

LETTER TO THE EDITOR

Poor responders after bariatric surgery – Are there second chances?**Respondedores pobres a cirugía bariátrica- ¿existen segundas oportunidades?***Dear Editor:*

During the past five years we have witnessed a significant progress in the management of type 2 diabetes mellitus (T2DM) and obesity,¹ often referred to as diabetes. Bariatric surgery has been proven to significantly exceed success rates of medical therapy in achieving not only substantial weight loss but also enabling T2DM remission as well as ameliorating metabolic syndrome-associated comorbidities. These effects have been proven to last beyond 10 years follow up.² However, regardless of good initial diabetes remission rate (around 80% after Roux-en-Y gastric bypass, 55% vertical sleeve gastrectomy and 95% biliopancreatic diversion) and weight loss (20–30% of total body weight), at five-year follow-up only 20–40% of patients maintain T2DM remission and 30–35% of lost weight is regained.^{2,3} Therefore, despite high success rates, a significant proportion of patients fail to achieve sustained control of diabetes following surgery.² Poor responders constitute a big challenge to manage for physicians, surgeons and allied healthcare professionals. With increasing number of performed bariatric procedures, the number of poor responders is also expected to rise, creating a large unmet clinical need.

Bariatric surgery has a potent physiological impact by affecting gastrointestinal signals to the brain as well as to other organs such as pancreas and liver. Based on this, poor responsiveness suggests inadequate physiological response that affects behaviour and metabolic control. In this context, there are some predictors of T2DM remission such as age, diabetes duration, preoperative C-peptide levels, insulin usage and poor early postoperative weight loss. In the same way, phenotypic features of adipose tissue remodelling, aberrant eating behaviour and the occurrence of depression or anxiety post-surgery is associated with poorer weight outcomes, whereas adherence to dietary and physical activity guidelines emerged as positive predictors of weight loss.⁴

Psychological interventions, pharmacotherapy and revisional surgery are the main interventional options in poor responders post bariatric surgery.

We have all witnessed the difficulty in making and sustaining changes in dietary intake and physical activity in obese individuals. Hence one reason for variable weight outcomes may be variation in the ability to adhere to post-surgery diet and activity recommendations and self-manage behaviour over time due to psychological factors.⁴ In this context, several psychological interventions could be applied in bariatric patients such as the cognitive behavioural therapy, the acceptance and commitment therapy or the dialectical behavioural therapy. They have been shown to improve eating disorder behaviours, body dissatisfaction, quality of life and acceptance of weight-related thoughts and feelings.^{4,5} However, whilst it would make intuitive sense that poor responders would benefit from additional support to promote maximal weight loss and prevent weight regain after surgery, there is no strong evidence yet to support this.^{4,5}

With regard to pharmacotherapy, the use of anorexigenic gut hormone analogues, such as glucagon like peptide 1 (GLP-1) analogue has been proven to be effective for glycaemic control and also for moderate weight loss in the absence or presence of T2DM in non-surgical patients. GLP-1 stimulates insulin release, improves glycaemic control, suppresses appetite and reduces food intake by potentially changing food preferences.⁶ Following a RYGB, large amounts of GLP-1 are secreted in response to a meal. However, it has been shown that poor responders secrete less GLP-1 during a standardised meal test compared to good responders after RYGB.⁷ Therefore, GLP-1 analogues have a potential to enhance surgical outcomes as shown in several retrospective observational studies.^{8,9} Another line of treatment can be provided by a relatively new group of glucose-lowering medications, sodium–glucose co-transporter-2 (SGLT2) inhibitors. They improve glycaemic control and also moderately improve weight and blood pressure, and reduce risk of death from cardiovascular causes by 38% in patients with T2DM and cardiovascular disease.¹ It terms of their use in poor surgical responders, some concerns have been raised regarding safety due to potential risk of dehydration and electrolyte disturbances. Another group of medications that can be considered after bariatric surgery are centrally acting ones such as lorcaserin, topiramate with phentermine and naltrexone with bupropion.¹

In poor responders it is crucial to exclude presence of anatomical abnormalities contributing to poor weight loss or regain or diabetes relapse. Surgical complications such as gastro-gastric fistula, dilatation of the gastric pouch

or gastrojejunal anastomosis post Roux-en-Y gastric bypass (RYGB), a “candy cane” (enlarged blind end of the Roux limb by the gastrojejunostomy site) and gastric band erosion or slippage should be ruled out. Whilst not all cases are eligible for revision surgery, its rate varies between 5% to even 50% after primary bariatric procedures with the highest rates in the gastric band group.¹⁰ When revising a RYGB, distalisation or conversion of a RYGB to a biliopancreatic diversion (BPD) can be considered. However, whilst the first approach may still not result in significant diabetes improvement, the latter brings increased risk of nutritional deficiencies. When revising sleeve gastrectomy patients refashioning of the sleeve or conversion to a RYGB or BPD are the most common interventions). Other options include adding an additional restriction with an adjustable gastric band or a ring over the existing sleeve or RYGB gastric pouch as well as endoluminal procedures.¹¹ Revision surgery has a potential of enhancing weight loss and improving diabetes control. However, due to complexity of these procedures, revisional bariatric surgery brings risk of increased morbidity. Therefore, re-operations should be carefully considered and performed by experienced laparoscopic bariatric surgeons.

There is still a limited knowledge of the aetiology of refractory diabetes following obesity surgery, which narrows the therapeutic options. For the very same reason, it is not possible to distinguish good responders from the poor ones prior to surgical intervention. More research in this field is required in order to guide a targeted and efficient treatment. Whilst this is awaited, a combined psychological, surgical and pharmacological therapy should be individually tailored to each patient’s needs and adjusted dynamically depending on their responsiveness.

Conflict of interest

The authors have no conflict of interest.

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