Review

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The effects of bariatric surgery on gut microbiota in patients with obesity: a review of the literature

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Obesity is a disease with a rapidly increasing prevalence all over the world in recent years. Genetic and environmental factors are involved in the etiology of obesity, and the effect of microbiota on obesity is becoming increasingly clear. Obesity treatment has various treatment modalities such as behavior modification, medical nutrition therapy, physical activity enhancement, and surgical intervention. When other treatment methods are not successful, bariatric surgery is usually resorted to as the treatment method. Some changes such as food choices, the level of hormones and enzymes due to anatomical changes, pH of the stomach, and microbiota are observed after bariatric surgery. Alteration in the microbiota composition after bariatric surgery has also been reported to be important in achieving body weight loss and preserving body weight loss.

Key words: obesity, bariatric surgery, microbiota

INTRODUCTION

Obesity is defined by the World Health Organization (WHO) as an accumulation of excess fat in the body to the extent that it can impair health [1]. Although excessive food intake and physical inactivity are usually thought of as the cause of obesity, the etiology of obesity is quite complex. There are many factors in the etiology of obesity, such as environmental, genetic, and lifestyle [2]. Besides, the microbiota has recently been reported as an important component in obesity etiology [3–6]. There are various treatment modalities such as medical nutrition therapy, medical treatment, and physical activity enhancement for obesity [2]. Besides these treatments, if the appropriate indications are present, bariatric surgery as a surgical intervention would be another treatment [7]. After the application of bariatric surgery, body weight loss occurs with changes in the metabolism of bile acids (BAs), in gastric pH, in the metabolism of hormones, and in microbiota [8].

OBESITY

Obesity is defined as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired [1]. This is considered a risk factor for a number of chronic diseases including cardiovascular diseases, hypertension, type 2 diabetes, nonalcoholic fatty liver disease, and colon cancer. Over the past 20 to 30 years, the prevalence of obesity has also been increasing rapidly in not only developed countries but also in developing countries. This is related to lifestyle changes, which include decreased physical activity and a Western-type diet with a high energy content [9]. In addition to physiological regulatory mechanisms, numerous complex factors that affect each other, such as environmental and genetic factors and psychological and cultural conditions, are among the causes of obesity [10]. Obesity is one of the most easily diagnosed but difficult to treat diseases. However, it should be treated to prevent various health problems. Obesity management should be planned specifically for each individual [11]. Nowadays, treatment methods for obesity as follows; diet therapy, behavior modification therapy, medical treatment, and surgical treatment [12].

BARIATRIC SURGERY

Bariatric surgery is one of the treatment methods that are effective in the treatment of obesity and complications [13]. Thanks to bariatric surgery, long-term permanent body weight loss is achieved, metabolic effects of obesity are reduced, many diseases are prevented, and quality of life is increased [14]. Body weight loss with bariatric surgery is achieved through reduction of nutrient digestion, alteration of food preferences, acceleration of gastric emptying, regulation of hormonal changes (e.g. glucagon-like peptide 1 [GLP-1] and peptide YY [PYY]) and alterations in the metabolism of BAs. Although bariatric surgery is suitable for obesity treatment, some complications such as gastric outlet obstruction, mesh erosion, slippage, gastroesophageal reflux, nutritional deficiencies, internal herniation, and marginal ulcerations can occur rarely [15]. Indications for bariatric surgery were established by the US National Institutes of Health in 1991 (Table 1) [16]. There are various bariatric surgical methods according to their effect mechanisms (Table 2) [17].

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Table 1. Indications for surgical operation [16]

• BMI=40 kg/m^2 or additional disease (type 2 diabetes, hypertension, sleep apnea, hyperlipidemia) together with BMI >35 kg/m^2
• Acceptance of surgical risk
• Failure of nonsurgical treatments
• Psychiatric stability, no alcohol and drug dependence
• Patients is well-motivated, knowing the operation and sequelae
• No medical problems that will harm the surgeon
• No uncontrolled psychotic and depressive disorder
• Complete family and social support

Table 2. Methods of surgical intervention [17]

Restrictive
Laparoscopic adjustable gastric banding (LAGB) Sleeve gastrektomy (SG) Vertical banded gastroplasty (VBG)
Malabsorptive
Biliopancreatic diversion (BPD) Jejunoileal bypass (JIB)
Combined restrictive and Malabsorptive
Roux-en-Y gastric bypass (RYGB) Duodenal switch (DS) with BPD

BARIATRIC SURGICAL METHODS

Roux-en-Y gastric bypass (RYGB) is the gold standard and the most commonly practiced bariatric surgery in the world [18]. This method consists of two steps. In the first step, the stomach capacity is left to be about 30 cm^3. Roux sputum can then be pulled up from the stomach, the front of the colon and back of the stomach, or behind the colon and stomach for gastrojejunostomy [19]. Intake of food and energy decreases due to the reduction in stomach volume. A small amount of fat malabsorption also occurs [20].

Laparoscopic sleeve gastrectomy (LSG) is the removal of the remaining long, 80% of lateral aspect of the stomach in a vertical fashion, leaving a long, tubuler gastric tube [21]. LSG is preferred for patients who have super obesity and a BMI <50 kg/m^2 [22]. Due to the reduction of gastric volume, nutrient intake and energy intake are restricted. However, there is a reduction in plasma levels of ghrelin [23].

Laparoscopic adjustable gastric banding (LAGB) involves the placement of an adjustable silicone band around the upper part of the stomach, thus forming a small gastric space over the gastric band. The size of the gap between the upper stomach space and the back of the stomach can be adjusted by filling it with sterile saline injected through the abdominal wall. Adjustment of the band can be done gradually over time during postoperative follow-up [24]. This method provides body weight loss by reducing nutrient uptake by a completely restrictive effect [17].

Biliopancreatic diversion (BPD) consists of three main components: a tube stomach with preserved pylorus, distal ileoanal anastomosis, and anastomosis of the proximal duodenal bile duct. Body weight loss is provided by the reduction of gastric volume and decrease of ghrelin hormone, increasing peptide-YY. In this technique, hormonal changes with anatomical changes are thought to lead to body weight loss [25]. Common bariatric surgical procedures are shown in Fig. 1 [19].

Hormones known to generate hunger, and reduce satiation and satiety, adapt to weight loss in a manner encouraging hunger and weight gain. There are sustained reductions in leptin, insulin, and peptide YY while levels of ghrelin and pancreatic polypeptide increase with intentional weight loss. The hormonal changes after the different techniques of the bariatric surgeon are summarized in Table 3 [26]. Surgery induces changes in both environmental and systemic factors, as well as anatomical changes in the digestive tract (Table 4) [27].

GUT MICROBIOTA

The microbiota is defined as a community of microorganisms located in a prominent ecological environment or place. It comprises commensal, symbiotic, and pathogenic microorganisms living in the human body. Microbiome is defined as the genetic pool of microbiota living in a specific place and their relation with the environment [28]. It is estimated that there are about 1,014 microorganisms in the human body, more than seventy percent of which are in the colon, and more than 35,000 bacterial strains in the gastrointestinal tract [29]. The microbiota is influenced by many factors such as delivery type, breastfeeding time, transition time to complementary feeding, diet, and use of antibiotics from birth to death [30]. The intestinal microbiota, composed mainly of anaerobic bacteria in which Bacteroides and Firmicutes are involved, has physiological, metabolic, immunological, and neural functions in the body [31]. It has been reported that the human intestinal microbiota is composed of more than 1,000 species. It can be classified into 6 bacterial clusters in healthy individuals. These include Firmicutes (including gram-positive strains of Clostridium, Eubacterium, Ruminococcus, Butyrivibrio, Anaerostipes, Roseburia, Faecalibacterium, etc.), Bacteroidetes (including gram-negative strains of Bacteroides, Porphyromonas, Prevotella, etc.), Proteobacteria (including gram-negative strains such as Enterobacteriaceae), Actinobacteria (including the gram-positive Bifidobacterium genus), Fusobacteria, and Verrucomicrobia (including Akkermansia, etc.) [32]. Bacteroidetes and Firmicutes constitute more than 90% of total intestinal microbiota. The most important components of the human intestinal microbiota are the obligate anaerobes of the genus Bacteroides, Eubacterium, Clostridium, Ruminococcus, Peptococcus, Peptostreptococcus, Bifidobacterium, and Fusobacterium and facultative anaerobes such as Escherichia, Enterobacter, Enterococcus, Klebsiella, Lactobacillus, and Proteus. Methanogenic archaea have also been reported

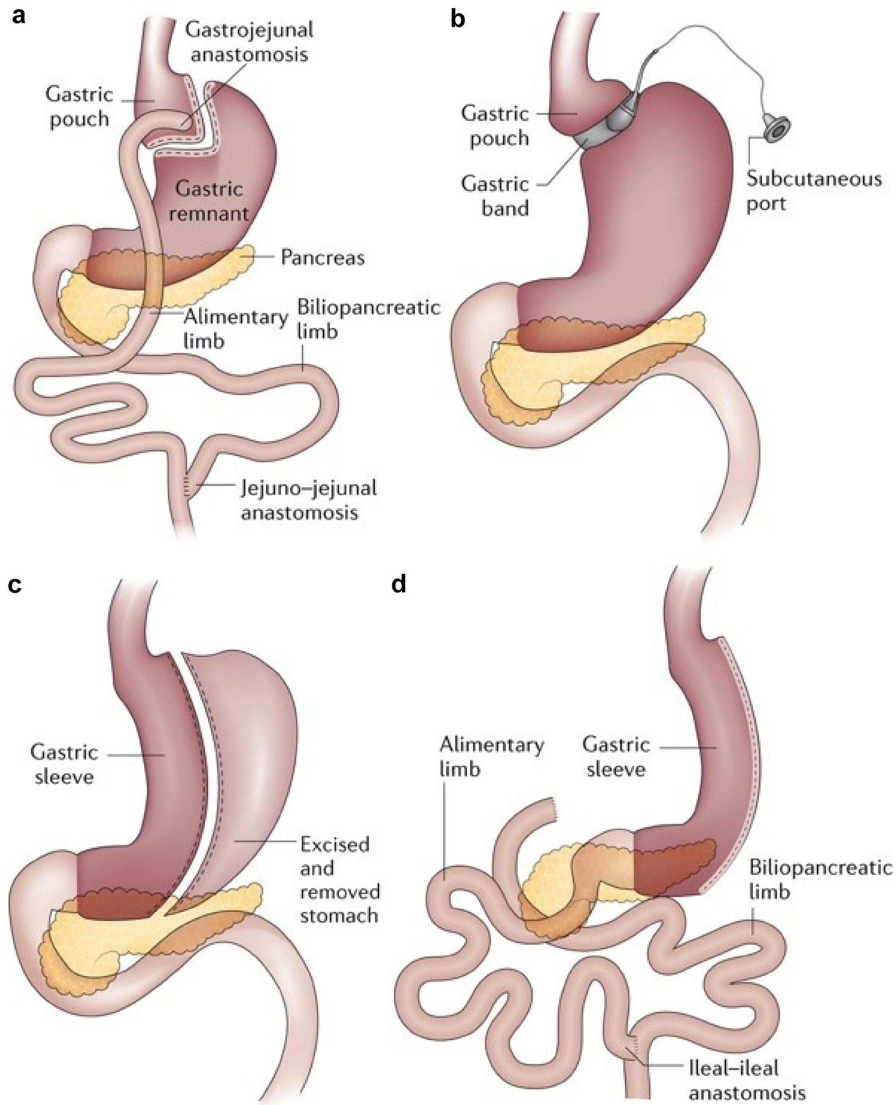

Fig. 1. Common bariatric surgical procedures [19].

a: Roux-en-Y gastric bypass; b: adjustable gastric banding; c: sleeve gastrectomy; d: biliopancreatic diversion with duodenal switch.

Table 3. A summary of the changes in key hormones related to energy balance and weight loss for each of the established surgical procedures and for intentional dietary behavioral weight loss [26]

	RYGB	LSG	LAGB	BPD	Behavioral weight loss
Leptin	▼	▼	▼	▼	▼
Insulin	▼	▼	▼	▼	▼
Adiponectin	▲	▲	▲	▲	▲
Glucagon	▲	?	—	?	▼
Ghrelin	▲, ▼, —	▼	▲, —	▲, —	▲
GLP-1	▲	▲	—	?	—
PYY	▲	▲	?	▲	—

▲: a substantial number of studies indicate an increase; ▼: a substantial number of studies indicate a decrease; —: a substantial number of studies found no change; ?: too few data.

RYGB: Roux-en-Y gastric bypass; LSG: Laparoscopic sleeve gastrectomy; LAGB: Laparoscopic adjustable gastric banding; BPD: Biliopancreatic diversion.

Table 4. Dietary and digestive changes induced by different types of bariatric surgery [27]

Changes	LAGB	LSG	RYGB
Time spent chewing	Increased	Increased	Increased
Food intake	Decreased	Decreased	Decreased
Food transit time	Decreased	No change	Increased
Food choices and preferences	Preference for pureed food and fewer fibre-containing foods	No change	Reduced preference for high-fat or high-sugar foods
Acid production	No change	No change	Disrupted
Ghrelin levels	No change	Decreased	No change
GLP1 and PYY levels	No change	No change	Increased

LAGB: Laparoscopic adjustable gastric banding; LSG: Laparoscopic sleeve gastrectomy; RYGB: Roux-en-Y gastric bypass.

extensively [33]. The most important Methanogenic archaeon in the human gut is Methanobrevibacter smithii.

Changes in microbiota content affect human health at a significant level. It is reported that many noncommunicable diseases such as obesity, type 2 diabetes, asthma, allergies, and atopic diseases, inflammatory bowel disease, metabolic syndrome, necrotizing enterocolitis, and atherosclerosis are closely associated with the intestinal microbiota [34].

GUT MICROBIOTA IN PATIENTS WITH OBESITY

It is reported that genetic and environmental factors influence the etiology of obesity. Researchers have also reported that intestinal microbiosis contributes to the regulation of energy and fat metabolism and that it affects obesity and its complications [35]. It has been reported that patients with obesity have less variability in the intestinal microbiota than thin individuals [36]. The important function that separates microbial strains from obese and thin individuals is the inability to produce fermentation. Another difference is that short-chain fatty acids cannot be produced from indigestable food items [37].

Intestinal microbiota studies in both humans and animal models have helped clarify the role of microbial activity in the etiology of obesity. It is reported that patients with obesity have fewer Bacteroides and more Firmicutes in their microbiota than normal-weight people. It has been stated that diets rich in saturated fatty acids lead to the development of hepatic steatosis and obesity, increasing the amounts of Firmicutes/Bacteroidetes ratio in the intestinal microbiota [38]. Fat and carbohydrate-restricted diets and body weight loss cause the amount of Bacteroidetes to increase [39]. On the other hand, some studies show that there is no relationship between body mass index and Firmicutes/Bacteroidetes [40, 41]. However other studies show an increase in Firmicutes/Bacteroidetes ratio in obesity and insulin resistance. Reduction of carbohydrate intake in patients with obesity decreases the butyrate levels in feces and level of Roseburia spp. and Eubacterium rectale [42]. The microbiota is affected by the loss of body weight caused by diet and exercise. It has been reported that the amounts of Bacteroides and Lactobacillus increase as a result of energy restriction and exercise in patients with obesity. However, no changes were seen in overweight adolescents who lost less than 2 kg in body weight [43]. In view of such information, intestinal microbiota modification may be a potential therapeutic treatment for prevention or reversal of obesity.

GUT MICROBIOTA AFTER BARIATRIC SURGERY

Significant changes are reported in the intestinal microbiota after bariatric surgery. Possible mechanisms for the changes in the intestinal microbiota include food choices and preferences, reduction of food consumption, and nutrient malabsorption [44]. Short-term dietary changes may cause rapid changes in the intestinal microbiota composition. Prevotella enterotypes have been reported to be associated with both complex carbohydrate-rich and simple carbohydrate-rich diets, while the Bacteroides enterotype is associated with a typical “Western diet” rich in animal protein and saturated fat [45]. In particular, low-fat, high-carbohydrate diets and high-carbohydrate, low-glycemic-indexed diets affect the amounts of specific strains differently in the intestinal microbiota [46]. Diet therapy after bariatric surgery also causes changes in microbiota due to these reasons.

A second factor affecting the change in microbiota after bariatric surgery has been reported to be BAs [8]. BAs can autoregulate their synthesis and intestinal reabsorption through modulation of the nuclear-located farnesoid X receptor (FXR). Another pathway of autoregulation is the G-linked protein TGR5, but this pathway is not yet fully understood [47]. Recently, the physiological role of BAs has been linked to the control of glucose homeostasis, beta-cell function, and energy consumption. These roles of BAs are associated with FXR and TGR5 [8]. Biliopancreatic extract biliary fluid and nutrients are separated from each other in RYGB. BAs come together with nutrients in the lower parts of the intestine. The distal jejunum and proximal ileum are excesseively exposed to the nutrients. Dietary lipids are surrounded by the Bas, while BAs cycling in the upper intestine becomes blunted. As a result, increased plasma BAs and FGF15/19 levels normalize the postprandial BAs response after surgery [48]. The mechanism underlying the beneficial effects of bariatric surgery has been reported to be alterations in BAs metabolism [43]. The change in BAs flow has a definite effect on the changes in microbiota after bariatric surgery, too. In the proximal jejunum, the absence of nutrient transit and decreased mobility lead to an increase in the number of bacteria [27]. The changes in BA flow also alter the 7α-dehydroxylation capacity of the intestinal microbiota, which is involved in the synthesis of the secondary (intermediate) BAs. Administration of a diet supplemented with the primary BAs colic acid to rats increase the presence of Firmicutes, which contains the enzyme 7α-hydroxylase such as Clostridium spp. [49].

Hormones such as leptin and ghrelin may change after bariatric surgery. The change in hormones is related to both energy metabolism and microbiota [50]. Although the relationship between the intestinal microbiota and ghrelin is not fully understood, it is reported that prebiotics modulates the intestinal microbiota and prebiotics decrease circulating levels of ghrelin [51].

Serum leptin levels in circulation have been reported to be positively correlated with Mucispirillum, Lactococcus, and the high amount of Lachnospiraceae which cannot be classified. Another study reported that leptin has a negative correlation with Bacteroides, Clostridium, and Prevotella, and a positive correlation with Bifidobacterium and Lactobacillus [52]. Studies have emphasized that further research is needed, although hormones have been reported to affect the intestinal microbiota [38, 53–55].

Another factor affecting microbiota is reported to be changes in pH. After surgery, pH increases as the volume of the stomach shrinks. The changing pH affects every part of the digestive system after the stomach. Increased pH can affect microbiota at a significant level. It has been reported that Bacteroidetes decrease due to pH changes after bariatric surgery, while Firmicutes and Actinobacteria increase [56].

After bariatric surgery, microbiota diversity changes due to the reasons mentioned above. Table 5 summarizes the way in which the numbers of microorganisms are affected after bariatric surgery [8].

CONCLUSION

Bariatric surgery is an important method in the treatment of obesity. It is quite effective in achieving and protecting weight loss. This effectiveness of obesity treatment after bariatric surgery is not only related to food consumption. The altered microbiota after bariatric surgery als have an impact on its effectiveness. Malabsorption status after bariatric surgery, changes in the metabolism of bile acids, changes in gastric pH, and changes in the metabolism of hormones lead to gut microbiota changes. Changes in microbiota also affect energy homeostasis. Because of these reasons, body weight loss is achieved after bariatric surgery.

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Table 5. Taxonomic profile of the gut microbiota after bariatric surgery [8]

Microbial richness	Reported change
Microbial richness	↑ (h)
Firmicutes	↓ (a,h)
Erysipelotrichales (Or)	↓ (a)
Lactobacillales (Or)/Lactobacillus spp.	↓ (a)
Lactobacillus reuteri	↓ (h)
Clostridiales (Or)	↓ (h)
Clostridium difficile	↓ (h)
Clostridium hiranonis	↓ (h)
Blautia spp.	↓ (h)
Dorea spp.	↓ (h)
Streptococcus spp.	↑ (h)
Staphylococcus epidermis	↓ (h)
Roseburia intestinalis	↓ (h)
Eubacterium rectale	↓ (h)
Dialister invisus	↓ (h)
Coprococcus comes	↓ (h)
Anaerostipes caccae	↓ (h)
Gemellasanguinis	↓ (h)
Faecalibacterium prausnitzii	↓ (h)
Veillonella spp.	↑ (h)
Veillonella parvula	↑ (h)
Veillonella dispar	↑ (h)
Bacteroidetes	↓ (h)
Bacteroides/Prevotella spp.	↑ (h)
Alistipes spp.	↑ (a,h)
Actinobacteria	
Bifidobacterium spp.	↓ (h) ↑ (h)
Nakamurella spp.	↓ (h)
Mycobacterium kansaii	↓ (h)
Chloroflexi	
Thermomicrobium roseum	↓ (h)
Fibrobacteres	
Fibrobacter succinogenes	↓ (h)
Verrucomicrobia	
Akkermansia muciniphila	↑ (a,h)
Proteobacteria	↑ (a,h)
Gammaproteobacteria (Cl)	↑ (a,h)
Escherichia coli	↑ (a,h)
Klebsiella pneumoniae	↑(h)
Shigella boydii	↑ (h)
Salmonella enterica	↑ (h)
Enterobacter cancerogenus	↑ (h)
Enterobacter hormaechei	↑ (a)
Citrobacter spp.	↑ (h)
Pseudomonas spp.	↑ (h)
Enterococcus faecalis	↑ (h)
Epsilonproteobacteria (Cl)	
Helicobacter spp.	↓ (h)
Spirochaetes	
Treponema pallidum	↓ (h)
Brachyspira hyodysenteriae	↓ (h)
Fusobacteria	
Fusobacterium nucleatum	↑ (h)
Fusobacterium periodonticum	↓ (h)
Archae (K)	↓ (h) ↑ (a)

a: animal studies; h: human studies.

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