

ASK THE EXPERT

Metabolic surgery and diabetes



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American Institute of Gastric Banding, a multicenter clinical facility based in Texas (USA). He is the Advisory Editor of the journal *Obesity Surgery*. He has published more than 250 papers in the medical literature, including several key studies on the effects of weight loss on diabetes and the long-term outcomes of bariatric surgical procedures. He has also been actively involved in conducting postgraduate courses and workshops on obesity and its treatments in Australia, Europe, the USA, Asia-Pacific countries, South America and Canada for the past 15 years.

Q Is there any sign of the diabetes & obesity epidemics slowing down?

Recent data from the National Health and Nutrition Examination Survey (NHANES) suggests that the rate of increase in obesity is slowing [1]. After more than doubling from 14.4% of the adult population in 1980 to 32.2% in 2004, an average increase of 0.74% per year, the prevalence was 35.7% in 2010, an increase at the rate of 0.62% per year in the last 6 years measured.

However, we must not see this as a problem being solved. We have been digging a hole and we may now be digging more slowly. But with more than a third of the US adult population, around 80 million individuals, now obese we are still down a very deep hole.

The growth in prevalence of Type 2 diabetes will be driven principally by the growth of obesity and the aging of the population. Boyle *et al.* used US prevalence data on diabetes and prediabetes to construct dynamic models from which they calculated that, from a baseline prevalence of 14% in 2010, the low estimate of the prevalence of diabetes in the adult population by the year 2050 to be 21% and the high estimate to be 33% [2]. These are frightening figures.

Q There has been a lot of focus on preventing diabetes & obesity. How achievable is this?

We have too much food and too little to do. As we observe the prevalence of obesity continuing to grow, albeit more slowly, it



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is clear we are not preventing the problem at a community level. There are no proven strategies for the prevention of obesity. In spite of multiple large community trials, we have no proven technique that could be applied across the population to prevent obesity occurring. As the disease of obesity remains common and as that group in the community ages, the prevalence of diabetes will inevitably rise. The prevention of the obesity and the diabetes epidemics needs political, social and economic change more than healthcare change. We should not expect it soon.

Q How does bariatric surgery improve diabetes?

Multiple factors combine to create Type 2 diabetes and its sequelae. Insulin resistance and β -cell failure are at the core. Elevated free fatty acid levels (lipotoxicity) and elevated plasma glucose levels (glucotoxicity) impair β -cell function. The incretins (GLP-1 and GIP) restore β -cell function. Obesity, along with reduced physical activity and an appropriate genetic setting, leads to insulin resistance in muscle and the liver. The increased demand on the β cell and its progressive destruction triggers the onset of diabetes.

The essential effect of bariatric surgery is to achieve substantial weight loss. If applied early in the disease, the restoration of insulin sensitivity reduces the damage by free fatty acids and glucose on the β cell before the β -cell mass is destroyed. β -cell function not only stabilizes but actually improves with weight loss. Additional primary effects of some bariatric procedures are being

investigated. The increased response in GLP-1 to a meal, which occurs after gastric bypass, has attracted a high level of interest. It remains unclear if this drives any further improvement of β -cell function [3].

Q Does surgery compare favorably with other options for the management of diabetes?

Bariatric or metabolic surgery will predictably lead to remission of Type 2 diabetes in a substantial proportion of patients. Remission of diabetes should be the key outcome to be measured. The definition of remission varies between studies but usually requires normal fasting blood glucose and normal HbA1c with no hypoglycemic therapy. There have now been three major randomized controlled trials comparing surgery with optimal medical care [4–6]. All show a superior effectiveness to the comparative nonsurgical programs with remission rates of 37% for sleeve gastrectomy [5], 44 and 75% for gastric bypass [5,6], 73% for gastric banding [4] and 95% for biliopancreatic diversion [6]. The nonsurgical programs had 0, 12 and 13% remission rates. Important differences between trials, as shown in Table 1, should be noted but do not obscure the greater effectiveness of the surgical option.

Q At what point should obese & diabetic subjects be recommended for bariatric surgery? Do you think metabolic surgery should be the core management option for subjects with Type 2 diabetes?

Apart from glycemic control, the central aim of any program of diabetes therapy

is to achieve weight loss, increase physical activity and preserve β -cell function. Lifestyle interventions are effective for some and must be the first option. In the Look AHEAD study a complete or partial remission was achieved in 11.5% of individuals at 1 year and 7.3% at 4 years [7]. For the obese individual who does not respond or relapses after such a lifestyle program, discussion of a surgical option with that patient is now strongly indicated. That discussion should occur as early as possible to minimize β -cell destruction. The discussion should emphasize that all bariatric procedures are effective. The decision about which procedure is to be recommended should be left to the surgeon and the patient, and should include discussion of the primary effectiveness, the durability of that effect, the complexity, risks and adverse events, and the costs.

Q What has been the most significant research in bariatric surgery in the last 5 years?

The trio of randomized controlled trials (RCTs) summarized in Table 1 that compare bariatric surgical procedures with optimal nonsurgical care are critically important. They demonstrate a major advance in the care of the diabetic patient by providing a path to improved control or even remission of the disease. They show an effect that is clearly greater than current nonsurgical options. Our knowledge of better care has moved up a significant notch. The translation of this knowledge into clinical practice should now be occurring.

Table 1. Key features of the three randomized controlled trials comparing bariatric surgery with nonsurgical therapy.

Study (year)	Procedures	Group size (n)	BMI range	Diabetes duration (years)	Initial HbA1c (%)	Study duration (years)	Definition of remission	Remission rate (%)	Ref.
Melbourne RCT (2008)	LAGB vs NST	30	30–40	<2	7.7	2	HbA1c <6.2%, off therapy	LAGB: 73 NST: 13	[4]
Cleveland RCT (2012)	RYGB vs SG vs NST	50	27–43	8.5	9.2	1	HbA1c <6.0%, therapy allowed	RYGB: 44 SG: 37 NST: 12	[5]
Rome RCT (2012)	RYGB vs BPD vs NST	20	>35	6	8.7	2	HbA1c <6.5%, off therapy	RYGB: 75 BPD: 95 NST: 0	[6]

BPD: Biliopancreatic diversion; LAGB: Laparoscopic adjustable gastric banding; NST: Nonsurgical therapy; RCT: Randomized controlled trial; RYGB: Roux-en-Y gastric bypass; SG: Sleeve gastrectomy.

Q What challenges remain in this field? What should research focus on for the future?

The greatest challenge is to generate a change in the mindset of the healthcare providers of the diabetic patient. Substantial weight loss must become one of the key aims when designing a management plan for the obese diabetic. With few exceptions, this will require bariatric surgery. And so the commitment to weight loss must therefore include the commitment to continue on to bariatric surgery if non-surgical weight loss programs are insufficient. We now know that bariatric surgery is more likely to lead to improved control or complete or partial remission than continued nonsurgical therapy. It also provides a number of secondary benefits with improvement in other health problems and a better quality of life.

However, our knowledge about the bariatric surgical option is still incomplete – we need to work on filling these gaps. Here are just four of the key questions that should be pursued:

- Does the effectiveness last? We must know more about the durability of effect. A transient improvement in glucose control is arguably of little value. We know from the RCTs that the effect lasts beyond 2 years. We know the weight loss

effect of gastric banding and gastric bypass lasts beyond 10 years [8]. We need to confirm that the effect on diabetes should be seen to last in the long term (>10 years). It will take time to accumulate these data. Questions about the durability of the gastric bypass effect have already been raised;

- How does it work? We must know more about the mechanisms of effect. Only by understanding these can we optimize the application of bariatric surgery in diabetes;
- Can we afford it? We must show cost-effectiveness. In a RCT comparing gastric banding with nonsurgical therapy, modeling of a lifetime has shown the surgery to have a ‘dominant’ effect – increased quality-adjusted life years at lower cost [9]. Confirmation of this in different cost environments and with other bariatric procedures is needed;
- What about the overweight diabetic? We must explore the benefits of weight loss in the overweight (BMI 25–30) individual with diabetes. We should be testing if a safe outpatient procedure such as gastric banding can provide better control of diabetes than current optimal medical care.

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The opinions expressed in this article are those of the interviewee and do not necessarily reflect the views of Future Medicine Ltd.

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