Obesity Surgery (2019) 29:1663–1674
https://doi.org/10.1007/s11695-019-03779-7

REVIEW ARTICLE

Changes in Gut Microbiota and Hormones After Bariatric Surgery: a Bench-to-Bedside Review

Mohsen Tabasi[1,2] · Fatemeh Ashrafian[3] · Jamil Kheirvari Khezerloo[4] · Sahar Eshghjoo[5] · Ava Behrouzi[3] · Seyed Alireza Javadinia[6] · Farid Poursadegh[7] · Sana Eybpoosh[8] · Sara Ahmadi[3] · Amin Radmanesh[2] · Ahmadreza Soroush[9] · Seyed Davar Siadat[3]

Published online: 22 February 2019

Abstract
Overweight and obesity are among the most prevalent non-communicable diseases which are generally treated successfully by bariatric or sleeve surgery. There are evidences affirming that sleeve surgery can manipulate the pH of the stomach and interact with the metabolism of fatty acids, carbohydrates, and bile acid transfer, leading to the overgrowth of gut microbiota. Therefore, this study aims to review the changes in gut microbiota and hormones after bariatric surgery.

Keywords Gastric sleeve surgery · Gut microbiota · Obesity

Introduction

Overweight and obesity are defined by the World Health Organization (WHO) as abnormal or excessive accumulation of body fat tissues with deleterious effects on individuals' health. In the recent decades, obesity has shown a global ascending trend, with complications such as diabetes and an increased risk of cardiovascular diseases (CVD). Currently,

Highlights
1. Gut microbiota community is considered a contributing factor in metabolic disorders such as obesity.
2. *Bacteroidetes* and *Firmicutes* are two important and dominant phyla in the human gastrointestinal tract.
3. After sleeve surgery, the frequency of *Bacteroides*, *Gammaproteobacteria*, *Ruminococcus*, and *Roseovarius* increased.
4. Bariatric surgery can help to prevent weight gain by reducing the size of the stomach.

✉ Seyed Davar Siadat
d.siadat@gmail.com

Mohsen Tabasi
Mohsen68tabasi@gmail.com

Fatemeh Ashrafian
fatemeh.ashrafian24@gmail.com

Jamil Kheirvari Khezerloo
miladkheirvari@yahoo.com

Sahar Eshghjoo
eshghjoo@medicine.tamhsc.edu

Ava Behrouzi
ava.behrouzi@gmail.com

Seyed Alireza Javadinia
Javadiniaa941@mums.ac.ir

Farid Poursadegh
PoursadeghF931@mums.ac.ir

Sana Eybpoosh
sana.eybpoosh@gmail.com

Sara Ahmadi
Sarahmadi@gmail.com

Amin Radmanesh
amin_radmanesh@yahoo.com

Ahmadreza Soroush
soroush1344@gmail.com

Extended author information available on the last page of the article

in addition to genetic factors, the incidence of obesity has shown to be influenced by environmental factors such as gut microbiota composition as well as by various diets.

Gut microbiota is a complex and diverse microbial community that colonizes gastrointestinal tract (GIT). Dysbiosis—an imbalance in the symbiosis of gut microbiota—which resulted from high-fat diet (HFD) could induce obesity through increased intestinal permeability, translocation of lipopolysaccharide (LPS) to circulation, and inflammation [1, 2].

The gut microbiota encompasses the bacteria, archaea, fungi, viruses, and protozoans. The bacteria often belong to the phyla of *Firmicutes*, *Bacteroides*, *Actinobacteria*, and *Proteobacteria* [3]. Although more than a thousand different bacteria are found in the human gastrointestinal tract, only 150 to 170 species are common between different individuals; thus, the microbiota is relatively specific for each individual [4]. Dysbiosis can occur in a variety of ways, including dietary changes, stress, host genetics, treatment with antibiotics, and contamination with pathogenic bacteria [5], and as a consequence of metabolic syndromes (such as obesity, type 2 diabetes, etc.), neurological diseases, allergies, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD) [6–9].

Due to its crucial role in energy homeostasis, the gut microbiota community is considered a contributing factor in metabolic disorders such as obesity. The central energy metabolism pathways in which the microbiota are involved include the elevated energy production medicated by the effect of metabolites like SCFA and the effect on host genomic regions such as those encoding lipoprotein lipase, AMP-activated protein kinase, and endocannabinoid system.

Due to the influential roles of the microbiota in the different metabolic pathways, we aimed to investigate the effects of gut microbiota in the process of obesity and the associated changes following gastric sleeve surgery.

Gastric Sleeve Surgery

Nowadays, bariatric surgery is one of the successful treatments for obesity. These operations include gastric balloon placement, sleeve gastrostomy, Roux-en-Y gastric bypass, vertical banded gastroplasty, duodenal switch, adjustable gastric band, and gastric plication. In general, obesity surgery can help to prevent weight gain by reducing the size of the stomach, lowering the appetite hormones due to the minimizing the size of stomach, and creating an earlier feeling of satiety (Fig. 1) [10].

The sleeve gastrostomy technique is one of the most popular limiting surgical procedures in which approximately 85% of the stomach is removed. This surgery is a safe and effective way to reduce the weight of obese patients who are at greater risk or are reluctant to undergo the weight loss surgery [11]. Effective factors in weight loss in sleeve gastrostomy are food restrictions, malabsorption, gastric emptying, rapid gastric emptying, increased appetite-regulating hormones (PYY, GIP, GLP-1, etc.), decreased hunger hormone (ghrelin), and increased bile acids. Although the size of the stomach is reduced in this type of surgery, its function remains normal. On the other hand, it reduces hunger sensation by decreasing the gastric volume which contains cells producing ghrelin hormone (which provokes hunger and causes starvation) [12].

It has been shown that the fasting ghrelin levels have not been changed significantly following RYGB surgery as an obesity surgery. On the other hand, in laparoscopic sleeve gastrectomy (LSG) surgery, a significant decrease in ghrelin levels was followed by appetite reduction and excessive weight loss. Moreover, YY peptide increased significantly after each of these operations [13]. Although it is now clear that obesity surgery mainly results in weight loss by inhibiting energy absorption and hormonal changes, studies on serum ghrelin levels are still contradictory, and many studies indicate that the level of ghrelin is not altered following the surgery. To further validate these findings, more studies are needed with larger sample size [10, 11].

Several studies have demonstrated that cholecystokinin (CCK) level is increased following the meals in people who undergo RYGB surgery [14, 15]. CCK is secreted by the endocrine I cells in duodenal mucosa. CCK induces secretion of bile acids to GIT lumen through contractions of gallbladder. In addition, certain surgeries such as RYGB which reduces the nutrient contact with most G cells also reduce the secretion of the gastrin hormone [11]. These results have been found in a wide range of individuals from those in the second week of surgery [14] to those at the age of one, after surgery [16]. Gastrin is produced in enteroendocrine G cells, found mainly in the gastric antrum and duodenum, and in response to food and stomach obstruction which thereby reduces the appetite.

The secretion gastric inhibitory polypeptide (GIP) is also stimulated by meals and promotes the production of insulin, the induction of satiety, glucagon enhancement, the conversion of glucose to fatty acid, and the storage in adipose tissue by increasing lipoprotein lipase (LPL) activity [11]. According to the previous studies, this peptide is decreased after surgery [17]; nevertheless, there are opposing observations in this regard [14, 18]. GLP-1, which is secreted from L cells, has been shown to be significantly elevated after surgery [14, 15, 19, 20].

Similar to GLP-1, oxyntomodulin and glicentin are produced from L cells originating from the proglucagon gene. Oxyntomodulin function is resembled to that of glucagon, although its role in obesity has not yet been clearly determined [11]. In a study by Laferrere et al., a significant increase in oxyntomodulin was reported after RYGB surgery [21]. However, one of the most important effects of bariatric surgery is the significant reduction of insulin levels. Insulin is secreted from beta-pancreatic cells, playing the integral role in regulating blood glucose.

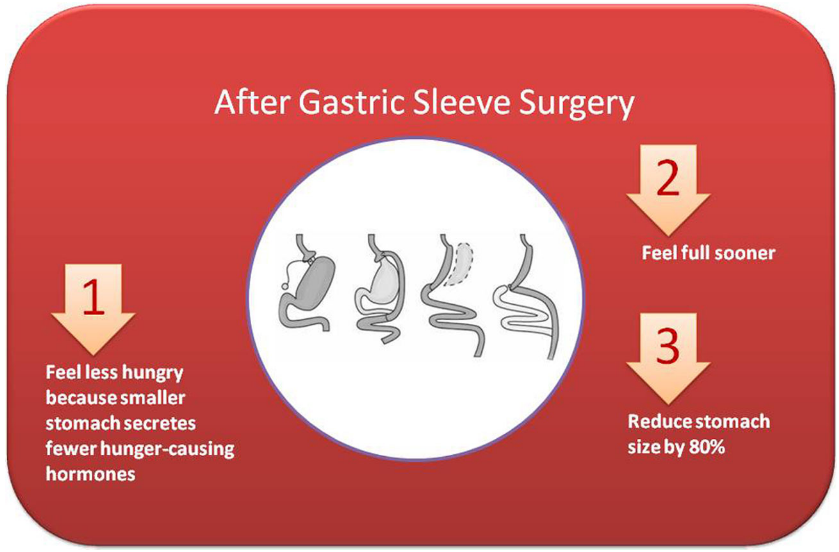

Fig. 1 Different factors affecting weight control in bariatric surgery

Obesity

Major Mechanisms Involved in the Process of Obesity

Obesity is one of the most common disorders in developed and developing societies. Nowadays, due to modern lifestyle and increased energy intake, the prevalence of obesity is in an ascending trend. It was shown that BMI of the British society has increased from 22 in 1985 to 31 in 2015. This can be mainly associated with the indicated factors and lack of mobility [22]. In addition, researchers' findings suggest that obesity is significantly correlated with genetic and environmental factors [23]. The characteristics of several mechanisms involved in obesity are described as follows.

Leptin

The leptin protein is produced by the adipose tissue and released into the bloodstream. It acts as a regulator of energy balance via inhibiting the hunger sensation [24]. Leptin also reduces the production of hypothalamic neuropeptide Y (NPY) and increases the alpha-melanocyte-stimulating hormone which is an appetite suppressor in the hypothalamus. Leptin functions also to increase the secretion of thyrotropin- and gonadotropin-releasing hormones (TRH and GnRH), and thus, increases energy consumption. In addition, during lipogenesis in adipocytes, leptin inhibits this process by reducing the sterol regulatory element–binding protein (SREBP) and thereby the production of fatty acids from a high-carbohydrate diet [25]. Briefly, leptin stimulates the expression of the proopiomelanocortin (POMC) gene, resulting in the production of melanocortin peptide which has various functions in the metabolism involved in obesity. A summary of the leptin mechanism of actions and its association with hypothalamus for weight loss is depicted in Fig. 2.

Neuropeptide Y

In the recent decades, neuropeptide Y (NPY) which has been studied extensively [26] is considered one of the most potent appetite stimulant neurotransmitters which is expressed in the arc of the hypothalamus [26].

Lack of Melanocortin 4 Receptor

It has been reported that a mutation in melanocortin 4 receptor (MC4R) is found in 2–3% of obese children and up to 5% of patients with severe primary obesity. These findings show that the lack of MC4R is one of the most common forms of genetic causes of severe obesity [27].

MRAP2

The MRAP2 is an additive protein for MC2R (MRAP) to transfer the MC2R to the surface of adrenal cells and responding to adrenocorticotropic hormone (ACTH). Researchers have shown that MRAP2 is regulated by MC4R, and obesity is reported in mice lacking MRAP2. However, more studies will be required to determine its precise downstream mechanisms of action [28].

Other Factors

Brain-derived neurotrophic factor (BDNF) is among the very factors in neural growth that activates signaling through tropomyosin tyrosine kinase B receptor–associated kinase B (TrkB) which may serve as the basis for the distal signaling of MC4R. Severe obesity in children has a significant association with mutations in the TrkB gene [29].

Another important factor in obesity is a mutation in single-minded 1 [30]. Studies have shown that SIM1 may affect

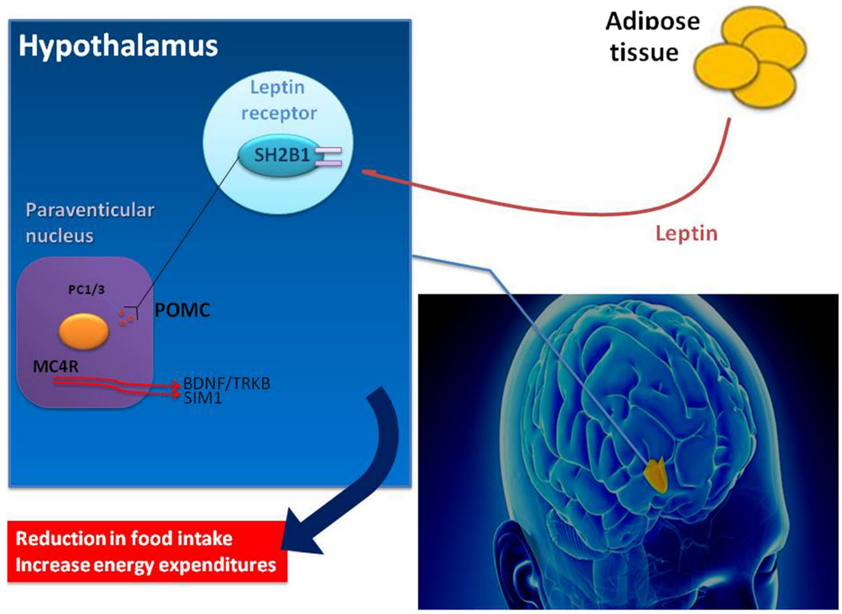

Fig. 2 The association between the hypothalamus and leptin and the associated effect on energy balance in the body

homeostasis by reacting with central melanocortin signaling pathways [31, 32].

Due to the consistency between the energy balance pathways in different species, genetic variations may influence the energy consumption. Multiple mutations in the kinase suppressor of Ras 2 gene (KSR2), a molecular scaffold protein implicated in the Ras-Raf-MEK signaling pathway (effective in cell division, differentiation, and growth), have been reported. It is indicated that the basal metabolic rate (BMR) is much lower than expected in people who have a mutation in the KSR2 [33]. BMR is also highly effective in controlling energy expenditure and phenotypic conditions [22, 27].

Gut Microbiota and Obesity

Gut Microbiota

Microbiota is an ecological community of commensal, symbiotic, and pathogenic microorganisms [34] which is also referred to as "microbial organs" [35]. More than 100 trillion, equal to more than 2 kg of microbial cells, reside in the human body contributing to the metabolic regulation of the host cells [36]. The intestinal flora has the highest number of bacteria and the highest number of species compared to other parts of the body [37]. Most of the bacteria belong to the genus of *Bacteroides*, *Clostridium*, *Faecalibacterium*, *Eubacterium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus*, and *Bifidobacterium* [38]. The collected data from the studies have identified 2172 isolates in human species which divided into 12 different phyla, of which 93.5% were *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, *Proteobacteria* [39, 40], *Bacteroidetes*, and *Firmicutes*, the dominant phyla in the human gastrointestinal tract [41]. The families of *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobiaceae* also constitute the other important members of gut microbiota [42].

The Effects of Gut Microbiota on Obesity

It has been demonstrated that the gut microbiota composition has significant differences between obese and lean subjects, with a higher ratio of *Firmicutes* to *Bacteroidetes* (F/B ratio) [41, 43]. Gut microbiota of obese people has a lower bacterial diversity compared to that in the lean individuals [44]. The ratio of *Bifidobacterium* to Clostridium was higher in women with normal weight than in obese women indicating the negative role of Clostridium in obesity. Many studies have reported that the frequency of important intestinal commensal bacteria such as *Faecalibacterium prausnitzii*, *Bacteroides*, *Akkermansia muciniphila*, and *Prevotella* is lower in obese people compared to normal-weight subjects [43]. In addition, gut microbiota is associated with insulin resistance. Cardiovascular and metabolic disorders are other complications associated with the changes in gut microbiota [45].

In a cross-sectional study on 74,946 children aged five to eight years, it was indicated that antibiotic consumption only increased the BMI in boys and showed a constant rate in girls [46]. In Denmark, a study on 28,354 children showed that antibiotic consumption before 6 months of age was associated with an increased risk of overweight [47]. Another study on 11,532 subjects reported that the children who have been consuming antibiotics less than 6 months of age are likely to be overweight at 38 months of age. However, this increase was not significant at the age of seven [48].

Long-term use of specific diets affects the gut microbiota composition [49–51]. However, scientists have discovered that the diet, even in the short term, changes the microbiota [52]. Still, short-term diets are not able to treat obesity or malnutrition [53]. The major impacts and mechanisms of changes in microbiota on accelerating obesity are described in Fig. 3. The proposed mechanisms are as follows.

Energy Harvest from Diet

The first mechanism involved in inducing obesity mediated by gut microbiota is the accumulation of energy from the bacterial metabolites. The fermentation of non-digestible fibers by the gut microbiota produces short-chain fatty acids (SCFAs). SCFAs are regulators of the levels of hormones involved in glucose and energy homeostasis [54]. SCFAs consist of propionate, butyrate, and acetate, stimulating de novo synthesis, liver triglyceride, and adipogenesis in adipose tissue, and acts as a signaling molecule by regulating signaling of immune and inflammation pathways. SCFAs stimulate the secretion of hormones such as insulin, amylin, glucagon-like peptide (GLP-1), and peptide YY (PYY) [55] that induce satiety and increase the plasma insulin. Acetate also plays a role in increasing the production of leptin hormone [56].

Polysaccharides and food proteins that escaped from the digestive process of the small intestine reach the colon and are fermented to the SCFAs by gut microbiota. The level of energy consumption is based on the gut microbiota composition and modulated through intertwined pathways [57].

It is estimated that up to 10% of the daily calories needed for the body and up to 70% of the cellular respiratory energy for the epithelial colon is provided from the SCFAs [58].

Gut Microbiota May Lead to Maintenance of Epithelium Integrity

One of the mechanisms that causes obesity is the effects of gut microbiota on the integrity of intestinal epithelium. Gut microbiota can play an important role in the development of intestinal epithelium. Increasing the density of the small intestine villi and their effect on physiology and intestinal movements increases the absorption of calories from consuming meals.

Gut Microbiota and Fasting-Induced Adipocyte Factor

Another regulatory route involved in the induction of obesity by microbiota is the effect of gut microbiota on the function of host genes such as fasting-induced adipose factor (FIAF). FIAF is secreted from the liver, intestine, and fat tissue, and acts as a lipoprotein lipase (LPL) antagonist [59]. Changes in gut microbiota composition decrease the FIAF expression and increase the LPL activity. When the increase in LPL activity occurs, the breakdown of serum triglyceride (TG) into free fatty acids accelerates which eventually increases the fat storage, and thus, augments obesity [60–62]. The fact that inhibition of FIAF by gut microbiota increases LPL may be a possible mechanism for the development of obesity caused by gut microbiota [54].

The Effect of Gut Microbiota on the Toning of eCB System

The other system whose function is affected by microbiota is the endocannabinoid system (eCB), which is responsible for

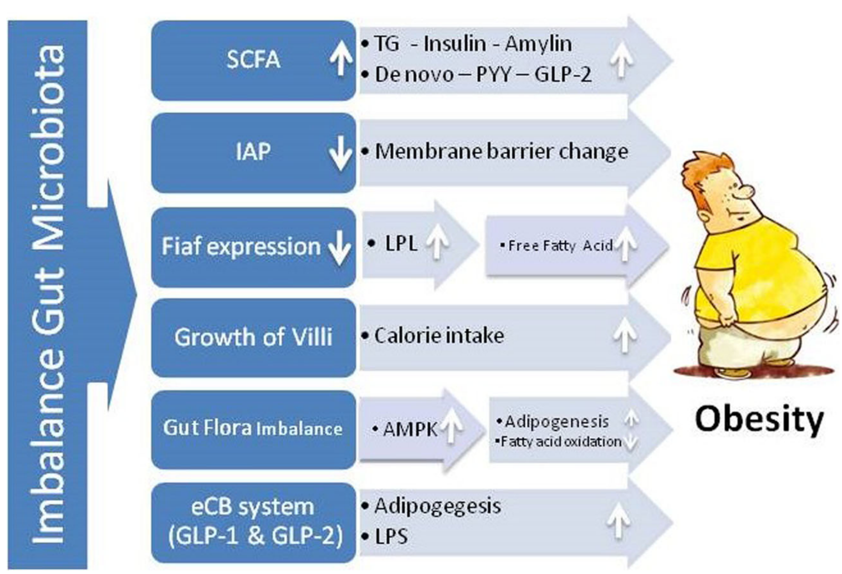

Fig. 3 Major mechanisms due to the microbiota changes causing obesity

Table 1 Literature review of the association of obesity surgery and microbiota changes on body metabolisms in animal specimens

First authors	Year	General subject	The population study	Numbers	Microbiota changes	Subsequent metabolic changes
Jahansouz C (Jahansouz et al., 2017)	2017	Sustainable changes in the microbiota after obesity surgery	Diet-induced obese mice	30	Abundance of family members of *Lachnospiraceae*, *Erysipelotrichaceae*, *Ruminococcaceae*, *Coriobacteriaceae*, and *Bifidobacteriaceae* was positively correlated with sample weight. Abundance of family members of *Porphyromonadaceae*, *Enterobacteriaceae*, and *Enterococcaceae* was negatively correlated with sample weight.	Decrease in insulin sensitivity Weight loss
Kim T (Kim et al., 2017)	2017	Microbiota changes in ZDF mice after duodenal endoluminal sleeve (DES)	ZDF rats after duodenal endoluminal sleeve (DES)	Not defined	Increased level of *Bacteroidetes* and *Verrucomicrobia*	Treating the metabolic defects, such as hyperphagia, obesity, dyslipidemia, and hyperglycemia
Jia V. Li (Li et al., 2011)	2011	Investigating the effect of obesity surgery on metabolic gut microbiota	Rats under RYGB surgery	30	Increased levels of *Proteobacteria* (especially *Enterobacter hormaechei*) Reduced levels of *Firmicutes* and *Bacteroidetes*	- Decrease in TCA cycle performance Changes in amino metabolites (increased level of putrescine and diaminoethane in the stool) - Changes in muscle metabolism - Changes in kidney metabolism - Change in the level of amino acids
Alice P. Liou (Liou et al., 2013)	2013	The study of changes in the gut microbiota due to gastric bypass	Obese male C57BL /6J mice after gastric bypass surgery	32	Increase in the abundance of the Verrucomicrobia (genus: *Akkermansia*) and Gammaproteobacteria (order: Enterobacteriales)	- Increase in fatty acid metabolism, such as glyoxylate and decarboxylate Reduced ratio of SCFA to BCFA in stool Decrease in acetate in cecum
Basso N (Basso et al., 2016)	2016	The effects of obesity surgery in	Male rat	60	Change in the pattern of gut microbiota The abundance of *Ruminococcus* decreased, and the incidence of *Lactobacillus* and *Collinsella* increased	Improvement in metabolic activity and type 2 diabetes Causes weight loss Reduces fat accumulation and liver glycogen Reduced levels of ghrelin and increased plasma GLP1 concentrations

Table 2 Literature review of the association between obesity surgery and microbiota changes on body metabolisms in human specimens

First authors	Year	General subject	The population study	Number	Changes in microbiota	Subsequent metabolic changes
Tremaroli V (Tremaroli et al., 2015)	2015	Microbiome changes in patients undergoing RYGB and VBG surgery and the associated effect on lipid regulation	Women under RYGB or VBG surgery	14	Increased class of *Gammaproteobacteria* Reducing the members of the *Firmicutes* (*Clostridium difficile*, *Clostridium hiranonis*, and *Gemella sanguinis*)	Effect on bile acid and TMAO* metabolism Increase in phosphoglycerate carriers, increased SCFA metabolism, tension in the outer membrane Increased salt stress, increased sulfur metabolism, increased motor stimulation, and increased cellular mobility Increased glutathione metabolism/glutathione synthesis from glutamate Increased phosphotransferase activity and increased transfer of monosaccharides such as xylose, rhamnose, allose, and arabinose
Palleja A (Palleja et al., 2016)	2016	A study of gut microbiota constant changes after RYGB surgery	Obese patients after RYGB surgery	33	Increase in diversity of microbiota changes in *Escherichia coli*, *Klebsiella pneumoniae*, *Veillonella* spp., *Streptococcus* spp., *Alistipes* spp., and *Akkermansia muciniphila* Decrease in *Faecalibacterium*	Increased glutathione metabolism/glutathione synthesis from glutamate Increased nitrogen metabolism, phenylalanine transfer, and ABC carriers Decreased tyrosine Increased urinary p-cresol derivatives Increased phosphotransferase activity Increased transfer of monosaccharides, such as xylose, rhamnose, allose, and arabinose
J Graessler (Graessler et al., 2013)	2013	The study of the microbiota changes before and after RYGB obesity surgery	Patients undergoing RYGB surgery with BMI > 40 and type 2 diabetes	6	Increase in *Proteobacterium*, *Enterobacter cancerogenus*, and *Shigella boydii* Reduction of *Firmicutes* (*Faecalibacterium prausnitzii* and *Coprococcus*) Decrease in the strains of *Nakamurella* and *Mycobacterium kansasii*	Increased consumption of bacterial carbohydrates
Damms-Machado A (Damms-Machado et al., 2015)	2015	The study of the effects of diet or surgery on microbiota compositions and drug absorption	People who have had a laparoscopic sleeve gastrectomy (LSG)	5	Change in the ratio of *Bacteroidetes* to *Firmicutes*	Decrease in the potential of microbiota energy absorption
Kong L-C (Kong et al., 2013)	2013	Examination of gut microbiota changes before and after Roux-en-Y surgery	Obese individual	30	37% increase in the gut microbiota abundance associated with gamma apoptosis (*Escherichia coli*) Reduction of *Actinobacteria* such as *Bifidobacterium*	Increased association between the expression of WAT genes and gut microbiota after surgery
Furet J-P (Furet et al., 2010)	2010	The study of compliance of gut microbiota after obesity surgery	Obese people with type 2 diabetes	43	Increased ratio of *Bacteroides* to *Prevotella* Decrease in *Bifidobacterium*	
Ishida RK (Ishida et al., 2007)	2007	Stomach microflora after obesity surgery	Patients undergoing RYGB surgery with obesity	37	Aerobic bacteria, anaerobic bacteria, fungi, and parasites were present before and after surgery Respiratory testing was positive in 40% of cases	Increased pH in stomach Clinical signs, such as diarrhea and malabsorption, have not been observed
Mallipedhi A (Mallipedhi et al., 2015)	2015	Correlation between fasting and nutritional status 6 months after obesity surgery	People with type 2 diabetes underwent for obesity surgery	24	–	Improved insulin sensitivity and the response of the incretin hormone
Youssef A (Youssef et al., 2014)	2014	Investigating the effects of sleeve surgery on appetite, acyl ghrelin, PYY3-36, and active GLP1 in non-diabetic obese people	Obese people undergoing LRYGBP surgery at age 46	10	–	Decreased concentration of acyl ghrelin, GLP1, leptin, lipid volume, and weight Increased PYY3-36

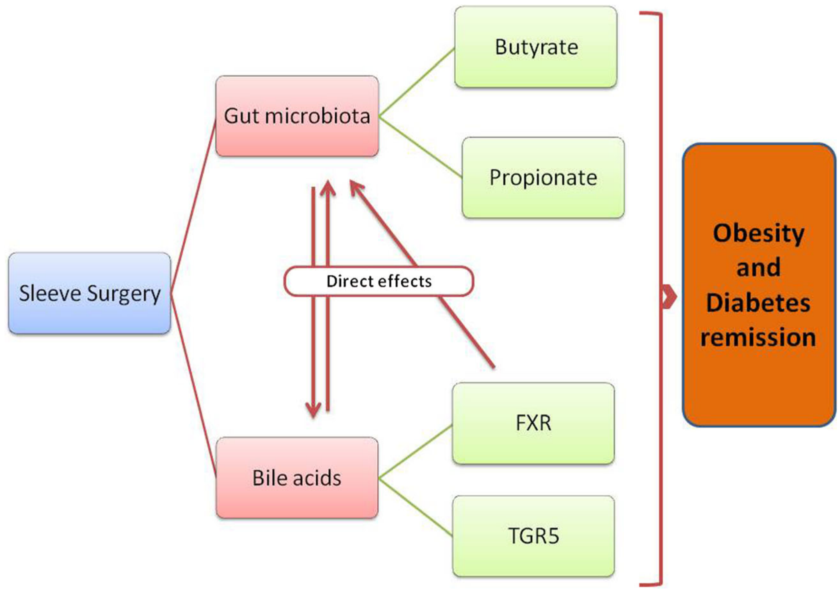

Fig. 4 Major effects of obesity surgery for controlling weight gain and diabetes

the reduction of the metabolic endotoxemia and inflammation. Also, the eCB system stimulates the production of peptides involved in controlling glucose homeostasis and GIT function. These peptides include GLP 1 and 2 and are produced and secreted from the intestinal L cells. The eCB system also induces adipogenesis either directly or through increasing the lipoplasty (LPS) which ultimately leads to obesity [63].

The Effect of Gut Microbiota on Intestinal Alkaline Phosphatase Enzyme

Intestinal alkaline phosphatase (IAP) is involved in breaking down the food lipids and plays an important role in the detoxification of LPS through the dephosphorylation of its lipid A moiety. The expression of this enzyme is controlled by the gut microbiota. In obese people, changes of gut microbiota composition results in a decrease in IAP activity and causes changes in cell membrane functions [64].

Gut Epithelium and Inflammation in Obesity

The permeability of gut epithelium is regulated through the expression and distribution of tight junction proteins. It has been known that the permeability of gut barrier increases during obesity due to the changes in gut microbiota composition. This eventually leads to the accelerated translocation of LPS

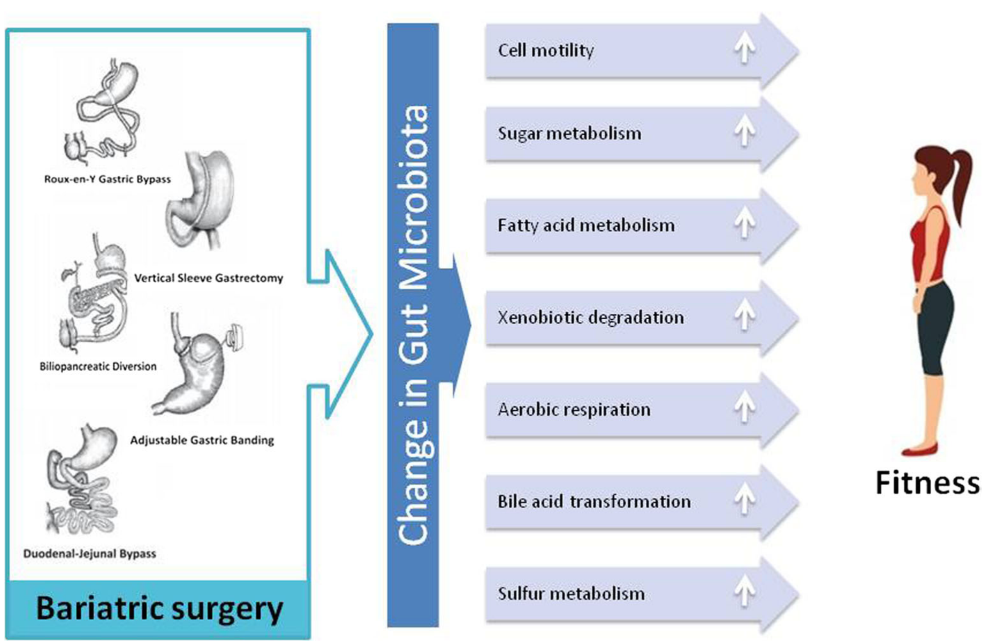

Fig. 5 The overall effects of obesity surgery on microbiota and body metabolism, leading to weight loss and fitness

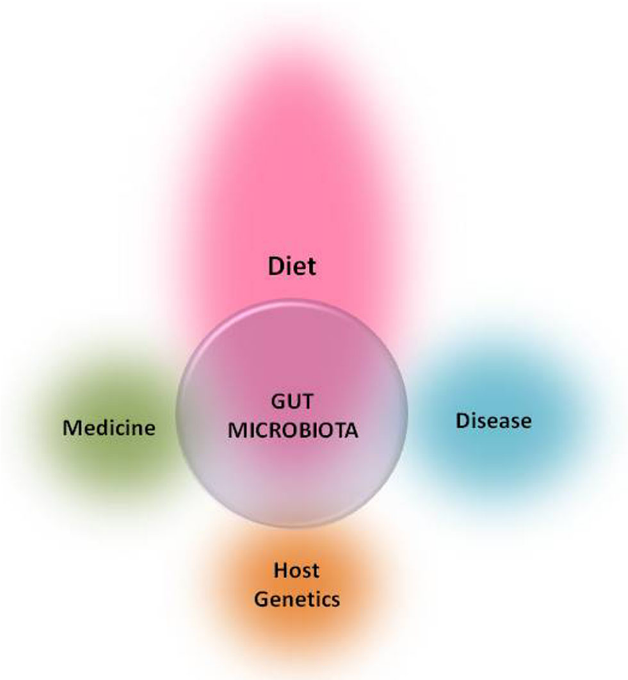

Fig. 6 General factors affecting gut microbiota

into circulation which causes metabolic endotoxemia and thereby induces a low-grade inflammation [65].

Low-Grade Inflammation Is the Turning Point of Obesity and Metabolic Syndrome

Fat, muscle, and pancreatic tissues are associated with inflammation during obesity and diabetes which leads to infiltration of immune cells into these tissues and causes the production of pre-inflammatory cytokines (IL1β, IL6, and TNFα), a serum amyloid protein (SAA), acute phase protein (CRP), and chemokines [66]. As a result, the balance between the cells producing inflammatory and anti-inflammatory cytokines is disturbed in obesity. On the other hand, due to the increased size of adipocytes in obesity, the cytokine production, chemokine, hypoxia, and even cell death are increased [67].

The Influence of Surgery on Microbiota and Obesity

All changes resulting from sleeve surgery cause a deregulation in the microbiota pattern of the human and animal intestinal tract. Studies have shown that the transmission of gut microbiota from obese mice to germ-free mice is associated with weight loss. Also, gut microbiota transmission from RYGB-administered mice to germ-free mice, which has been shown to decrease the weight, highlights the important role of the gut microbiota in weight balance. After sleeve surgery, the frequency of *Bacteroides*, *Gammaproteobacteria*, *Ruminococcus*, and *Roseovarius* is increased which leads to changes in the gut microbiota pattern [68–70].

Several mechanisms associated with bariatric surgery and gut microbiota changes in animal and human studies are presented in Tables 1 and 2, respectively. *Firmicutes* increases in obese subjects; however, this phylum is decreased after bariatric surgery.

It was also reported that following obesity surgery, the secretion of bile acid (BA) increases in the intestine and circulatory system through affecting various organs such as the hypothalamus. It has a direct and indirect role in this regard from controlling food intake and energy consumption to the controlling of blood glucose, which are depicted in Fig. 2. In addition to the involvement in fat absorption, bile acid can be identified as the FXR ligand which regulates the transcription of bile acids, glucose metabolism, lipids, and energy, and can also regulate the GLP1 by activating another regulator called TGR5 [71]. This evidence suggests that through FXR signaling, BA affects both directly and indirectly the abundance and gut microbiota compositions. In contrast, gut microbiota may alter the BA concentration through microbial enzymes. These changes ultimately alter the hemostasis of the BA and FXR signaling [72]. The major effects of obesity surgery on suppressing weight gain and controlling diabetes are described in Fig. 4.

The molecular mechanisms underlying the correlation of gut microbiota with energy metabolism are assumed to be the lipid accumulation and host immunity. However, the mechanisms connecting the differences between the gut microbiota compositions, the incidence of obesity, and metabolic diseases are still unknown [36].

So far, very few human studies have addressed the gut microbiota changes after sleeve gastrostomy and the probable role of gut microbiota on the outcome of obesity surgery and post-surgical weight loss before surgery. If such an association and the identification of bacterial strains affecting the outcome of obesity surgery were determined, it might lead to promising probiotic strategies. As outlined in Tables 1 and 2, a broad range of mechanisms has been reported on the effects of obesity surgery on microbiota changes and body metabolism. Most of these mechanisms are illustrated in Fig. 5.

Conclusion

In summary, after bariatric surgery, the microbial abundance is increased in GIT [73, 74], and the elevation of *Firmicutes* is largely associated with extensive changes [44, 70, 75]. In addition, following the surgery, the pH of the stomach increases [76] which can be beneficial for the growth of some bacteria while fatal for others [77]. This is one of the main factors affecting microbiota, as well as the results of the obesity surgery.

An obesity surgery affects the metabolism of fatty acids, carbohydrates, bile acid transfer, and several other metabolisms through gut microbiota, leading to weight loss. Taken together, gut microbiota is affected by the various factors described in Fig. 6, among which the most important factor is diet.

Acknowledgments This article is part of the work by Mohsen Tabasi to fulfill the requirement for a PhD degree. We extend our heartfelt gratitude to all who have worked hard to make this project a success.

Funding This work was financially supported by the Pasteur Institute of Iran (grant no.TP-9567).

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Statement This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Statement Informed consent was obtained from all individual participants included in the study.

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Affiliations

Mohsen Tabasi[1,2] • Fatemeh Ashrafian[3] • Jamil Kheirvari Khezerloo[4] • Sahar Eshghjoo[5] • Ava Behrouzi[3] • Seyed Alireza Javadinia[6] • Farid Poursadegh[7] • Sana Eybpoosh[8] • Sara Ahmadi[3] • Amin Radmanesh[2] • Ahmadreza Soroush[9] • Seyed Davar Siadat[3]

[1] Department of Molecular Biology, Pasteur Institute of Iran, Pasteur Ave., Tehran 13164, Iran

[2] Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran

[3] Department of Mycobacteriology and Pulmonary Research, Microbiology Research Center, Pasteur Institute of Iran, Tehran, Iran

[4] Young Researchers and Elite Club, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran

[5] Microbial Pathogenesis and Immunology Department, Texas A&M University, Bryan, TX, USA

[6] Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Islamic Republic of Iran

[7] Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Islamic Republic of Iran

[8] Department of Epidemiology and Biostatistics, Research Centre for Emerging and Reemerging Infectious Diseases, Pasteur Institute of Iran, Tehran, Iran

[9] Obesity and Eating Habits Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran