‘Bariatric surgery for type 2 diabetes always produces a good outcome’

For

Dr Robert C Andrews1,2 and Dr Mimi Z Chen1,3
1School of Clinical Sciences, University of Bristol, Bristol UK
2Department of Diabetes and Endocrinology, Taunton and Somerset NHS Foundation Trust, Taunton, UK
3Department of Diabetes and Endocrinology, Royal United Hospital Bath NHS Trust, Bath, UK

Weight is very important in type 2 diabetes (T2DM); 1 kg of weight gained annually over 10 years is associated with a 49% increase in risk of developing T2DM in the subsequent 10 years. In patients with T2DM a weight loss of 5–10% results in a 0.5% reduction in HbA1c, a 5mmHg decrease in systolic blood pressure and diastolic blood pressure, a 0.13mmol/L increase in HDL cholesterol, and a 0.45mmol/L decrease in triglycerides. For these reasons the ADA and EASD recommend that weight loss should be strived for in all patients who have T2DM.

In spite of this recommendation, few patients with T2DM are offered comprehensive weight loss programmes; instead treatment focuses on using medication to control glucose, blood pressure and lipids, with many of these medications causing weight gain. In the past, excuses for not targeting weight loss have been that it is hard to maintain weight loss in the long-term without high levels of contact or continuation of weight loss drugs.

Bariatric surgery, however, does not suffer from the above problems. The mean 20 years’ weight reduction in the Swedish Obese Subjects study, a very large prospective study, was 15–25% dependent on the type of surgery performed, and contact levels required post surgery were low.2

This and other studies have led NICE to state that bariatric surgery should be offered to patients with a BMI of 35–40kg/m² who have obesity-related conditions such as diabetes mellitus or obstructive sleep apnoea, or in those with a BMI of 40kg/m² or greater regardless of weight-related comorbidities. Updated NICE guidance due in the New Year is likely to suggest that the BMI cut-off for surgery in patients with T2DM should be lowered to 30kg/m².

In spite of these NICE recommendations, many physicians are reluctant to refer patients for bariatric surgery. The common reasons stated for this are: there are no long-term data that bariatric surgery improves diabetes control; there are no outcome data on macro- and microvascular diabetes complications; there are no data that bariatric surgery is better than medical therapy; bariatric surgery is very risky; complication rates are high and can be very serious; there are no cost-effective data; and most of our patients do not want surgery. The following takes each of these statements in turn.

There are no long-term data that bariatric surgery improves diabetes control

There is no doubt that bariatric surgery improves glucose control in patients with T2DM. A systematic review that looked at 22 094 patients in 136 studies, of which five were randomised controlled trials (RCTs), found that 86.6% of patients showed improvement in their glycaemia, with 78.1% achieving remission.3

A recent review of long-term outcomes of bariatric surgery found two high-quality studies with data on 80% of patients for longer than five years out from surgery. Adams et al. report a 62% remission rate in 88 patients six years after a Roux-en-Y gastric bypass (RYGB).4 and Caiazzo et al. demonstrate a 14% remission rate but a 63% ideal control rate (HbA1c<7% [53mmol/mol]) in 22 patients five years post laparoscopic adjustable gastric banding (LAGB).5 When using less stringent follow-up rates, a number of studies are found that report long-term data. For example, in the Swedish Obesity Study of 343 patients with T2DM who were operated on, diabetes remission rates were 72.3% (219/303) at two years and fell to 38.1% (90/236) and 30.4% (35/115) after 10 and 15 years, respectively.6 In this study, follow-up data are only available on 88% of patients at two years, 69% at 10 years and 34% at 15 years.

It is interesting to contrast what length of follow-up data we consider significant before a diabetes medication use becomes commonplace. For example, in many Clinical Commissioning Groups around the country, lixisenatide is the first-line GLP-1 agonist to be prescribed and to date the longest reported use data are 76 weeks.7

There are no outcome data on macro- and microvascular diabetes complications

In the UKPDS, better blood pressure control and better glycemic control were associated with reduced rates of both macrovascular and microvascular complications. Based on this evidence one would assume that any therapy that improves glycemic control would also have an impact on these complications. Until recently this has been the assumption, with many oral hypoglycaemics being licensed without data on these outcomes (metformin, sulphonylureas, glitazones and meglitinides). Recently, though, new hypoglycaemic agents can only gain a licence if they show that they do not increase macrovascular disease rates.

A recent Cochrane review of the use of sulphonylureas concluded that there is insufficient evidence from RCTs to support the decision to initiate sulphonylurea monotherapy and that data on mortality and diabetes complications were sparse and inconclusive.8 Similarly, a meta-analysis of metformin found that, compared to other treatments, metformin treatment had no effect on the risk of all-cause mortality (RR: 0.99; 95% CI: 0.75–1.31) or cardiovascular mortality (RR: 1.05; 95% CI: 0.67–1.64). They also found no evidence that metformin protected against the development of microvascular complications.9 For newer hypoglycaemic agents, all have been shown to not increase macrovascular risk but only one has been shown to improve this (pioglitazone). None
of the newer agents have presented any data showing a reduction in microvascular risk.

There are no large RCTs that are looking at (or have looked at) the effect of bariatric surgery on macrovascular and microvascular complications in patients with T2DM. What evidence we have comes from prospective and retrospective studies.

In two large prospective control studies, bariatric surgery has been shown to significantly reduce the mortality in patients with T2DM (9% vs 28% or 92% risk reduction). These reductions in death were mainly attributed to a reduction in cardiovascular disease.

Reduced incidences (50% and 67%) of microvascular diabetes complications were seen in two large prospective studies. In one of these studies, reduction in events was only seen in patients who had T2DM for less than four years at the time of surgery.

Smaller studies have attempted to examine the effect of surgery on microvascular disease progression. These studies suggest that bariatric surgery improves glomerular filtration rate (GFR) in patients with normal GFR and in those patients with chronic kidney disease stages 2 and 3. Microalbuminuria improves, with some studies showing complete resolution, and in established diabetes nephropathy improvement is seen in 53% of patients and stabilised in the remaining 47%.

In patients with no pre-existing eye disease, progression to disease is rare and, if seen, only results in the development of background retinopathy. There is a paucity of data on diabetes neuropathy following bariatric surgery.

There are no data that bariatric surgery is better than medical therapy

Four small studies have attempted to answer this question. In an RCT of 60 patients recently diagnosed with T2DM, LAGB induced greater diabetes remission at two years compared to conventional medical therapy (73% vs 13%).

Mingrone et al. performed a trial in which 60 obese patients with diabetes were randomised to intensive medical therapy, RYGB, or a biliopancreatic diversion (BPD). After two years of follow up, remission of T2DM was observed in 15 of 20 subjects and in 19 of 20 subjects randomised to RYGB and BPD, respectively. None of the medically treated subjects achieved remission.

Schauer et al. randomised 150 obese patients with diabetes with HbA1c greater than 7% (53mmol/mol) to either intensive medical therapy, RYGB, or sleeve gastrectomy (SG) procedures. The primary endpoint at a year of improvement of HbA1c to less than 6% (42mmol/mol) was achieved in 12% of the intensive medical therapy group, compared to 42% and 37% of the RYGB and SG groups, respectively.

Ikramuddin et al. compared RYGB and intensive medical therapy in 120 obese patients with T2DM. The primary endpoint was control of T2DM: HbA1c less than 7% (53mmol/mol), low density lipoprotein cholesterol less than 100mg/d, and systolic blood pressure less than 130mmHg. The use of medications to achieve these goals was allowed in both groups. At one-year follow up, 49% of the RYGB group achieved the triple endpoint compared to 19% of the intensive medication therapy group.

All four of these small studies demonstrate that bariatric surgery is better than medical therapy at improving glycaemic control.

Interestingly, we do not expect new diabetes drugs to show that they are better than current therapy. They just have to demonstrate that they are as effective as those currently used.

The surgery is very risky

The increased frequency with which these operations are carried out and the use of laparoscopic techniques mean that the risks of bariatric surgery are low, comparing favourably with the risk of having a gallbladder operation. LAGB is the safest of the three operations having a mortality rate of 1 in 2000, compared to ~1 in 1000 for SG and 1 in 500 for RYGB. Surgical morbidity is also relatively low for these procedures.

Complications rates are high and can be very serious

It must be remembered that use of oral hypoglycaemics and insulin is associated with complications. Metformin, the safest of the oral hypoglycaemic agents, causes B12 deficiency in many patients. Sulphonylureas cause weight gain and an increased risk of hypoglycaemia, with over 40% of patients experiencing mild and 14% experiencing severe hypoglycaemia over a 12-month period. Their use has also been associated with an increased risk of heart disease when used with metformin. Pioglitazone has been linked with an increase in bladder cancer and is known to increase the risk of long bone fractures. Insulin causes weight gain, hypoglycaemia and has been linked to increased cancer rates.

Long-term metabolic risks of bariatric surgical procedures do occur but, provided they are identified and treated, they rarely cause serious problems. Calcium absorption is reduced after all bariatric procedures putting patients at risk of metabolic bone disease and secondary hyperparathyroidism, thus calcium replacement and monitoring are recommended for all bariatric surgery patients. Patients are also at high risk for micronutrient deficiencies, especially vitamins D, B1, B6 and B12, as well as folate and iron. For these reasons all patients are recommended to take multivitamins (two per day) and vitamin D with RYGB, and SG patients also asked to take iron tablets and three-monthly B12 injections.

Changes in the absorption of certain solutes in gastric bypass patients can also lead to problems. Enhanced absorption of ethyl alcohol leads to a higher rate of alcohol consumption, and increased absorption of oxalate leads to an increased rate of kidney stones (2% to 14%) with a small subset at risk of renal dysfunction if measures are not taken to lower oxalate.

In a small subset of patients (1%), significant hypoglycaemia can be seen which requires adjustment in food intake. A small percentage of these patients require additional therapy to control these events.

There are no cost-effective data

For diabetes, cost-effectiveness of therapies is calculated using models. When bariatric surgery has been looked at with these models it has been found to be more cost-effective than the use of oral hypoglycaemic
agents. In these models, surgery costs were also fully recovered after 26 months. Costs of hypoglycaemic agents are never recovered.

Not what the patients want

There is a paucity of data on what obese patients with diabetes think about bariatric surgery and whether they feel that losing weight is a greater priority than control of their diabetes. Of those patients who have gone forward for bariatric surgery with us, even for patients who have had complications, few have regretted the decision to elect for surgery.

Conclusion

We still need to strive to obtain more data on the effect of bariatric surgery on glycaemic control, diabetes complications, side effects and patient-reported outcomes. However, the current data we have on bariatric surgery are comparable with data on other diabetes treatments and in many circumstances demonstrate a better evidence base and greater efficacy (see Table 1). Based on this, bariatric surgery should be offered to patients with diabetes who meet NICE criteria. It is then up to the patient to decide, with help from the multidisciplinary team, if they want to go forward for surgery.

Declaration of interests

Dr Andrews is a principal investigator on the National Institute for Health Research HTA-funded By-Band study: gastric bypass or adjustable gastric band surgery to treat morbid obesity. Dr Chen has no conflict of interests.

References


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Table 1. Benefits and risk of interventions for treatments of type 2 diabetes. Arrows represent the direction of changes seen, with ↓ indicating a reduction, → indicating no change and ↑ indicating an increase. One arrow suggests a small effect, two a moderate effect, three a large effect, and four a very large effect.
Against

Dr Jennifer Logue, Clinical Senior Lecturer in Metabolic Medicine, Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK

Bariatric surgery is touted as the cure for type 2 diabetes. It can result in large amounts of weight loss and is thought to be very cost-effective due to savings in diabetes care costs and wider economic gains through improved health. There are recommendations that we should be performing more and more bariatric surgery procedures and, in particular, be offering it as a treatment option to those with T2DM at lower body mass indices.

The long-term benefits for T2DM are uncertain

There is lack of relevant long-term data on the outcomes of bariatric surgery for patients with T2DM. Published randomised controlled trials looking at the effect of a variety of bariatric surgical procedures on glycemic control have only two to three years follow up, though they do show a large percentage of patients achieving diabetes remission, that is HbA1c <42mmol/mol off all hypoglycaemic medication.1,2 Beyond this the majority of long-term data for surgery come from the Swedish Obese Subjects (SOS) study. This is an observational study of 2010 patients who underwent one of three different bariatric surgery procedures in Sweden between 1987 and 2001. They were matched to a comparator group who had non-surgical weight management. A total of 345 participants in the surgery group and 262 controls had T2DM at recruitment. This study showed a rate of ‘recovery’ from T2DM of 72% at two years, much in keeping with recent trials, but by 10 years in general, less hypoglycaemic medications will be required and may only have microvascular disease benefits if done early after the development of diabetes. Yet when the cost-effectiveness of bariatric surgery is discussed, it is with the assumption of reduced diabetes care costs. It is the case that, in general, less hypoglycaemic medications will be required to obtain the same level of glycemic control,3 but there is no evidence to support stopping statins, antihypertensives (except if symptomatic) or decreasing retinal screening and monitoring for microalbuminuria at this point. It could also be argued that metformin, where tolerated, should be continued in the hope of maintaining ‘remission’. For glycemic control and micro- and macrovascular risk reduction, bariatric surgery is simply another (very expensive) tool in the armoury rather than any kind of miracle cure.

Complications

As a surgical procedure being performed on patients with high body mass and comorbidities, complications are inevitable, though the actual rate of complications, the procedures required to manage complications, and the effect they have on quality of life and employment are unknown. Despite the complex patient group, in-hospital therapy at time of recruitment and this is reflected by a mean total cholesterol of 5.8mmol/L. There was treatment indication with total cholesterol concentration; only those with a total cholesterol >5.8mmol/L had a cardiovascular benefit from bariatric surgery. Given the mean cholesterol in more contemporary studies is below 5mmol/L, it may be that the effectiveness of bariatric surgery for cardiovascular disease was simply a reflection of poor risk factor management in the control groups and the result would not be repeated in a study today.

The evidence for microvascular disease reduction is also reliant on the historical SOS data. At a median 17.6-year follow up there was a 56% reduction in microvascular complications.6 However, when the patients were stratified by duration of diabetes, there was no benefit for those who had diabetes for four or more years suggesting that irreversible changes may occur – so-called metabolic memory.

So bariatric surgery does not lead to lasting remission of diabetes in all patients, probably does not reduce macrovascular events in patients with adequate risk factor control, and may only have microvascular disease benefits if done early after the development of diabetes. Yet when the cost-effectiveness of bariatric surgery is discussed, it is with the assumption of reduced diabetes care costs. It is the case that, in general, less hypoglycaemic medications will be required to obtain the same level of glycemic control,3 but there is no evidence to support stopping statins, antihypertensives (except if symptomatic) or decreasing retinal screening and monitoring for microalbuminuria at this point. It could also be argued that metformin, where tolerated, should be continued in the hope of maintaining ‘remission’. For glycemic control and micro- and macrovascular risk reduction, bariatric surgery is simply another (very expensive) tool in the armoury rather than any kind of miracle cure.
mortality is low, with a recent study from the US reporting 0.3\% mortality.\(^8\) It goes without saying that any death as a consequence of bariatric surgery is devastating and, however small the risk, must be taken account of when assessing the risks of surgery compared to the benefits. What are more common are short- and longer-term complications from intestinal obstruction, leak, vitamin deficiencies and chronic dumping syndrome (15\%) after gastric bypass, and band slippage or pouch dilatation (15\%) after gastric banding which usually results in a revisional bariatric procedure.\(^7\) This need for revisional surgery adds to the costs of surgical services, and can be poorly resourced when not factored into the overall costs of a surgical service; recent data from the English National Bariatric Surgery Registry show that 6.3\% of bariatric surgery procedures recorded were revisions of previous procedures. What is unknown is the effect that complications have on the patient’s recovery from bariatric surgery and how much it attenuates the benefits on quality of life, psychological wellbeing and economic productivity. There are no data on simpler complications such as surgical site infections, poor wound healing and chronic pain as these are dealt with as outpatients or in primary care, yet these are complications that would be predicted in a population who are obese and have diabetes. There are also theoretical risks on bone health and increased fracture risk which remain unexplored. As bone density is closely related to weight (bones only need to be strong enough to support your current mass), it is hard to unpick physiological from pathophysiological bone mass loss. Also, vitamin D can be low after surgery but equally can be low in obese individuals without bariatric surgery.

However, one retrospective study of 258 women who mainly had gastric bypass, showed a 2.3-fold increase in the rate of fractures after a follow-up period of 7.7 years.\(^10\) Generally, there is reduction in cancer risk with bariatric surgery, but a recent observational study from Sweden suggests that there may be a 2-fold increase in colorectal cancer risk 10 years after bariatric surgery regardless of the surgery type.\(^11\) 

### Psychological outcomes

Psychological comorbidity is common in obesity and seems to be particularly prevalent in those who choose to undergo bariatric surgery. In general, bariatric surgery leads to improvement in scores for anxiety, depression and binge eating disorders, but there have been reports on increased suicide after bariatric surgery.\(^12\) It may be that those who choose surgery over non-surgical weight loss do so due to greater psychological distress and a perceived need for solution; if the surgery does not alleviate this distress they may resort to suicide. An alternative explanation is physiological; there is an increase in suicide after gastric ulcer surgery\(^13\) raising the question of a possible effect of vagotomy on mood and suicidal ideation. There is also an increase in alcohol use disorders two years after bariatric surgery, seen most often in those having gastric bypass surgery. There is currently no evidence on how best to screen for psychological disorders prior to bariatric surgery and what should constitute an absolute contraindication. There is also no evidence for which psychological interventions can help improve psychological distress and reduce the risk of adverse outcomes after surgery.

### Stratified approach required

For many patients bariatric surgery will be a life changing intervention with the potential for rare but serious complications, unknown long-term sequela and a poor evidence base for how to deliver care in a safe yet cost-effective service. It can have life changing benefits for a large percentage of those who receive it, but the cost-effectiveness when long-term follow up, length of remission of comorbidities and managing any complications are accounted for is likely to be far less favourable than currently claimed. The fact that bariatric surgery is such a popular procedure worldwide is an indication of the growing twin epidemics of diabetes and obesity and lack of a viable alternative treatment. Due to this lack of an alternative treatment option we are increasing our provision of bariatric surgery locally; a move I am in support of as long as patients are carefully selected and well managed. However, there is an urgent need to address these gaps in the evidence for the safe selection and management of bariatric surgery patients\(^14\) while also pursuing alternative treatment options.

### Declaration of interests

Dr Logue is Chief Investigator of the NIHR funded Surgical Obesity Treatment Study, a prospective cohort study on the long-term outcomes from bariatric surgery.

### References