

## Review Article

# The Impact of Bariatric Surgery Procedures on Type 2 Diabetes, Hyperlipidemia and Hypertension

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**O**verweight and obesity, especially abdominal obesity, are associated with type 2 diabetes, hyperlipidemia, hypertension, coronary heart disease, stroke, peripheral arterial disease and other comorbidities.<sup>1</sup> Type 2 diabetes in particular is so strongly linked with obesity that some researchers are starting to consider these two epidemics as a single disease, referring to it as "diabesity" in the medical literature.<sup>2</sup> Bariatric (better termed metabolic) surgery procedures achieve long-term weight reduction and a dramatic improvement in diabetes, hyperlipidemia and hypertension (long before there is any weight loss) leading to a significant reduction in overall mortality.<sup>3</sup>

## Bariatric surgery procedures

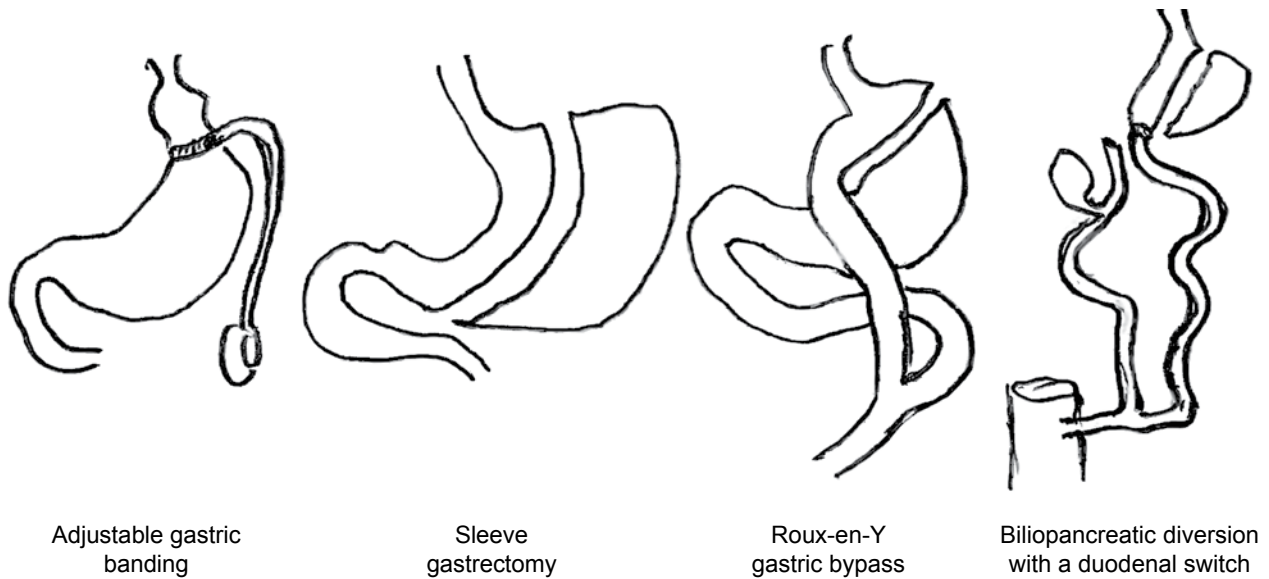
Bariatric surgical procedures are divided into restrictive, malabsorptive and mixed.<sup>4</sup> Restrictive bariatric surgery procedures reduce the size of the stomach, resulting in early satiety and decreased caloric intake. The most frequent restrictive procedures are vertical banded gastroplasty, sleeve gastrectomy, and the laparoscopic adjustable gastric band.<sup>5</sup> Malabsorptive procedures decrease the functional length of the small intestine, leading to

decreased nutrient absorption.<sup>4,6,7</sup> Roux-en-Y and biliopancreatic diversion with duodenal switch are mixed procedures, with both restrictive and malabsorptive aspects, and they are the most effective (Figure 1).<sup>4,7,8</sup>

## Bariatric surgery and type 2 diabetes

Medical treatment for type 2 diabetes has limited success in metabolic control particularly amongst obese diabetics, with many of these patients not achieving recommended targets. Besides that, some antidiabetic medications, including insulin, can result in weight gain.<sup>9</sup>

Bariatric surgery appears to offer a novel endpoint in obese diabetics: complete diabetes remission.<sup>10-12</sup> In an original article by MacDonald in 1997, reporting on 154 morbidly obese diabetics after a Roux-en-Y gastric bypass operation, the mean glucose levels fell from 187 mg/dL preoperatively and remained less than 140 mg/dL for up to 10 years of follow up. At the end of the study only 8.6% of the surgical group required medical treatment compared to 31.8% preoperatively. The mortality rate also fell to 9% compared to 28% in the control group (78 age-matched morbidly obese diabetics). This improvement in mortality rate was mainly due to



**Figure 1.** Most common bariatric surgical procedures.

a decrease in cardiovascular events.<sup>13</sup> In a meta-analysis of 136 studies and 22,094 patients, diabetes was completely resolved in 76.8% and resolved or improved in 86.0% of the patients. Diabetes mellitus resolved in 48% of the patients after laparoscopic gastric banding, in 68% after vertical banded gastroplasty, in 84% after Roux-en-Y, and in 98% after biliopancreatic diversion.<sup>14</sup> In another large meta-analysis (621 studies, 135,246 patients), 78.1% of obese diabetics had complete diabetes resolution after a bariatric surgical procedure, and 86.6% showed improvement or resolution of the disease. More specifically, 95.1% of patients had diabetes resolution after biliopancreatic diversion with duodenal switch, 80.3% after gastric bypass, 79.7% after gastroplasty, and 56.7% after laparoscopic adjustable gastric banding.<sup>15</sup> Diabetes resolution was achieved in 89% and 99% of 26 and 111 obese diabetics, up to 2 years after Roux-en-Y gastric bypass and a variant of biliopancreatic diversion, respectively.<sup>16</sup> Among 23,106 operated obese patients with metabolic syndrome, the one-year remission rate of diabetes was 28% for gastric banding, 52% for sleeve gastrectomy, 62% for Roux-en-Y gastric bypass, and 74% for biliopancreatic diversion with duodenal switch.<sup>17</sup> All bariatric procedures improve glucose homeostasis, with gastric bypass and biliopancreatic diversion being the fastest and most effective. The underlying mechanisms responsible for the favorable effects of bariatric surgery on obe-

sity comorbidities, which are still not very clear, are: changes in secretion of gut hormones and adipocytokines (Table 1), weight loss due to malabsorption and caloric restriction, changes in gut microbiota, and changes in neural impulses transmitted through vagal pathways.<sup>8,18,19</sup>

Interestingly euglycemia and normal insulin levels occur within days after surgery, long before there is any significant weight loss.<sup>20,21</sup> The mechanisms of the favorable effects of bariatric surgery procedures on glucose metabolism are not well understood, and seem to be the result of endocrine and neural signals that affect appetite and satiety, as well as a complex interaction of malabsorption and gastric restriction. Two main hypotheses have been suggested in order to explain the acute increase in insulin sensitivity following bariatric surgery: the Upper and the Lower Intestinal Hypothesis.<sup>22</sup> According to the former, gastric bypass results in reduced secretion of factors such as ghrelin (an orexigenic hormone) and anti-incretins that decrease insulin release and/or increase insulin resistance. According to the Lower Intestinal Hypothesis the rapid nutrient delivery to the lower intestine stimulates the L cells, resulting in increased secretion of incretins (such as the anorexigenic hormones peptide YY and glucagon-like peptide 1-GLP1), which in turn enhances insulin secretion and/or action.<sup>22</sup> In addition to these endocrine changes, neural impulses

**Table 1.** Changes in gut hormones and adipocytokines after bariatric surgery.

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•	Leptin levels drop after laparoscopic adjustable gastric banding, gastric bypass and biliopancreatic diversion
•	Adiponectin levels rise following laparoscopic adjustable gastric banding, gastric bypass and biliopancreatic diversion
•	Resistin: conflicting results
•	Peptide YY (basal and meal stimulated) increases after vertical banded gastroplasty, Roux-en-Y gastric bypass and jejunioleal bypass
•	Ghrelin: reduced levels after gastric bypass, no change after gastric banding
•	Oxyntomodulin: increased in glucose loading after gastric bypass
•	Glucagon-like peptide 1 and 2 (GLP1, GLP2): increased postprandial after Roux-en-Y gastric bypass. GLP1 is also increased but at a lower level after gastric banding
•	Glucose-dependent insulinotropic polypeptide: conflicting data. Probably decreased after Roux-en-Y gastric bypass
•	Obestatin: increased 6 months after gastric banding. No change 2 years after Roux-en-Y gastric bypass
•	Cholecystokinin: No changes in fasting or postprandial cholecystokinin were seen after Roux-en-Y gastric bypass, vertical banding gastroplasty, or jejunioleal bypass
•	Neurotensin and motilin: decreased after gastric banding
•	Vasoactive intestinal peptide: No changes in plasma vasoactive intestinal peptide have been found after either Roux-en-Y gastric bypass or vertical banding gastroplasty

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through vagal pathways may influence eating behavior, resulting in weight loss and improvement of glucose homeostasis.<sup>23</sup>

In the recent recommendations of the International Diabetes Federation for the management of type 2 diabetes, bariatric surgery is considered as an appropriate treatment for type 2 obese diabetics (body mass index, BMI $\geq$ 35 kg/m<sup>2</sup>) not achieving recommended targets (with medical treatment). Mildly obese diabetics (BMI 30-35 kg/m<sup>2</sup>) are also considered eligible for bariatric surgery under certain circumstances.<sup>24</sup>

Considering all of the above, is type 2 diabetes an operable disease, despite the fact that after vertical banded gastroplasty or Roux-en-Y gastric bypass, only 36% of prior diabetic patients remained free of the disorder at 10 years?<sup>25</sup>

### Bariatric surgery and hyperlipidemia

Bariatric surgery results in an improvement in hyperlipidemia. In a systematic review and meta-analysis, hyperlipidemia improved in over 70% of operated patients.<sup>14</sup> In particular, total cholesterol, low-density lipoprotein and triglycerides decreased by an average of 0.86 mmol/L, 0.76 mmol/L and 0.90 mmol/L respectively, while high-density lipoprotein showed no significant change.<sup>14</sup> In the same meta-analysis, patients who underwent vertical banded gastroplasty or gastric banding showed an increase

in high-density lipoprotein of 0.13 mmol/L and 0.12 mmol/L, respectively. In an original report by Arribas del Amo, out of 80 operated obese patients who underwent vertical banded gastroplasty, serum total cholesterol normalized in 34.28% and triglycerides in 77.77%.<sup>26</sup> In another study of 310 patients who underwent gastric bypass surgery, 87% of those with hyperlipidemia and also 87% of those with hypertension, resolved or improved these conditions.<sup>27</sup> The prospective controlled Swedish Obese Subjects (SOS) study showed that, 2 and 10 years after bariatric surgery, patients exhibited an improvement in hypertriglyceridemia and an increase in high-density lipoprotein compared with conventionally treated matched controls.<sup>25</sup> These benefits were less marked at 10 than at 2 years, but remained significant.<sup>25</sup>

### Bariatric surgery and hypertension

In overweight and obese individuals, among other comorbidities, arterial hypertension is a serious one. Bariatric surgery offers resolution or improvement in arterial hypertension. In a systematic review and meta-analysis by Buchwald et al, 61.7% of hypertensive obese patients showed postoperative resolution of hypertension, and 78.5% showed resolution or significant improvement of this condition.<sup>14</sup> In another retrospective original study, hypertension resolved in 65.5% of the hypertensive obese patients who underwent vertical banded gastroplasty.<sup>27</sup> In

the same study, out of 310 patients who underwent gastric bypass surgery, 87% of those with hypertension resolved or improved this condition. In an observational 2-cohort study of operated patients and matched severely obese controls, 82% of the patients experienced a significant reduction in cardiovascular disease.<sup>28</sup> Improvement of hypertension has also been reported in non-severely obese patients with BMI < 35 kg/m<sup>2</sup>.<sup>29</sup> In a meta-analysis of 52 studies involving 16,867 obese patients, a significant decrease in cardiovascular risk factors, including hypertension, diabetes, and hyperlipidemia, has been shown. Mean systolic pressure reduced from 139 to 124 mm Hg and diastolic pressure from 87 to 77 mm Hg. Also observed was a 40% relative risk reduction for 10-year coronary heart disease risk, as determined by the Framingham risk score.<sup>30</sup> In addition to the above discussed obesity comorbidities, bariatric surgery seems to benefit a large list of comorbid conditions (Table 2).<sup>8</sup>

On the other hand, bariatric surgical procedures have many detrimental effects and appear to be costly compared with non-surgical interventions.<sup>31</sup> Weight regain is a major complication, more prevalent after restrictive types of operation. Deficiencies in vitamins and micronutrients, mainly due to malabsorption, can lead to anemia, osteoporosis, peripheral neuropathy and central nervous system deficits, sensorimotor disturbances, night blindness, coagulopathy, rash, alopecia, pellagra, acrodermatitis, and cardiomyopathy, and patients need lifelong postoperative substitution therapy.<sup>8</sup> Other potential problems are drug malab-

sorption, renal stones due to oxalosis and liver failure. Skin excess, laxity and ptosis result in unpleasant hygienic and cosmetic consequences requiring expensive cosmetic surgeries.<sup>8</sup> In addition, some studies have shown an increased mortality due to accidents and suicides after bariatric surgery.<sup>31</sup> Venous thromboembolism, sepsis, anastomotic leaks, bleeding, infections, small bowel obstruction, hernias, dumping syndrome, nausea, vomiting, diarrhea, gastritis, bile reflux, and gallstones are postoperative complications.<sup>8,31,32</sup> Nevertheless the mortality rate is low and at 30 or less days, according to a meta-analysis, was 0.1% for the restrictive procedures, 0.5% in patients after gastric bypass operation, and 1.1% in patients undergoing biliopancreatic diversion with or without duodenal switch.<sup>14</sup> The mortality rate after bariatric surgery seems to be equivalent to that of minimal abdominal surgery, such as laparoscopic cholecystectomy (0.3-0.6%).<sup>33</sup>

In summary, bariatric surgery is significantly effective not only as regards the long-term reduction of body weight, but also for the resolution or improvement of obesity comorbidities, such as type 2 diabetes, hyperlipidemia and hypertension. These beneficial effects are achieved because of long-term weight loss, but also because of endocrine changes induced by the gastrointestinal surgery, the latter appearing within the first postoperative days. It is now generally accepted that bariatric surgery reduces the morbidity and mortality of cardiovascular events in particular. In a meta-analysis (8 trials, 14,052 operated patients and 29,970 controls) gastric banding and

**Table 2.** Beneficial effects of bariatric surgery.

- Weight loss
- Diabetes mellitus: improvement or resolution
- Lipid profile improvement (total cholesterol, LDL cholesterol and triglycerides decreased, no significant change in HDL cholesterol)
- Arterial hypertension: improvement or resolution
- Increase in left ventricular wall thickness, increase in left ventricular ejection fraction, and improvement in overall cardiac function
- Improvement in chronic venous insufficiency, leg ulcers, superficial thrombophlebitis and deep vein thrombosis
- Obstructive sleep apnea: improvement or resolution
- Gastroesophageal reflux disease: improvement (probably due to the decrease in intra-abdominal pressure)
- Non-alcoholic fatty liver disease improvement
- Hyperandrogenemia: improvement and restoration of menstrual cyclicity and fertility in females, improvement in hypoandrogenism and erectile dysfunction in males
- Decrease in cerebrospinal pressure and relief of related symptoms, such as headache and tinnitus
- Improvement in degenerative joint disease and pain, and decrease in the need for orthopedic surgery
- Reduction in the risk of chronic kidney disease progression
- Improvement in quality of life and psychosocial functioning

gastric bypass were associated with a reduced risk of global mortality (odds ratio, OR=0.55), cardiovascular mortality (OR=0.58), and all-cause mortality (OR=0.70).<sup>3</sup> The SOS study, which is a prospective controlled study of 2010 operated obese patients and 2037 matched controls treated conventionally, showed a reduced number of cardiovascular deaths (28 of 2010 patients versus 49 of 2037 in the control group; adjusted hazard ratio, HR=0.47). It was also shown that the total number of first-time cardiovascular events (myocardial infarction or stroke) was lower in the surgery group (199 events among 2010 patients) than in the control group (234 events among 2037 controls; adjusted HR=0.67).

In conclusion bariatric surgery offers resolution or at least improvement in obesity comorbidities, particularly type 2 diabetes, hyperlipidemia and hypertension, and is associated with a reduced risk of cardiovascular events and death.

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