

Obesity

Low-calorie diets – a cure for type 2 diabetes?



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It is commonly believed that the natural history of type 2 diabetes has the inevitable outcome of pancreatic beta-cell failure and insulin dependence (Heine et al, 2006). This view, combined with findings from landmark studies demonstrating beneficial effects of intensive glycaemic control (Turner et al,

1999), has resulted in treatment intensification through early use of insulin therapy. However, the outcomes following bariatric surgery have challenged this perceived inevitability of beta-cell failure, since diabetes remission (although defined differently by different studies) can occur in a significant number of people with extreme obesity, including those on insulin therapy (Dixon et al, 2008; 2012; Buchwald et al, 2009).

In the Swedish Obese Subjects (SOS) study (Sjöström et al, 2004), a non-randomised prospective study, diabetes remission occurred in 72% of participants with diabetes who underwent bariatric surgery at 2 years, although this diminished to 36% at 10 years. Since the publication of this study, several other groups have demonstrated the impact of bariatric surgery on diabetes.

In an Italian study (Mingrone et al, 2012), obese people with diabetes ($n=60$) were randomised to receive gastric bypass (GB), biliopancreatic diversion (BPD), or medical therapy (MT). Diabetes remission (fasting glucose <5.6 mmol/L and $HbA_{1c} <48$ mmol/mol [$<6.5\%$] for ≥ 1 year without antidiabetes medications) was achieved in 95% of those who underwent BPD, 75% GB, and 0% with MT. In a study from Taiwan, Lee et al (2011) randomised obese people with diabetes ($n=60$) to GB or sleeve gastrectomy (SG). Diabetes remission (fasting glucose <7.0 mmol/L or $HbA_{1c} <48$ mmol/mol [$<6.5\%$] without antidiabetes medications) was observed in 93% of the GB, and 47% of SG, groups. A US study randomised obese people with poorly controlled diabetes ($n=150$) to GB, SG or MT and at 12 months post-surgery 0% of the MT group achieved an HbA_{1c} level $<6\%$ (42 mmol/mol) without antidiabetes medications, compared with 42% and 27% of the GB and SG groups, respectively (Lim et al, 2011). These studies have and will attract widespread attention, but comprise few subjects and will need to be replicated in larger populations.

Prior to bariatric surgery, candidates are commonly placed on a calorie-restricted diet, usually for a 4–6-week period. Calorie restriction

has been observed to result in significant diabetes improvement or remission prior to surgery (Lim et al, 2011), suggesting that calorie restriction *per se* is an important mediator of diabetes improvement or remission.

The study by Malandrucco et al (2012; summarised alongside) examined the impact of a 400-kcal/day diet for 1 week on 14 people with extreme obesity (BMI >40 kg/m²) and diabetes. Using hyperglycaemic clamps, they observed improvements in first and second phase insulin secretion, but did not observe any changes in insulin sensitivity.

The improvement in diabetes after bariatric surgery are the result of a combination of calorie restriction, weight loss, and alterations in metabolic hormones and adipocytokines. Furthermore, enhanced incretin response – particularly following GB and BPD – is believed to be involved (Chandarana and Batterham, 2012). However, caloric restriction studies suggest that low-calorie diets may play a major role in diabetes improvement or remission – but long-term maintenance of dietary interventions is challenging, and Sumithran et al (2011) suggest that the hormonal changes associated with calorie restriction in fact promote weight regain. These hormonal changes also tend to persist potentially explaining not only weight regain once the restriction is removed, but also additional weight gain.

A major indication for bariatric surgery is weight loss maintenance, making it practically the best, sustainable option for extreme obesity complicated by diabetes that is currently available. Whether it may be possible to use less restrictive dietary approaches, which might be more tolerable and sustainable, to treat type 2 diabetes requires further study.

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CLINICAL NUTRITION

Very-low-calorie diet improves metabolic profile

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 Caloric restriction is known to rapidly improve glycaemic control in obese people with T2D; however, the early effects of a very-low-calorie diet (VLCD) on insulin sensitivity and insulin secretion in morbidly obese people with type 2 diabetes are unclear and are the subject of this investigation.

2 The authors sought to investigate the relative contributions of insulin sensitivity and insulin secretion to improvement in glucose metabolism following a 1-week VLCD severely obese people with type 2 diabetes.

3 Hyperglycaemic clamps were used before and after a 7-day VLCD (400 kcal/day) in 14 participants (BMI, >40 kg/m²) who had good glycaemic control ($HbA_{1c} <7.5\%$ [<58 mmol/mol]) prior to the intervention.

4 The VLCD caused a $3.22 \pm 0.56\%$ weight loss ($P < 0.001$).

5 A significant decreases in fasting plasma glucose ($P < 0.05$) and triglycerides ($P < 0.01$) were also found and the mean capability to dispose of a glucose load increased from 59.0 ± 6.3 to 75.5 ± 6.3 mL/min/m² ($P < 0.01$) due to improvements in both first- and second-phase insulin secretion ($P < 0.02$). No significant changes in insulin sensitivity were found ($P = 0.33$).

6 The authors concluded that the marked improvement in metabolic profile in severely obese people with T2D after a short VLCD was due primarily to the amelioration of beta-cell function and not improved insulin sensitivity.

Malandrucco I, Pasqualetti P, Giordani I et al (2012) Very-low-calorie diet: a quick therapeutic tool to improve β cell function in morbidly obese patients with type 2 diabetes. *Am J Clin Nutr* **95**: 609–13

DIABETES CARE

Resistance training improves metabolic features, reduces abdominal fat in T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 To assess differences between the effects of aerobic and resistance training on HbA_{1c} (primary outcome) and several metabolic risk factors in people with T2D, and to identify predictors of exercise-induced metabolic improvement, the authors undertook the present study.

2 People with T2D ($n=40$) were randomly assigned to aerobic training or resistance training for 4 months; baseline and 4-month follow-up HbA_{1c}, glucose clamp-measured insulin sensitivity, oral glucose tolerance test-assessed beta-cell function, body composition by dual-energy X-ray absorptiometry, visceral (VAT) and subcutaneous (SAT) adipose tissue by magnetic resonance imaging, cardiorespiratory fitness and muscular strength were measured.

3 After training, increase in peak oxygen consumption was greater in the aerobic group (interaction $P=0.045$), while increase in strength was greater in the resistance group (interaction $P<0.0001$). HbA_{1c} level, total and truncal fat, VAT and SAT were similarly reduced in both groups, and insulin sensitivity and lean-limb mass were similarly increased.

4 Improvement in HbA_{1c} after intervention was independently predicted by baseline HbA_{1c} and changes in peak oxygen consumption and truncal fat.

5 The authors concluded that resistance training improves metabolic features and insulin sensitivity and reduces abdominal fat in people with T2D, similar to aerobic training. Bacchi E, Negri C, Zanolin ME et al (2012) Metabolic effects of aerobic training and resistance training in type 2 diabetic subjects: a randomized controlled trial (the RAED2 study). *Diabetes Care* 35: 676–82

ARCH PEDIATR ADOLESC MED

Increased diabetes risk associated with excess BMI-years

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors sought to evaluate the relation between excess BMI-years (the degree to which an individual's BMI exceeds the reference BMI and the duration for which he or she carries excess BMI) and incident diabetes.

2 This was a longitudinal analysis of 8157 adolescents and young adults

aged 14–21 years from 1981 through to 2006 in the USA.

3 Higher levels of excess BMI-years were associated with an increased risk of diabetes; for a given level of excess BMI-years, younger compared with older and Hispanic and black compared with white individuals had a higher risk of developing diabetes

4 The authors concluded that, because younger compared with older individuals have a higher risk of self-reported diabetes for a given level of excess BMI-years, interventions should target younger adults.

Lee JM, Gebremariam A, Vijan S, Gurney JG (2012) Excess body mass index-years, a measure of degree and duration of excess weight, and risk for incident diabetes. *Arch Pediatr Adolesc Med* 166: 42–8

SURGERY FOR OBESITY AND RELATED DISEASES

Abnormal GTT common following gastric bypass

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 During follow-up examinations of people who had undergone Roux-en-Y gastric bypass (RYGB), the authors noted those with weight regain complaining of fatigue shortly after eating and decided to study glucose tolerance test (GTT) results in a cohort of post-RYGB participants.

2 People ($n=63$; six with diabetes) who had undergone RYGB (>6 months postoperatively) were studied (mean age, 48.5 years; mean percentage of excess BMI lost, 64.5%; mean weight regain at follow-up, 5.3 kg) for a mean follow-up period of 47.9 months.

3 Some 49 participants were found to have abnormal GTT results; 43 had evidence of reactive hypoglycaemia at 1–2 hours after the glucose load

4 The authors concluded that abnormal GTT is a common finding after RYGB and that hypoglycaemia may contribute to weight regain post-RYGB.

Roslin MS, Oren JH, Polan BN et al (2012) Abnormal glucose tolerance testing after gastric bypass. *Surg Obes Relat Dis* Jan 27 [Epub ahead of print]

SURGERY FOR OBESITY AND RELATED DISEASES

Physicians unwilling to refer patients for bariatric trials

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors sought to investigate physicians' attitudes towards referring obese patients with T2D for bariatric surgery.

2 Physicians at an academic medical centre ($n=142$) and community-

based physicians ($n=197$) in the USA likely to treat T2D were sent a survey about their perceptions of the safety and efficacy of bariatric surgery as a treatment for obesity and T2D.

3 Physicians who returned the survey (response rate, 27.4%) had positive impressions of bariatric surgery for obesity and T2D (79.6% and 67.4%, respectively); yet only 20.8% reported that they would be likely to refer their patients with T2D with a BMI 30–34.9 kg/m² to a research trial of bariatric surgery.

Sarwer DB, Ritter S, Wadden TA et al (2012) Physicians' attitudes about referring their type 2 diabetes patients for bariatric surgery. *Surg Obes Relat Dis* Jan 30 [Epub ahead of print]

“Because younger compared with older individuals have a higher risk of self-reported diabetes for a given level of excess BMI-years, interventions should target younger adults.”