Clinical DIGEST 3

Obesity

Who benefits from bariatric surgery for diabetes?



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ith the increasing levels of more severe obesity complicated by comorbidities such as T2D, the number of bariatric surgery procedures is increasing worldwide. A recent report, based on an email questionnaire, estimated the number of bariatric procedures

worldwide to be 340 768, with 46.6% being the Roux-en-Y gastric bypass, 27.8% being the sleeve gastrectomy and 17.8% being the gastric band (Buchwald and Oien, 2013). While bariatric surgery was initially used for weight loss, it has been associated with improvement and remission of type 2 diabetes; however, the extent of these benefits are dependent on the type of study, the definitions employed for improvement and remission of diabetes and the bariatric procedure used (Leong and Taheri, 2012). The metabolic benefits have been highlighted with the designation of this type of surgery as "metabolic" surgery (Rubino et al, 2013). Some have suggested that bariatric surgery could also be beneficial for diabetes complications (Miras et al, 2012; Heneghan et al, 2013), although further study is required. Apart from metabolic improvements after bariatric surgery, there are improvements in cardiovascular function (Ashrafian et al, 2008) and renal function (Jose et al, 2013) and a reduction in mortality (Sjöström et al, 2007).

As with many treatments, not all individuals lose weight with various bariatric procedures, and some who do lose weight fail to maintain this weight loss in the long term. Similarly, not all people with diabetes have resolution of their diabetes, and some who go into diabetes remission relapse over time. Several studies have examined this, including the recent study by Dixon and colleagues, who examined the factors predicting diabetes improvement and resolution after gastric bypass surgery in a Chinese population (summarised in this section). The factors identified to be of importance in predicting remission included shorter duration of diabetes, higher C-peptide levels (suggesting greater pancreatic beta-cell reserve) and greater BMI (≥35 kg/m²).

These findings agree with another recent study by Arterburn and colleagues (summarised alongside), who retrospectively studied over 4000 individuals with diabetes who underwent gastric bypass surgery. Arterburn and colleagues also

identified male gender, older age, lower HbA_{1c} and less dependence on insulin and oral antidiabetes medication as favourable predictors of diabetes remission.

In the Swedish Obesity Study, a prospective cohort study of bariatric surgery, diabetes remission after 2 years occurred in 72% of the surgery group compared with 21% in the nonsurgical control group; after 10 years, diabetes remission reduced to 36% and 13% in the surgical and non-surgical groups, respectively (Sjöström et al, 2004). Arterburn and colleagues observed remission of diabetes in 76.9% of participants, with a 35.1% relapse in diabetes at 5 years. They examined the predictors of relapse in study participants, which included: older age at surgery; female gender; higher HbA, at surgery; dependence on insulin and oral antidiabetes medication; and duration of diabetes. This and previous studies suggest that early intervention with bariatric surgery for diabetes should be considered. Also, with emerging information, it should become increasingly possible to provide a more realistic expectation of diabetes outcomes post-surgery. Identifying individuals with diabetes who respond to bariatric surgery and remain in diabetes remission will assist informed consent. manage individuals' expectations and eventually tailor bariatric procedures better.

Ashrafian H, le Roux CW, Darzi A, Athanasiou T (2008) Effects of bariatric surgery on cardiovascular function. *Circulation* 118: 2091–102

Buchwald H, Oien DM (2013) Metabolic/bariatric surgery worldwide 2011. *Obes Surg* **23**: 427–36

Heneghan HM, Cetin D, Navaneethan SD et al (2013) Effects of bariatric surgery on diabetic nephropathy after 5 years of follow-up. Surg Obes Relat Dis 9: 7-14

Jose B, Ford S, Super P et al (2013) The Effect of biliopancreatic diversion surgery on renal function: a retrospective study. *Obes Surg.* Available at: http://1.usa.gov/Zn32gl (accessed 18.3.13)

Leong WB, Taheri S (2012) The role of bariatric surgery in the treatment of type 2 diabetes mellitus. *J R Coll Physicians Edinb* **42**: 194–8

Miras AD, Chuah LL, Lascaratos G et al (2012) Bariatric surgery does not exacerbate and may be beneficial for the microvascular complications of type 2 diabetes. *Diabetes Care* **35**: e81. doi: 10.2337/dc11-2353

Rubino F, Shukla A, Pomp A et al (2013) Bariatric, metabolic and diabetes surgery: What's in a name? *Ann Surg.* Available at: http://1.usa.gov/107QHOV (accessed 18.3.13)

Sjöström L, Lindroos AK, Peltonen M et al (2004) Lifestyle, diabetes and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 351: 2683–93

Sjöström L, Narbro K, Sjöström CD et al (2007) Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 357: 741–52



Long-term remission and relapse following gastric bypass

Readability	1111
Applicability to practice	1111
WOW! factor	111

The aim of this retrospective cohort study was to identify the long-term rates and clinical predictors of diabetes symptoms subsiding and returning in people undergoing gastric bypass surgery.

The study, carried out in the USA, involved 4434 adult participants with uncontrolled or medication-controlled T2D, who had undergone gastric bypass in the period between 1995 and 2008.

The authors found that, within 5 years of the surgery, 68.2% of participants experienced diabetes remission. Within the same time-frame, 35.1% of this group had experienced a relapse.

Important predictors of remission and relapse were found to be poor preoperative glycaemic control, insulin use and longer diabetes duration.

The authors concluded that for many obese adults with T2D, gastric bypass surgery is linked to durable remission, but around one-third of such people experience a relapse within 5 years of remission.

The authors claim that their study emphasises the significance of preoperative patient selection and counselling when one of the desired outcomes of surgery is durable diabetes remission. They concluded that more research was necessary to understand the mechanisms of diabetes relapse and the most effective time for surgery so as to ensure durable remission.

Arterburn DE, Bogart A, Sherwood NE et al (2013) A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. *Obes Surg* **23**: 93–102



Clinically relevant predictors of diabetes remission

Readability	1111
Applicability to practice	1111
WOW! factor	111

- In this longitudinal study, the authors aimed to find clinically relevant preoperative predictors of diabetes remission and inadequate glycaemic control following gastric bypass surgery.
- According to the authors, achieving an optimal outcome following the surgical treatment of T2D is possible if the people best suited to undertake bariatric surgery are selected, yet an effective system to categorise and predict outcomes of metabolic surgery is lacking.
- The authors examined the preoperative details of 154 participants, all of whom were ethnically Chinese and had T2D. The data were assessed for their influence on glycaemic outcomes at 12 months following gastric bypass.
- A total of 107 participants (69.5%) were in remission 1 year after surgery. The authors identified three independent and clinically significant preoperative factors that were associated with outcomes of bariatric surgery in ethnically Chinese participants following gastric bypass.
- They found that longer duration of diabetes, lower C-peptide level and lower BMI lessened the likelihood of the subject responding to surgery. The authors concluded that their data supported and clarified previous findings in non-Asian populations.

Dixon JB, Chuang LM, Chong K et al (2013) Predicting the glycemic response to gastric bypass surgery in patients with type 2 diabetes. *Diabetes Care* **36**: 20–26

DIABETES CARE

Impact of sleep duration on obesity in people with T2D

Readability	111
Applicability to practice	111
WOW! factor	111

- The aim of this prospective study was to determine the relationship between sleep duration, obesity and glycaemic control in people with T2D. The study comprised 4870 Japanese participants with T2D.
- The authors found that both a short and long sleep duration

had an important influence towards higher HbA_{1c} levels in participants with T2D. The authors established a U-shaped association between sleep deprivation, obesity and HbA_{1c} levels. This was not found to be linked to potential confounding factors, such as total energy intake, regular exercise, depressive symptoms and obesity.

The authors concluded that, since sleep duration is modifiable, it could prove to be a significant factor in the clinical management of T2D.

Ohkuma T, Fujii H, Iwase M et al (2012) Impact of sleep duration on obesity and the glycemic level in patients with type 2 diabetes mellitus: the Fukuoka Diabetes Registry. *Diabetes Care* 12 Nov [Epub ahead of print]

More research is necessary to understand the mechanisms of diabetes relapse and the most effective time for surgery so as to ensure durable remission."



Obesity and higher mortality a year after T2D diagnosis

Readability	
Applicability to practice	111
WOW! factor	111

The aim of this study was to examine the relationship between BMI – within a year following the diagnosis of T2D – and all-cause, cardiovascular, cancer and respiratory mortality in the medium term.

The study examined the records of 106 640 patients, taken from the Scottish Care Information Diabetes Collaboration (SCI-DC) database.

The authors found that, within a year of T2D being diagnosed, patients who had been classed as normal weight or obese showed variably higher mortality outcomes compared with the overweight group. The authors concluded that the results of their study confirmed a U-shaped association of BMI with mortality.

Logue J, Walker JJ, Leese G et al (2012) The association between BMI measured within a year after diagnosis of type 2 diabetes and mortality. *Diabetes Care* 8 Nov [Epub ahead of print]

DIABETES CARE

Day-night pattern of FGF-21 levels

Readability	////
Applicability to practice	11
WOW! factor	11

In this interventional study, the authors sought to elucidate the day—night pattern of fibroblast growth factor (FGF)-21 levels and its connection with free fatty acids. Despite the interest in FGF-21 as a therapeutic target in diabetes, little is known about the potential day—night

variation pattern and responses in the energy-repleted and energy-deprived conditions.

The authors found that a day—night variation in the levels of FGF-21 occurs in young, lean women in the isocaloric fed state. They also found that leptin replacement restored the approximate entropy of the FGF-21 time series, but not the energy deprivation-induced changes of FGF-21 levels.

Foo JP, Aronis KN, Chamberland JP et al (2012) Fibroblast growth factor 21 levels in young healthy females display day and night variations and are increased in response to short-term energy deprivation through a leptin-independent pathway. *Diabetes Care* 27 Nov [Epub ahead of print]