



Gut Microbiome and Bariatric Surgery

Arun Dhir^{1,2,3} · Dora Huang⁴

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Introduction

Bariatric surgery remains the most effective therapeutic mode of achieving sustainable weight loss and modulation of obesity-related comorbidities. It was traditionally understood that surgical alterations in gut anatomy result in physical caloric restriction and nutrient malabsorption; however, these may not be the only means to weight loss and metabolic success. A more complex mechanism is thought to be at play. The role of the human gut microbiota may offer an additional explanation in the modulation of metabolism and disease pathology following bariatric surgery.

Gut Microbiota and Obesity

It is well known that the human gut microbiota affects energy balance by influencing calorie harvest, usage and storage. Hence, the composition of the microbiota provides important metabolic capabilities. Ongoing research is attesting to these capabilities and discovering potential links to many chronic diseases besides obesity.

The gut microbiota produces short-chain fatty acids, which are bacterial metabolites from the fermentation of otherwise indigestible oligosaccharides, dietary plant fibres and non-digested proteins. This interaction is particularly important in the pathophysiology of obesity, as short-chain fatty acids stimulate satiety hormone production (GLP-1 and PYY), as

well as playing a role in lipid metabolism, inflammation and insulin sensitivity.

In obesity, the gut microbiome has been shown to play a role in increased energy harvesting. Obesity is associated with specific microbial phyla composition. It is commonly associated with an increased ratio of *Firmicutes* to *Bacteroidetes*—a dysbiotic energy-harvesting microbiome [1]. Reduced microbial gene richness is also characteristic to the obesity state [2].

The intimate relationship between gut nutrient processing and the microbiome is evidenced in faecal microbial transplant. In murine models, transplanted faecal microbiota from obese mice into wild-germ free animals resulted in modest fat gain, compared to mice colonised with lean microbiome. Human studies involving faecal matter transplant have also shown beneficial effects with obesity [3], metabolic syndrome and transient insulin sensitivity, after transplant from lean individuals to obese patients.

Gut Microbiota and Bariatric Surgery

Changes in the gut microbiota following bariatric surgery have been explored in various studies [4–10]. Depending on the type of surgery and extent of alteration, gut microbiota may directly or indirectly change due to environmental, systemic and anatomical changes post-operatively. Modification in gastric size will affect diet and acid exposure. Altered nutrient flow due to shortened small bowel may affect oxygen nutrient exposure to the more distal gut. Gut microbes will be affected by changes in gut hormone production, as well as altered mixing of bile acids and pancreatico-biliary secretions with nutrients. Lastly, nutrient flow in shortened small bowel segments will vary.

The literature suggests that overall there is a dramatic shift in the composition and richness of gut microbiota after surgery, most profoundly in Roux-en-Y gastric bypass (RYGB) and a modest shift with sleeve gastrectomy. The most prominent phyla alteration observed is the overall decrease in the relative abundance of *Firmicutes* and increase in *Bacteroidetes* (post-gastric

✉ Dora Huang
dorahuang4@gmail.com

Arun Dhir
arun@melbournegastrosurgery.com.au

¹ Northern Health, Epping, VIC, Australia

² Melbourne Gastro Surgery, Melbourne, VIC, Australia

³ Monash University, Melbourne, VIC, Australia

⁴ Austin Health, Heidelberg, VIC, Australia

sleeve) [4, 10] and *Proteobacteria* (post-Roux-en-Y gastric bypass) [4, 5, 7–10]. The microbial gene richness is frequently seen to increase post bariatric surgery.

Roux-en-Y Gastric Bypass

RYGB involves bypassing the majority of the stomach and only 50 cm of the duodenum resulting in mostly a restrictive effect and a moderate malabsorptive effect.

The potential beneficial effect of the post-RYGB gut microbiota has been evidenced in faecal matter transplant rodent and human studies [10]. The exogenous transfer of the gut microbes from RYGB mice to wild germ-free mice resulted in significant reduction in adiposity and weight gain, in comparison with transfer from mice that underwent sham surgery.

In terms of phyla changes, a significant increase of *Bacteroides* and *Proteobacteria*, and a decrease of *Firmicutes* are observed in patients after RYGB [4, 6, 9, 10]. Furthermore, alterations in *Escherichia* (which belongs to the *Proteobacteria* phylum) are described frequently [5, 6, 9]. RYGB displays the greatest symbiotic microbiota changes and increase in microbial gene diversity compared to other types of bariatric surgery [5, 10]. Most changes in microbiome occurred within the first year postoperatively and this effect persisted until 9 years of follow-up in one smaller study [9].

Human translational research showed consistent increase in *Roseburia* genus in patients with successful resolution of diabetes after both RYGB and sleeve gastrectomy (SG) [8]. Such microbiome changes associated with faecal metabolite alterations may be relevant for modulating epigenetic mechanism; *Roseburia* are butyrate producers. Butyrate can promote epigenetic remodeling intestinal stem cells. This example signifies the potential for bariatric surgery-induced microbiome modification to alter host physiology, which requires intense exploration in the future.

Sleeve Gastrectomy

SG involves the removal of approximately 80% of the stomach by stapling along the greater curvature. This causes a restriction of food intake, acceleration of gastric emptying and alteration of gut hormones affecting satiety and appetite.

Several studies have investigated the influence of SG on the gut microbiome. SG has been reported to produce only modest microbial changes compared with RYGB [8]. In a large SG study (n = 110), microbial richness and gene count substantially increased 3 months post-operatively, approaching those of lean controls [11]. This is contrasted by smaller studies that did not find statistical significance in microbial diversity in SG patients [8]. Most studies investigating SG describe a decrease in *Firmicutes* and increases in *Proteobacteria*, *Bacteroidetes* and the *Bacteroidetes/Firmicutes* ratio (a surrogate marker for the microbiome of lean controls) [7, 12].

Adjustable Gastric Banding

Adjustable gastric banding (AGB) is a restrictive bariatric procedure that involves the placement of an adjustable band approximately 3 cm proximal to the gastro-oesophageal junction. Two studies assess the effect of AGB on microbiome [5, 9]. AGB is associated with microbial richness increased within 3 months post-surgery and reached statistical significance at 12 months. However, alterations in microbiome of the GB patients were not as profound when compared to the changes observed after RYGB or SG.

Bilio-intestinal Bypass

Bilio-intestinal bypass (BIB) and duodenal switch are hybrid surgical procedures combining gastric volume restriction with variable extents of small bowel bypass. Only two small studies explore gut microbial changes after this procedure [13, 14]. Results on the microbial changes after BIB were highly heterogeneous between patients. It appeared that the *Bacteroidetes* to *Firmicutes* ratio did not alter after BIB.

One-anastomosis Gastric Bypass/Mini Gastric Bypass (OAGB/MGB)

To our knowledge, there are no studies to date examining the relationship between OAGB and gut microbiome. Addressing this gap in the literature, our centre is currently conducting an Australian pilot study to examine these potential changes.

Conclusion and Future Perspective

We believe that work in this space will continue to evolve and shed more light on our understanding of how the gut microbiome is altered after bariatric surgery. Whether the altered gut microbiome is the cause or the effect of the metabolic effects seen after bariatric surgery is a harder question to answer.

This is an exciting time in the history of evolution of bariatric surgery and enriches our understanding of how it works. It also calls for greater collaboration between various disciplines of basic and clinical sciences, to further this objective.

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