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14

Metabolic surgery: Action via hormonal milieu changes, changes in bile acids or gut microbiota? A summary of the literature

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A B S T R A C T

Obesity and type 2 diabetes remain epidemic problems. Different bariatric surgical techniques causes weight loss and diabetes remission to varying degrees. The underlying mechanisms of the beneficial effects of bariatric surgery are complex, and include changes in diet and behaviour, as well as changes in hormones, bile acid flow, and gut bacteria. We summarized the effects of multiple different bariatric procedures, and their resulting effects on several hormones (leptin, ghrelin, adiponectin, glucagon-like peptide 1 (GLP-1), peptide YY, and glucagon), bile acid changes in the gut and the serum, and resulting changes to the gut microbiome. As much as possible, we have tried to incorporate multiple studies to try to explain underlying mechanistic changes. What emerges from the data is a picture of clear differences between restrictive and metabolic procedures. The latter, in particular the roux-en-Y gastric bypass, induces large and distinctive changes in most measured fat and gut hormones, including early and sustained increase in GLP-1, possible through intestinal bile acid signalling. The changes in bile flow and the gut microbiome are causally inseparable so far, but new studies show that each contributes to the effects of weight loss and diabetes resolution.

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Introduction

Obesity and type 2 diabetes are a worldwide epidemic. Medical weight loss through proper diet and exercise are essential to good health, but some patients require bariatric surgery in addition. Bariatric surgery has proven to be safe and effective in inducing weight loss and improving or even curing type 2 diabetes. Although all bariatric surgery procedures end up changing the patient's diet, the alteration to patient anatomy and/or nutrient flow has effects that are independent of the restriction on diet.

Weight loss surgery can generally be divided into three classes: restrictive, metabolic, or both. The restrictive procedures discussed here are: the adjustable gastric band (AGB), which simply encircles the cardia of the stomach with an inflatable silicone ring; and the sleeve gastrectomy (SG), in which most of the greater curvature of the stomach is removed. After these procedures, nutrients follow their pre-surgical course, but the patient is limited in the rate of food intake. There are many metabolic procedures, some of which also include a restrictive component. Here we review several procedures, as their similarities and differences in anatomical rearrangement and downstream effect can be compared to draw insight into the underlying physiology. The duodenal-jejunal bypass (DJB) involves separating the duodenum from the stomach outlet, and connecting a jejunal limb in its place. This procedure has a restrictive component; nutrients bypass the duodenum, which as a result is exposed to undiluted bile, and the bile and nutrients mix in the jejunum. Similar is the biliary-pancreatic diversion (BPD), which involves a much longer intestinal bypass, wherein the alimentary limb is anastomosed to the ileum. The BPD also usually involves a gastrectomy of varying types. BPD can lead to severe nutrient deficiencies, and is falling out of favour as RYGB and SG become more common [1,2]. Finally, the roux-en-Y gastric bypass (RYGB) involves separating the stomach into a small upper pouch, which is anastomosed to a roux jejunal limb, while leaving the remnant stomach attached to the biliary limb, into which the bile still drains. It is thus both restrictive and metabolic. The RYGB has been proven to induce greater weight loss and resolution of diabetes than the restrictive procedures, with a good safety record [3]. Each weight loss intervention has its pros and cons; their various differences also induce different changes in patient physiology, leading to direct effects on weight loss and diabetes resolution.

The last 10–15 years has seen a great increase in research in the hormone environments of the gut and the adipose tissue as they relate to weight loss. The stomach and intestine are now known to be crucial in the production of hormones such as ghrelin and glucagon-like peptide (GLP)-1. Further, adipose tissue is under homeostatic control by leptin and adiponectin. Weight loss procedures all have differing effects on these and other hormones; RYGB, in particular, is known to have an incretin effect, through both the 'foregut' mechanism, whereby bypass of the proximal small intestine leads to decreased anti-incretin effects, and the 'hindgut' mechanism, whereby direct flow nutrients to the distalsmall bowel cause a direct increase in incretin hormones. Disentangling the surgical changes from the changes induced by weight loss and diet are keys to understanding both the underlying physiology of obesity as well as the success of bariatric surgery.

Metabolic bariatric surgery has long been known to exert at least some of its effects through altered bile flow, including decreased absorption of fatty acids and increased bile production by the liver. Bile acids are now understood as signalling molecules in their own right; mechanistic studies of oral bile acid sequestrants have shown a significant incretin effect from altered bile flow [4]. Mechanistic studies of bile flow after surgery are difficult, and only few have been accomplished. Still, new evidence points to a causal link between the altered bile flow in malabsorptive procedures and the subsequent incretin effect.

The alterations in diet and bile flow that accompany weight loss surgery lead to changes in the gut microbiome. The techniques that are now used to profile the gut microbiome are relatively new, so mechanistic studies of bariatric surgery and changes in gut bacteria are only now beginning to come out [5]. Studies of the microbiome after change in diet, weight loss, bariatric surgery, probiotics, and antibiotics have all given new insights into how changes in the gut bacteria lead to profound changes in host physiology.

Here, we report a review of the impact of known weight loss procedures on gut and adipose hormones, bile acids, and the gut microbiome. From the large body of research that has been amassed, we can begin to glean new insights into the mechanism of weight loss and diabetes resolution after weight loss surgery.