8%. In the medical group, hypoglycemic events were observed in 81% of the patients and weight gain was seen in 7% [9]. All medications have potential side effects and lifetime medical therapy carries a financial burden as well. In Shimizu's paper their review of 18 studies, 477 patients, observed a mortality rate of 0% with a morbidity rate (major and minor) of 10.3% [13]. The Federal Agency for Healthcare Research and Quality and recent clinical studies has shown improved safety in bariatric surgery [15]. Overall mortality rates range from 0.1 to 0.2% and overall risk of major complication is 4.3% [15,16].

The concept of 'healthy obesity' or the 'obesity paradox' described by the author is a dangerous concept that underscores the severity of

obesity and its related comorbidities. Kramer *et al.* recently published a meta-analysis providing strong evidence that obesity is not benign. They reviewed eight studies with 61,386 people to determine the effect of metabolic status on all-cause mortality and cardiovascular events in normal weight, overweight and obese individuals. Their results showed that compared with metabolically healthy normal-weight individuals, obese persons are at increased risk for death and cardiovascular events even in the absence of metabolic abnormalities. They also showed that metabolically unhealthy individuals at normal, overweight or obese had a similar elevated risk [17].

Conclusion

We agree that long-term evidence-based studies may be needed before recommending metabolic surgery as a first-line modality for the treatment of Type 2 diabetes for BMI <35. This will likely need to be done under an IRB-approved protocol in the USA as we still use 1991 NIH guidelines for patient selection in bariatric surgery. However, the current studies show that metabolic surgery can provide durable short-term remission and improvement of Type 2 diabetes in BMI <35. In short- to medium-term follow-up

bariatric surgery produces 80% remission and 92% reduction in diabetes-related deaths [18]. Should we be satisfied with our current management for obese patients with Type 2 diabetes? Do we need to wait for our diabetic patients who are obese to reach a higher BMI to qualify for bariatric surgery? Or even worse, have patients deliberately gained weight to get needed therapy? This time period can result in a continued decline in β -cell function and decrease in insulin secretion, leading to decreased rates of diabetes remission and resolution. We believe obese patients with Type 2 diabetes would benefit from metabolic surgery and that metabolic surgery should be included in an algorithm for those patients who fail intensive medical management.

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