Obesity

The impact of bariatric surgery on diabetes outcomes – long-term trials are needed

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Bariatric surgery is increasingly recommended for treatment of people with diabetes (Leong and Taheri, 2012), with several guidelines now advocating treatment at lower BMIs than previously implemented (Fried et al, 2014). Clearly, bariatric surgery has a significant impact on weight loss, which improves quality of life, and the mechanical effects of excess body weight. Randomised controlled trials (RCTs) of bariatric surgery in people with diabetes have been small with only brief follow-up, and most available data are derived from observational studies, which have also been collated into systematic reviews (Buchwald et al, 2009).

Recently, Schauer and colleagues reported the 3-year outcomes of the STAMPEDE (Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently) trial (summarised alongside), in which people with uncontrolled type 2 diabetes were randomised to intensive medical management alone or intensive medical management plus bariatric surgery (Roux-en-Y gastric bypass or sleeve gastrectomy). The authors observed significant reductions in body weight and HbA_{1c}, as well as significant improvements in quality of life. While a higher proportion of participants in the surgery group achieved the predetermined glycaemic target, the majority of the overall cohort (62%) did not achieve it.

Sjöström et al (2014) have also recently reported long-term findings from the observational SOS (Swedish Obese Subjects) study. They assessed the incidence of vascular complications in obese people with diabetes who underwent bariatric surgery and a matched control group who received conventional diabetes and obesity treatment. They observed that the incidence of both macrovascular and microvascular complications of diabetes was significantly reduced in the surgery group after a median follow-up of 17.6 years, but only in people with a diabetes duration of <4 years.

Cardiovascular disease remains the major cause of mortality in type 2 diabetes. In STAMPEDE, significant reductions in body weight and HbA_{1c} were observed, while important cardiovascular measures, such as blood pressure, LDL-cholesterol and carotid intima–media thickness, were unaffected. Although its design and endpoints were different, STAMPEDE shares the improvements in HbA_{1c} that were seen in people with a similar diabetes duration in the ACCORD (Action to Control Cardiovascular Risk in Diabetes), ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) and VADT (Veterans Affairs Diabetes Trial) studies (Dluhy and McMahon, 2008; Duckworth et al, 2009; ACCORD Study Group, 2011; Coca et al, 2012). These three major trials did not demonstrate any reduction in cardiovascular events despite improving LDL-cholesterol levels and blood pressure – factors that were not affected in STAMPEDE.

Given the participant numbers and cardiovascular biomarker findings, it is unlikely that a reduction in cardiovascular events will be observed with bariatric surgery over longer-term follow-up of STAMPEDE. Thus, evidence supporting cardiovascular event and mortality reductions following bariatric surgery is still limited to dated observational studies. Furthermore, there are no RCT-derived data on whether the changes in body weight and HbA_{1c} that result from bariatric surgery are maintained or have an impact on the microvascular complications of diabetes over the long term. Many questions regarding the potential long-term benefits of bariatric surgery remain, and they will require RCTs to answer. ■

References on next page

N Engl J Med

Bariatric surgery improves effects of intensive medical therapy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The authors report on the 3-year outcomes of the STAMPEDE (Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently) trial, the 1-year results of which have already been published.

2 A total of 137 obese people with uncontrolled T2D underwent either intensive medical therapy alone or intensive medical therapy plus bariatric surgery (Roux-en-Y gastric bypass or sleeve gastrectomy).

3 At 3 years, the primary endpoint of an HbA_{1c} level of 42 mmol/mol (6.0%) was achieved by 5% of people in the medication group, compared with 38% in the gastric bypass group ($P<0.001$) and 24% in the gastrectomy group ($P=0.01$).

4 The surgery groups also had superior outcomes in terms of BMI, body weight, waist circumference and quality of life; however, blood pressure, LDL-cholesterol levels and carotid intima–media thickness were not significantly different between the surgery and medication groups.

5 Some adverse events resulting from surgery were reported, but were of low severity and rarely occurred after the first year.

6 Overall, 36% of the participants had a BMI of 27–34 kg/m^2 at baseline, and these patients had similar improvements in glycaemic control compared with those with a BMI of ≥35 kg/m^2; this suggests that the benefits of bariatric surgery are not limited to the latter group of patients.

Schauer PR, Bhatt DL, Kirwan JP et al (2014) Bariatric surgery versus intensive medical therapy for diabetes – 3-year outcomes. *N Engl J Med* **370**: 2002–13

Diabetes Metab Res Rev

Exenatide in people with T2D, obesity and NAFLD with elevated liver enzymes

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 T2D in conjunction with obesity and non-alcoholic fatty liver disease (NAFLD) with elevated liver enzymes is difficult to treat, as sulphonylureas, thiazolidines and biguanides are all metabolised in the liver and can cause damage.

2 The authors evaluated the effects of exenatide, a glucagon-like peptide-1 agonist, in 60 people with this disease profile.

3 Participants were randomised to receive either exenatide plus insulin glargine, or insulin aspart plus insulin glargine.

4 After 12 weeks, there were similar improvements in glycaemic control and lipid levels between the two groups.

5 Body weight and waist circumference were reduced in the exenatide group but increased in the intensive insulin group. The levels of alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transpeptidase were reduced in both groups, but to a greater extent in the exenatide group ($P<0.001$).

6 Regression from a greater to a lower degree of fatty liver was more common in the exenatide group (93.3% vs 66.7%; $P<0.01$).

7 The authors conclude that exenatide had a better hepatic-protecting effect than intensive insulin therapy, and that it may be a useful treatment adjunct for patients with T2D, obesity and NAFLD with elevated liver enzymes.

Shao N, Kuang HY, Hao M et al (2014) Effects of exenatide on obesity and NAFLD with elevated liver enzymes in patients with type 2 diabetes. *Diabetes Metab Res Rev* **30**: 521–9

Diabet Med

Predictive factors for gestational diabetes in obese women

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The authors assessed an array of clinical measurements and biomarkers in terms of their ability to predict the risk of gestational diabetes in 106 obese pregnant women in their second trimester.

2 The 29 participants (27.4%) who developed gestational diabetes were more likely to be older (median, 34 vs 31 years), to be of parity of two or more, to have higher blood pressure (mean, 123/76 vs 119/73 mmHg) and to be black.

3 Of the biomarkers measured, only adiponectin was independently associated with the condition.

4 If these results are validated in a large, prospective study, these factors could form a useful algorithm to predict gestational diabetes.

Maitland RA, Seed PT, Briley AL et al (2014) Prediction of gestational diabetes in obese pregnant women from the UK Pregnancies Better Eating and Activity (UPBEAT) pilot trial. *Diabet Med* **31**: 963–70

J Diabetes Complications

Effect of bariatric surgery on diabetic retinopathy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓

1 Rapid improvements in glycaemic control can result in a counterintuitive exacerbation of microvascular complications such as diabetic retinopathy (DR).

2 These authors sought to assess the incidence and progression of DR in 40 obese people with T2D who underwent bariatric surgery, a procedure that often results in rapid improvement in glycaemic control.

3 Unsurprisingly, surgery resulted in significant reductions in mean weight and HbA_{1c} (20 mmol/mol [1.8%]).

4 Participants without DR at baseline had a low risk of developing DR, and those with minimal DR had low risk of progression; however, those with moderate DR had a high risk of progressing to pre-proliferative DR.

5 People with moderate DR or worse should be closely monitored for DR progression following bariatric surgery.

Thomas RL, Prior SL, Barry JD et al (2014) Does bariatric surgery adversely impact on diabetic retinopathy in persons with morbid obesity and type 2 diabetes? A pilot study. *J Diabetes Complications* **28**: 191–5

J Clin Endocrinol Metab

Adipose tissue stiffness in obesity

Readability	✓✓✓
Applicability to practice	✓✓
WOW! Factor	✓✓✓

1 Liver and white adipose tissue (WAT) fibrosis are characteristics of obesity, and are in turn associated with tissue stiffness.

2 The current authors sought to determine the link between tissue stiffness, WAT and liver fibrosis, and obesity phenotypes in 404 obese people undergoing bariatric surgery.

3 WAT fibrosis was associated with body fat mass and BMI, and with clinically significant weight loss following bariatric surgery.

4 Subcutaneous WAT stiffness was associated with WAT fibrosis, as well as impaired glucose control.

5 WAT stiffness is associated with tissue fibrosis, obesity and diabetes-related traits, and may be a useful measure in clinical practice.

Abdennour M, Reggio S, Le Naour G et al (2014) Association of adipose tissue and liver fibrosis with tissue stiffness in morbid obesity: links with diabetes and BMI loss after gastric bypass. *J Clin Endocrinol Metab* **99**: 898–907

> ***"Exenatide had a better hepatic-protecting effect than intensive insulin therapy, and may be a useful treatment adjunct for patients with obesity, non-alcoholic fatty liver disease with elevated liver enzymes and type 2 diabetes."***

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