

Fat: bariatric surgery and procedures

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Who would have thought? Surgery as a 'cure for type 2 diabetes (T2DM)'. I would like to introduce one of my patients, Sarah, a 46-year-old woman. She presented 10 years ago, living with obesity (BMI 44) and poorly controlled T2DM. She had been taking insulin for eight years, plus additional GLP-1 agonists and metformin. She underwent several lifestyle interventions for weight loss with little success. She subsequently underwent a Roux-en-Y gastric bypass (RYGB) and was able to come off all insulin and oral antiglycaemic medications. She only takes the recommended multivitamin replacement post-bariatric surgery now. Her HbA_{1c} has been well controlled for several years.

History of bariatric surgery

The first bariatric surgical procedure for weight loss dates back to the tenth century and was carried out in Spain on Sancho, King of Leon also known as 'Sancho the Fat'.¹ King Sancho was living with such severe obesity that 'he could not walk, ride a horse or pick up a sword' and lost his throne. He was escorted by his grandmother to Cordoba, where he was treated by a famous Jewish physician who sutured the King's lips so that he could only be fed a liquid diet through a straw. King Sancho lost half his weight, returned to Leon on his horse and regained the throne!

The 'true' history of bariatric or metabolic surgery started nearly 100 years ago, in line with 100 years of insulin. The story began in 1925, when a report in the *Lancet* described a 'side effect' of a gastrointestinal operation to treat a peptic ulcer.² Physicians noticed resolution of glycosuria which, at the time, was used to diagnose 'diabetes'. Similar observations were made in the following decades, with the first metabolic surgical procedure, the proximal-jejunal bypass, carried out by Mr Kremen in 1954.³ During the 1980s and 1990s, resolution of T2DM after bariatric surgery was noted and reported, including a landmark report by Pories *et al* involving more than 120 patients.⁴ In 1999, it was observed that nearly all patients undergoing a biliopancreatic diversion (BPD), a malabsorptive weight loss procedure, had normalised glucose levels post-operatively.

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Professor Rubino, Chair of Metabolic Surgery at King's College London, attempted to carry out clinical trials comparing metabolic surgery to medical therapy in 1999, but at the time they were not deemed ethical. He performed initial studies in rats in 2004 by taking a lean diabetes model and constructing a duodenal-jejunal bypass with preservation of gastric volume.⁵ He observed a significant improvement in glucose tolerance following the duodenal-jejunal bypass in this rodent model.

The anti-diabetes effect of duodenal-jejunal exclusion has also been observed with the use of endoscopic medical devices. One of these, the Endobarrier or duodenal sleeve, is a 60 cm impermeable implantable endoscopic duodenal-jejunal liner positioned along the first part of the intestine. It has been shown to induce significant improvement in glycaemic control in patients with T2DM.⁶ In the Revise-Diabetes clinical trial, patients with T2DM were randomised to Endobarrier alone, Endobarrier and GLP-1 agonist liraglutide 1.2 mg or liraglutide 1.2mg alone.⁷ The Endobarrier with additional liraglutide demonstrated the greatest weight loss and improvement in HbA_{1c}.

A further procedure, duodenal mucosal resurfacing, uses a heat balloon to resurface the duodenum and has been shown to give improvements in HbA_{1c}, albeit with a relatively small effect on weight loss.⁸ These medical devices which involve manipulation of the duodenum support the notion that the first part of the intestine is mechanistically important for regulation of glucose control and weight.

Trial results

Over the last decade, several randomised trials of bariatric surgery vs. pharmacotherapy for the treatment of T2DM have been published.⁹ These trials have shown surgical superiority in terms of remission of T2DM, defined as an HbA_{1c} of 6.5% or less in individuals off all diabetes medications for at least one year. The compelling evidence in favour of surgery eventually led to the publication in 2016 of international guidelines for metabolic surgery as a recommended treatment for T2DM among select individuals.¹⁰ In the UK, NICE recommends consideration of metabolic surgery in T2DM for patients with a BMI as low as 30, or 27.5 in South East Asians. The most common procedures worldwide include the RYGB and the sleeve gastrectomy, although insertion of the gastric band has been popular in the past. The BPD is performed less frequently and is the most malabsorptive, although it achieves the greatest remission of T2DM.

Obese Subjects (SOS) trial, a prospective controlled study following patients on lifestyle vs. bariatric procedures, showed

sustained weight loss of about 25% in the RYGB arm 20 years post-operatively.¹¹

Why does metabolic surgery work and why do patients feel less hungry after surgery? Traditionally, it was thought that this could be explained by gastric restriction and a smaller stomach size in addition to malabsorption. However, it is clear that significant biological changes take place after a RYGB and a sleeve gastrectomy, which lead to dramatic changes in gut hormones and contribute to a reduction in appetite. Indeed, the GI tract is an endocrine organ and there are significant endocrine differences between diet-induced weight loss and weight loss after metabolic surgery. For example, there is a decrease in the hunger hormone ghrelin and increases in satiety hormones including GLP-1 and PYY after metabolic surgery but increases in ghrelin and decreases in GLP-1 and PYY following diet-induced weight loss.¹² There is a decrease in energy expenditure after a diet but an increase after surgery. There are additional metabolic changes after bariatric surgery, including increases in bile acids and favourable changes in gut microbiota, which lead to increased insulin secretion, increased insulin sensitivity and increased satiation and weight loss.¹³

Duration of remission

How long does remission of T2DM diabetes last after bariatric surgery? The SOS study suggests a remission rate of 72% two years post-operatively which decreases to 36% at 10 years.¹⁴ Remission rates for other studies depend on the definition of remission and the duration of diabetes at baseline. Earlier surgical intervention in those with a shorter duration of T2DM results in a significantly greater resolution of diabetes. Studies also suggest improvements in quality of life, and a reduction in microvascular and macrovascular complications, following metabolic surgery.¹⁵ Factors which make remission of T2DM less likely are age >50 years, duration of T2DM >5 years, use of glucose-lowering drugs other than metformin, use of insulin and baseline HbA_{1c} >53 mmol/mol or 7.3%.¹⁶

Bariatric surgery is also available for patients with T1DM who are living with obesity. A systematic review in patients with a mean age of 38 and mean BMI of 43 has shown reductions in insulin usage and HbA_{1c} levels in these patients.¹⁷ Bariatric surgery in patients with T1DM needs careful assessment and MDT discussion; it should be advocated in patients when weight loss is likely to be beneficial in management of glycaemic control.

Bariatric surgery is useful in remission of several metabolic complications of obesity, including improvement in fibrosis in up to 70% of patients at five years in patients with severe obesity and NASH.¹⁸ Metabolic surgery has been shown to give reductions in major CV outcomes, in nephropathy, all-cause mortality and heart failure in the surgical arm compared to the control arm in patients living with obesity and T2DM.¹⁹ A recent Lancet meta-analysis in more than 174,000 individuals looked at survival in patients with and without diabetes after metabolic/bariatric surgery. It showed a significant reduction in overall mortality by 50% but a greater treatment effect in the T2DM cohort, with a 9.4 longer median life expectancy in this group vs. 5.1 years longer in the non-diabetes group in favour of the surgical arm.²⁰ Studies have also shown benefits in terms of



Key messages

- Reports of resolution of glycosuria after gastric surgery were published as early as 1925
- Several randomised clinical trials have shown superiority of metabolic surgery vs pharmacotherapy for remission of type 2 diabetes in patients living with obesity
- Metabolic surgery is safe, with mortality rates lower than a laparoscopic cholecystectomy in expert bariatric centres

COVID-19 outcomes, with patients who underwent bariatric surgery showing a decreased need for hospitalization, and a reduction in severe COVID outcomes as defined by ITU admissions, mechanical ventilation and death compared to matched non-surgical controls.²¹

Is metabolic surgery safe? There safety data are generally good, with 30-day and 5- year re-admission rates from our bariatric centre at King's College Hospital at lower rates compared to other common surgical procedures including hernia repairs and cholecystectomies.²² Mortality rates are lower than for a laparoscopic cholecystectomy in centres which carry out large volumes of metabolic surgery. Patients will need to be on life-long multivitamins after surgery and there is a risk of nutritional complications if they are not compliant.

The UK currently performs about 5,000 NHS bariatric procedures per year which compares with annual figures of around 50,000 bariatric procedures in France and more than 200,000 hip and knee replacements in the UK. We need to increase the number of metabolic procedures significantly as there are many individuals who will not be able to manage their weight and complications by lifestyle or pharmacotherapy alone.

Summary

The metabolic surgical road has been a long and arduous one. It started in 1925, with reports of the resolution of glycosuria after gastric surgery. Several reports in the 1980s and 1990s observed the resolution of diabetes after bariatric surgery. Experimental evidence in rats linked gastro-intestinal surgery and glucose metabolism. Over the last decade, several randomised clinical trials have shown sustained benefits of surgical treatment for T2DM. This finally led to the publication of much needed guidelines for the surgical treatment of diabetes. Metabolic surgery has been shown to be safe and cost-effective. It has demonstrated remission of T2DM and reduction in overall mortality and cancer risk. It is a life-saving intervention, essential for patients like Sarah.

Looking ahead, there are significant challenges in the provision and delivery of services for people living with complex and severe obesity. Only 50% of the UK offers multi-disciplinary Tier 3 weight management services, which are the stepping stone for Tier 4 ser-

vices where bariatric surgery is offered. We need to increase access to service provision across the UK in order to tackle the significant health inequalities in obesity care and provide cost-effective metabolic surgery to those that need it most.

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