

# The effects of bariatric surgery procedures on the gut microbiota, features of genetically mediated predisposition to obesity, forecasting algorithms for surgical treatment outcomes. Literature review

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Obesity is one of the major challenges facing modern medicine in the 21st century. Medically complicated obesity cases lead to a significant deterioration in quality of life and are associated with excess morbidity and increased mortality. According to the WHO, more than 24% of the world's population over 18 years of age is overweight. About 3.9 million people of working age died in 2018 due to obesity and its complications. Today, bariatric surgery is the most effective in treating obesity, as it allows achieving optimal metabolic outcomes. After bariatric surgery, the desired effect can be produced by the response of the intestinal microbiome to postoperative anatomical and physiological changes in the gastrointestinal tract.

**THE AIM** of this study was to conduct a comprehensive literature review and evaluate the effects of bariatric surgery on the human intestinal microbiome.

The literature review revealed a stable correlation between quantitative and qualitative characteristics of the intestinal microbiota and bariatric surgery, regardless of the type of a bariatric surgical operation. Roux-en-Y Gastric Bypass, Mini-Gastric Bypass and Sleeve Gastrectomy are the most commonly used bariatric operations in the world. The outcomes of these procedures show a sharp change in the proportion of different microbial phyla, including *Firmicutes*, *Bacterioides* and *Escherichia*, as well as changes in the gene expression parameters of these groups at different time periods after surgery.

An increasing number of the reported bariatric interventions worldwide necessitates the study of pathophysiological mechanisms of intermicrobial relationships, which can contribute to better outcomes of surgical treatment of obesity and the development of algorithms for predicting them.

## **KEYWORDS**

obesity, obese patients, Roux-en-Y gastric bypass, research, body mass index, gut microbiome, weight loss.

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In the 21st century, the global spread of obesity became pandemic. Obesity takes one of the highest positions in the rankings of causes of death from complications and factors associated with deterioration in the quality of life. It is one of the most challenging and urgent issues in world medicine.

According to the World Health Organization (WHO), obesity is defined as the excessive accumulation of adipose tissue in the human body, which results in weight gain and the development of chronic diseases that significantly impair quality

of life. Obesity is recognized as a risk factor in the development of diseases such as hypertension, atherosclerosis, type 2 diabetes, non-alcoholic liver disease, colorectal cancer, hypercoagulation [56].

Obesity is one of the most challenging public health issues in Ukraine. According to the research conducted in 2012, 53% of Ukrainians were overweight, out of which about 20% were diagnosed with obesity, and their number is constantly increasing. According to the data presented by the WHO in 2016, 58.4% of people over 18 years

were overweight and 25% of adults were obese. In Ukraine, 48.9% of the adult population were overweight in 1990 [56].

The continuously increasing number of obese people worldwide is strong evidence of its global spread which is associated with malnutrition and hypodynamics, constant psychological stress, neurological and endocrine disorders. In the highly developed industrial countries, including the United States, the United Kingdom, European countries, China, etc., there has been reported an increase in the prevalence of obesity both among adults and among children [39].

Obesity is an extremely mild disease to diagnose and one of the most difficult to treat. The condition is most commonly managed by diet therapy, lifestyle modifications, drug therapy and bariatric surgery, which is a leader among the methods of radical treatment of obesity.

Bariatric surgery is recognized by the world medical community as the most effective in treating obesity due to its low comorbidity rates and an ability to improve the quality of life. The effects of bariatric surgery on weight loss and comorbidity rates depend, among other factors, greatly on the intestinal microbiome, which is an important system, even an organ that plays a leading role in the regulation of lipid and glucose metabolism [13].

Nowadays, the most frequently performed surgical interventions in the world are Roux-en-Y Gastric Bypass, and Sleeve Gastrectomy. RYGB combines two powerful mechanisms of weight loss that are defined as restrictive and malabsorptive. The procedure includes the creation of a small (30–50 ml) gastric «pouch», which ensures the exclusion of the larger part of the stomach from the digestive process, and the formation of the Roux-en-Y anastomosis, which makes it impossible to pass food through the distal stomach, duodenum and proximal jejunum, and at the same time, doesn't block the entry of bile and pancreatic juices into the intestinal tract distal to an entero-entero anastomosis, thus ensuring a full digestive process. Sleeve Gastrectomy is an example of an isolated restrictive effect [4, 11]. A powerful metabolic effect is achieved due to the resection of the stomach along with the compulsory removal of its fundus and the formation of «sleeves» with a volume of 100–150 ml. The surgery reduces the amount of food stored and digested in the stomach by dozens of times as well as decreases the «satiety threshold» afferent impulses in response to stomach fullness. After surgery, weight loss is also achieved due to the total reduction in the synthesis of ghrelin, a hormone that induces hunger, resulting from the removal of the gastric fundus, which is the

main location of APUD-system cells that synthesize this hormone [9].

There are 3 types of surgical treatment for obesity. The restrictive surgical procedures include Laparoscopic Gastric Banding and Sleeve Gastrectomy. The malabsorptive surgical procedures are known as biliopancreatic diversion and jejunioileal bypass, but they are not used today in view of their low efficacy and severe complications. The combined type of surgical treatment, which is most often used due to its potent metabolic effect, comprises Roux-en-Y Gastric Bypass and biliopancreatic bypass [47].

Due to postoperative anatomical changes and some surgical peculiarities of the operated areas, there are numerous functional changes within the gastrointestinal tract: a hypertrophy of the villi of the small intestinal mucosa in response to malabsorption; nodular lymphoid hyperplasia of the small intestine in response to low amounts of chyme and hydrochloric acid and an increase in the amount of infectious agents in the intestinal lumen; an increased reactivity of APUD-system due to lack of mechanostimulation and chemostimulation in the gastrointestinal tract; a hypertrophy of muscle fibers in the intestinal wall, as a reaction to insufficient mechanical processing of chyme in the stomach and changes in the intestinal microbiota, which is one of the least studied issues [12].

A microbiota is a «community» of microorganisms that live, reproduce, and function in a particular environment. Among the whole set of microbes that function in the human body, it is common to distinguish commensals, symbiotes and pathogens. Another concept related to the classification of microorganisms that colonize the human body is the microbiome. A microbiome is a pool of genetic material of microorganisms that live in a specific environment and function in conjunction with the biological, physical and chemical laws of this «area» [15].

It is known that the human body is colonized by about 1.4 billion microbial organisms, of which about 90% colonize the gastrointestinal tract. More than 35,000 bacterial families are classified in the colon, among which the most common are *Firmicutes* (including gram-positive species *Clostridium*, *Eubacterium*, *Ruminococcus*, *Butyrivibrio*, *Anaerostipes*, *Roseburia*, *Faecalibacterium*, etc.), *Bacteroides* (including gram-negative species *Bacteroides*, *Porphyromonas*, *Prevotella*, etc.), *Proteobacteria* (including gram-negative *Enterobacteriaceae*), *Actinobacteria* (with gram-positive *Bifidobacterium*), *Fusobacteria*, and *Verrucomicrobia* (including *Akkermansia*, etc.). These families, groups and species represent more than 90% of the total colon microbiome. The most important, in terms of the proper functioning of the

colon, microorganisms are obligate anaerobes from the *Bacteroides*, *Eubacterium*, *Clostridium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus*, *Bifidobacterium* species, and *Fusobacterium*, and facultative anaerobes such as *Escherichia*, *Enterobacter*, *Enterococcus*, *Klebsiella*, *Lactobacillus* and *Proteus* [1, 18].

Presently, some fundamental theses on the functioning of the intestinal microbiome are known. One of the most important discoveries in this field of science is the so-called microbial genome (MG), which, similarly to DNA molecules in the nuclei of human cells and fingerprints, is unique to each person [31]. The microbial genome is the totality of all genetic material synthesized in the nuclei of all microbial cells present in the human gastrointestinal tract. It is able to affect the synthesis of enzymes and proteins that are directly and indirectly involved in the metabolism of trace elements, nutrients and their derivatives that are absorbed or partially metabolized in the intestinal lumen. According to «Iuliu Hatieganu» University of Medicine and Pharmacy, Cluj-Napoca, Romania, the number of substances encoded by genes of microbial origin, which regulate (directly or indirectly) the process of intra-intestinal metabolism in the human body, is 6–9 % of the total number [37].

Adults have the intestinal microbiome as one of the most variable organs of the human body, so it shows a very high rate of changes in microbial homeostasis and intercolonial relationships in response to changes in external or internal state of the «host organism». One of the most powerful triggers for such changes is a change in a diet. Changes in the microbiome occur 4 days after the start of the diet, regardless of its aim – a decrease or increase in body weight [11].

Some genetic and environmental factors may alter the etiopathogenesis of obesity. The scientists have also concluded that the intestinal microbiome has a significant effect on energy metabolism, fat and carbohydrate metabolism, which affects the processes leading to obesity and its consequences. The researchers report that obese people have less variability in intestinal microorganisms than patients with normal body mass index (BMI), as well as the inability of microorganisms that colonize the large intestine to produce enzymes that metabolize fats and fatty acids [32].

In any environment, there are some differences in body weight among individuals. These variations are partly the result of genetic factors. The idea that obesity may have a genetic component is not new, given that it has long been known that obesity is often a familial pathology [12, 19]. In fact, some studies have shown that children's BMI strongly

correlates with parental obesity. The children whose both parents are obese have a higher risk of the development of obesity compared to the children with parents who do not suffer from this pathology. However, it is difficult to distinguish in family studies whether this correlation is the result of genetic predisposition or environmental factors. In part, this issue could be addressed by studying twin or foster children by providing evidence of genetic influence on BMI. A meta-analysis of 31 twin studies showed that for adults, the variation in BMI due to genetic differences ranges from 47 % to 80 % [44]. More recent study by Silventoinen et al. [30] presented analysis of 87,782 pairs of twins and their parents and concluded that genetic factors play an important role in increasing BMI. According to these data, studies of adopted children have shown no reliable link between their body weight and obesity of their parents. These studies have shown that the BMI of adopted children is strongly correlated with biological parents, and less with foster parents [20].

It is known that genes contribute to differences in body weight within a single population. Interestingly, some genes identified as causing obesity in rodent models [2] have also been determined as contributing to severe obesity in humans. Non-syndromic monogenic forms of obesity are the result of mutations in one gene and affect ~5 % of the population. These mutations in loss of function are rare and usually cause differences in eating behavior and parameters of energy homeostasis. The major parts of these mutations have been identified in the genes LEP (leptin synthesis), leptin receptor (LEPR), melanocortin-4 receptor (MC4R) and pro-opiomelanocortin (POMC). And a recent study has discovered a deletion of the POMC gene with a 12 % allele frequency in Labrador Retrievers, which affects their body weight and food behavior, showing the importance of genetically mediated changes in leptin/melanocortin parameters for the obesity phenotype [16].

In turn, polygenic obesity is the most common form of obesity in modern society, where the environment contributes to weight gain due to the availability of large amounts of food and lack of physical activity. With the development of technology and the completion of the Human Genome Project, our knowledge of the genetic basis of obesity has increased significantly in recent years. Several studies have identified more than 100 loci in the human genome associated with BMI when comparing groups of people with normal weight and obesity. The first locus that is undoubtedly associated with obesity by approach of the World Gene Association (GWA), was a gene associated with mass and obesity (FTO).

Subsequent GWA studies and meta-analyses have identified a number of options associated with widespread obesity. The latest GWAS meta-analysis have identified 97 BMI-associated loci (56 of which were new) in a study of 339,224 European adults, representing 2.7 % of BMI variation [19].

It is known that obese patients have quantitative changes in the families of colon microbes, namely, a decrease in the number of *Bacteroides* and an increase in members of the *Firmicutes* family. The scientists have noted that a diet rich in fatty acids leads to the development of fatty liver disease, visceral obesity, and an increase in the number of *Bacteroides* against the background of declining *Firmicutes* population among intestinal microbiomes. Some studies, refuting all previous claims, show that there is no relationship between weight gain and the volume of *Bacteroides* and *Firmicutes* [8].

Some investigations suggest that the microbiota, as a large organ and a huge cluster of genetic material, plays a significant role in the development of metabolic syndrome and obesity. However, there is limited evidence of the behavior of the intestinal microbiome in the case of BMI  $\geq 30$ , as the vast majority of microbiome studies have been performed with people who have a BMI  $\leq 30$  [26].

A study conducted by a team of scientists, including endocrinologists, nutritionists, gastroenterologists at the University of Malaga, Spain [44] examined fecal samples from 28 obese patients who underwent surgery using RYGB and SGE techniques. Patients received only surgical treatment using these techniques, and therefore they were divided into two groups: 1a – patients after RYGB; 2a – patients after SGE. All patients were examined 3 weeks before surgery and 3 months after surgery. The results were contradictory. There was a significant difference in the characteristics of bacterial colonies of the intestine after the use of two different methods of surgical treatment of obesity. The researchers concluded that despite the extremely short postoperative period, the intestinal microbiome changed significantly in both groups of patients, so the adaptive capacity of the intestinal flora was extremely high, and that was caused not by weight loss but by dynamic replacement of some clusters of microbes by others. Changes in intra-intestinal pH in response to surgery indicate the likely impact of surgical treatment of obesity on the microbiome [10, 41].

In 2018, J. Aron-Wisniewski et al. from the Institute of Microbiology and Nutrition filled some gaps in the knowledge of the intestinal microbiome. In the course of their research, they found that different behaviour patterns of intestinal microorganisms,

namely gene expression of proteins involved in lipid metabolism, principles of colony formation, growth rate and death of opportunistic pathogens and «beneficial» flora, are dependent on the «microbial gene richness» (MGR). This gene significantly correlates with the incidence of cardiovascular and metabolic diseases in obese patients [3].

The study, based at the Pitié-Salpêtrière Hospital Obesity Unit in Paris, involved 61 women with a BMI  $\geq 35$  kg/m<sup>2</sup> who were offered bariatric intervention, namely RYGB. On dividing into two cohorts, including women with and without MGR, and in the absence of episodes of antibiotics within 3 months before the study, and anamnestic data on acute gastrointestinal diseases, patients were examined for many parameters, namely: anthropometric data, clinical and biochemical blood profiles, a lipid profile, a glucose tolerance test, as well as DNA sequencing of fecal samples for the formation of quantitative indicators of microbial colonization of the intestine, and determination of serum MGR. These indicators were studied during several visits: one week before RYGB, 1, 3 and 12 months after the intervention. The results showed that 75 % of observed and operated women with BMI  $\geq 35$  kg/m<sup>2</sup> had a high level of MGR in serum one week before RYGB. One year after bariatric obesity correction, MGR levels decreased in most patients, and lipid and glucose profiles showed significant improvement, pointing at a direct effect of bariatric surgery on the evolution of intestinal microflora in response to malabsorption [23].

A series of studies of the intestinal microbiome of laboratory mice were conducted at Iuliu Hatieganu, University of Medicine and Pharmacy, Cluj-Napoca, Romania. The researchers formed two cohorts: mice, which from birth to the time of the study had no external effects on their own microbiome, and were raised in conditions as close as possible to natural. And the 2nd group of mice, grown in the most comfortable conditions for weight gain, but a week before the experiments they were transplanted feces from mice of the first group. As a result, it was found that mice from the 1st cohort showed an increase in body weight by 42 %, despite the lack of food, and mice in cohort N 2 gained about 60 % of the initial weight. Analyzing these data, we can assume that in cases of adaptation to stressful conditions, the intestinal microbiome influences body weight more than a diet itself [58].

In the course of this study, it was found that in sterile raised mice, a deficiency of 4 nutrients, namely vitamin A, iron, folic acid and zinc, provokes the breakdown of groups of microorganisms characteristic of humans. For example, a lack of vitamin A in

the diet leads to the growth of colonies of *Bacteroides vulgatus*, a deficiency of vitamin B<sub>12</sub> encourages the growth of *Faecalibacterium prausnitzii* and *Roseburia*, resulting in a decrease in the number of *Escherichia coli*. There has also been a reduction in the colonies of *Firmicutes* and *Bacteroidetes* in response to reduced production of antioxidant nutrients (vitamins C and E), and at the same time the formed «gap» in the microbial ecosystem has been filled with *Shigellae* and *Salmonellae* microbes [54]. This study was confirmed by E. O. Verger and J. Aron-Wisniewsky, who analyzed the results of micronutrient deficiency in patients 1 year after RYGB [11, 54], and by D. Ciobârcă et al., who also analyzed changes in the intestinal microbiome in terms of deficiency of micronutrients during the postoperative period after bariatric surgery [13].

The simultaneous study conducted at Iuliu Hatieganu, University of Medicine and Pharmacy, Cluj-Napoca, Romania evaluated the effects of bariatric surgery on the intestinal microbiome. Analysis of the long-term effects of RYGB and gastric resection on the microbiota consisted of fecal mass transplantation both from operated human patients 9 years after surgery and from obese people to non-obese laboratory mice. Two weeks after transplantation, laboratory mice-recipients of feces of operated patients gained  $46 \pm 7.3\%$  less weight than mice-recipients of feces from obese people, under exactly the same living conditions and diets [20].

M. Osto et al. at the University of Veterinary Physiology in Zurich studied the effects of bariatric treatments for obesity, namely RYGB, on the intestinal microbiome of rats. The RYGB method was chosen because of its effectiveness in weight loss, reduction of hyperglycemia, and changes in postprandial hormonal reactions [40, 57].

Analysis of the intestinal microbiota from fecal samples taken from rats and humans after RYGB shows a decrease in colonies of microorganisms from the groups *Firmicutes* and *Bacteroidetes*, which, according to the scientists from the Institute of Veterinary Physiology, plays a significant role in postoperative weight loss and changes in metaprandial and postprandial fats [7].

For the study, there were selected 16 male rats, acclimatized in the conditions of individual living at a temperature of  $21 \pm 2$  °C, with an unlimited amount of food and water during a week. Out of 16 individuals, two groups were randomly selected. The first group underwent RYGB surgery and the second group underwent laparotomy with gastrostomy and gastrojejunostomy (control group). A group of 8 rats underwent a classic RYGB with the formation of biliopancreatic and alimentary

loops and a common canal about 25–32 cm long. A similar approach was applied in the control group, which had gastrostomy and gastrojejunostomy performed. In both groups, the survival rate after surgery was 93.7% (15 out of 16 patients underwent surgery) [7, 9].

The operations resulted in a significant weight reduction in the rats, which underwent RYGB, compared with the control group. The study demonstrated that the volume of bacterial colonies in the alimentary and biopancreatic loops in RYGB-transferred rats was significantly higher than the volume of bacteria in the small intestine of control rats. For groups of microbial organisms, there was an increase in the *Bifidobacterium* and *Lactobacterium* groups, and a decrease in the *Firmicutes* and *Bacteroidetes* groups. The scientists believe that the exclusion of the proximal segment of the small intestine from the digestive process has a major impact on the microbiocenot, which is most likely a decisive factor causing changes in the intestinal microbial system as humoral agents are produced in the proximal small intestine. Additionally, these changes are independent of changes in body weight. The experiments did not reveal a plausible relationship between quantitative or qualitative changes in the microbiota and changes in body weight. Therefore, the conclusion is obvious – changes in the intestinal microbiome do not seem to occur due to weight change, but due to cessation or change in the regulation of postprandial humoral agents [49]. A similar study was conducted by Y. Shao et al., who proved identical changes in the microbiome in response to changes in the anatomy of the gastrointestinal tract of rats [22].

An experiment involving laboratory rats was performed at the Department of Medical Microbiology, Utrecht University Medical Center, Utrecht University, and Surgery Department, Catharina Hospital Eindhoven. Fourteen rats that had previously been kept on a specific diet to provoke morbid obesity (an increase in body weight by an average of  $44.4 \pm 6.2\%$ ) were involved and examined to determine the microbiological patterns of colonization of their colon. From the 14 rats, 9 were selected, which were operated by RYGB and Sleeve Gastrectomy (6 and 3, respectively), the others represented the control group. Out of 9 operated rats, 3 died from postoperative complications, and six others showed a steady decrease in body weight by an average of  $36.0 \pm 2.7\%$ , without correlation with surgery type. Five unoperated rats included in the control group underwent fecal microbiota transplantation, which resulted in an average weight loss of  $25.7 \pm 2.3\%$ . To sum it up, the effectiveness of surgical treatment of

morbid obesity significantly depends on the microbiological component [48]. The analogical experiment conducted by Y. Kang et al. showed similar results [29].

In 2018, at the Department of Public Health, the University of Auckland in New Zealand, there was found a close correlation between changes in the gut microbiome after RYGB and SG and type II diabetes regression, which was confirmed in the R. Murphy et al. study [17]. The method of research was DNA typing of fragments of the microbial genome obtained from fecal samples. The study involved 14 patients of different sex and age suffering from morbid obesity and type II diabetes. Patients were randomly divided into two groups of 7 patients in each. 1 year after surgery, 100 % regression of hyperglycemia was achieved (HbA1c within  $4.8 \pm 1.1$  %) without drug compensation in both groups [32]. The DNA study of microbial genome fragments in fecal samples resulted in a sharp increase in *Firmicutes* and *Actinobacteria* genetic material and a decrease in *Bacteroidetes* from RYGB patients, and a decrease in *Bacteroidetes*-specific genetic fragments of patients after gastric tube resection. Patients in both groups (namely 12 out of 14) showed an increase in the presence of *Roseburia* genome in the fecal samples. Conclusion: patients who underwent RYGB showed more significant functional and quantitative changes in the intestinal microbiome than patients after sleeve gastrectomy [49].

A study at the Hvidovre Clinic in Denmark highlights the metabolic effects of surgery and their impact on the microbiome of patients who participated in the experiment. The study included 13 people (5 men and 8 women), who were selected according to the following criteria: age over 20 years; BMI  $\geq 40$  kg/m<sup>2</sup>, or BMI  $\geq 35$  kg/m<sup>2</sup> and comorbid conditions in the preoperative period, such as type II diabetes mellitus and/or hypertension; method of surgical treatment — RYGB. Patients were examined in two directions — metabolic parameters, studied by pre- and postoperative blood serum, and fecal microbiome, namely its quantitative and qualitative changes, and all patients followed a specially designed, individual diet during 3 months, which provoked weight loss by an average of 8%. Thus, from the 13 patients in the experiment, seven had type 2 diabetes mellitus, one had impaired glucose tolerance, and five had normal pre- and postprandial serum glucose levels, respectively. Biomaterial collection for fecal microbiome was performed three times — 3 months before surgery, the day before surgery and one year after surgery [21].

Microbial DNA was extracted from 200 mg of each portion of frozen faeces using the Illumina

HiSeq 2000 apparatus. On average, 77 % of the genetic material was organized into the genetic catalog of each patient with subsequent interpretation and grouping according to the Kyoto Encyclopedia of Genes and Genome. It allowed grouping the genetic patterns of microbial families of fecal microbiocenosis quantitatively and qualitatively and determining the biological reality of the experiment [19].

As a result, there was a 100 % change in the qualitative and quantitative pattern of the microbiome. 10 patients did not have statistically significant changes in the microbiome after a course of diet therapy, and three patients had an increase in *Lactobacilli*, *Actinomyces* and *Escherichia coli*, respectively. In contrast, in all samples taken 1 year after surgical treatment of obesity, there were statistically significant ( $p \geq 0.05$ ) changes in the microbiome, most noticeable in the *Actinomyces*, *Proteobacteria*, *Klebsiella pneumoniae*, and *Enterococcus faecalis* groups. Considering the outcomes of surgical treatment in terms of changes in metabolic parameters, 5 patients had a positive effect in the form of a decrease in plasma glucose by an average of  $1.4 \pm 0.4$  mmol/L and 8 patients had no significant metabolic effect after surgery. Summing up the results of the described experiment, it can be concluded that obese patients (BMI  $\geq 40$  kg/m<sup>2</sup>) with comorbid conditions had quantitative and qualitative changes in the intestinal microbiome during the postoperative period after RYGB, and statistically significantly ( $p \geq 0.05$ ) improved tolerance to glucose during postoperative period [3, 51].

Various authors describe changes in the intestinal microbiome, especially after restrictive bariatric surgery. The study, which involved 110 operated patients who underwent gastric sleeve resection, showed a significant increase in total microbial quantity and genetic representation of the microbial flora of the colon within 3 months after SG, which lasted from 1 to 2 years. In contrast, R. Murphy et al. [16] did not find any significant changes in the intestinal microbiota of 13 patients within 3 months after SG, but observed an increase in the number of colonies of *Roseburia intestinalis* associated with glycemic reduction for all 13 patients [17].

The scientists at the Department of Medical Microbiology, Utrecht University Medical Center, Utrecht University, and I. Ulker and H. Yildiran, Faculty of Food Hygiene, Ankara, Turkey, studied the change in microbiome of patients after surgical treatment of obesity. In the postoperative period, 2 major factors influencing the variability of intestinal microbiome patterns were identified: changes in food behavior and malabsorption. The researchers also identified several microbiological

patterns, so-called enterotypes, that can be observed depending on the diet followed by patients after bariatric surgery. For example, an enterotype with a prevalence in the microbial population of the *Prevotella* family is formed when a person follows a diet rich in carbohydrates. The enterotype, where *Bacterioides* predominate, is more usual for the so-called Western diet, which is rich in animal proteins and fats [53].

The Department of Upper GI Surgery, Beaumont Hospital, Ireland was the first to create a model that allows, by selecting several criteria, determining the optimal method of surgical treatment of obesity. In other words, the decision-making model is a mathematical, programmable process aimed at choosing the most effective, in terms of metabolic effect, as well as the most beneficial treatment strategy [34].

Researchers Y.- C. Lee and W. L. Wu searched for a decision-making model for bariatric treatment of obesity. They analyzed the outcomes of 3 types of surgery, including RYGB, SG (sleeve gastrectomy) and OAGB (one-anastomosis gastric bypass/mini-gastric bypass), in terms of the number and severity of complications, objective clinical and metabolic improvements and a change in the patient's quality of life [57].

The simulated analysis of the decisions made was carried out after the creation of special software TreeAge Pro Software 2019, which reproduced a virtual «reference patient», based on a five-year analysis of 9757 operated patients. The reference patient is a mathematically calculated virtual human model, objective and clinical data of which is a statistical sample of all analyzed patients, and this patient was a woman with a BMI—40.1 kg/m<sup>2</sup>, aged 40 years, with concomitant type 2 diabetes. The international scale QALY (quality adjusted life years) was also developed, which is based on 2 main criteria — the lifespan and the quality of life. One point on the QALY scale is one year of an ideal life.

The findings showed that RYGB received an average of 3.47 points on the QALY scale, OAGB — 3.65 points and SG — 3.80 points over a 5-year period. In terms of metabolic effect and the number and severity of complications, the leader among all interventions was RYGB, after which the metabolic and clinical effect was 86 % (22.0—88.5 %), OAGB — 71.8 % (60.0—95.7 %) and SG with a result of 75.3 % (52.0—86.4 %).

Based on the statistical calculations of the analyzed parameters, the researchers found that the highest efficiency in terms of the probability of achieving metabolic effect and quality of life in the postoperative period was RYGB (probability — 80.0 % (69.0—89.9 %)), which was slightly inferior

to OAGB (probability — 75.9 % (69.0—93.0 %)) and SG (probability — 72.2 % (55.0—95.5 %)). However, the decision-making strategy modeled on the TreeAge Pro Software 2019 platform showed that OAGB, which was statistically significantly different from RYGB, should be the method of choice in the treatment of a «reference» patient [6].

## Conclusions

Obesity, as a global pandemic, requires both a comprehensive approach to treatment and modern solutions. Bariatric surgery plays a crucial role in the treatment of obesity and the elimination of its comorbidities. This review of the literature shows that bariatric surgery and the elimination of metabolic disorders are closely related to changes in the intestinal microbiome. However, it is not clear yet whether these changes in the intestinal microbiome lead to an improvement in the patient's metabolic status, and whether the microbiome in the postoperative period corresponds to the average concept of «healthy microbiome». Discovering the exact correlations between changes in the microbiome after bariatric surgery is a complex and long-term process and opens new strategic directions for the treatment of obesity and its associated conditions, as well as predicts the effectiveness of the chosen surgical treatment.

## DECLARATION OF INTERESTS

The author declares no conflicts of interest.

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## Вплив бариатричних методик лікування ожиріння та його коморбідних процесів на стан кишкової мікробіоти, особливості генетично-опосередкованої схильності до ожиріння, прогнозування результатів хірургічного лікування. Огляд літератури

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У XXI ст. ожиріння є однією з найбільших проблем сучасної медицини, оскільки це захворювання і його ускладнення призводять до значного погіршення якості життя людини та є чинником ризику розвитку багатьох патологічних процесів і смерті. За даними ВООЗ, понад 24 % населення світу віком понад 18 років мають надлишкову масу тіла. Близько 3,9 млн осіб працездатного віку померли в 2018 р. унаслідок ожиріння та його ускладнень. Нині золотим стандартом лікування хворих на ожиріння є бариатрична хірургія, яка має доведену ефективність (оптимальний метаболічний ефект). Один із механізмів, що дають змогу досягти бажаної мети після бариатричних операцій, — реакція кишкового мікробіому на зміну анатомії та багатьох фізіологічних процесів шлунково-кишкового тракту.

Проведено аналіз світових літературних джерел для визначення зв'язку між бариатричною хірургією та змінами в кишковому мікробіомі людини. Виявлено стійкий зв'язок з кількісними та якісними характеристиками кишкової мікробіоти незалежно від різновиду бариатричної операції. Результати операцій, які найчастіше виконують у світі (Roux-en-Y Gastric bypass, mini-gastric bypass, рукавна резекція шлунка), демонструють різку зміну співвідношення мікробних кластерів, переважно *Firmicutes*, *Bacteroides* та *Escherichia*, а також параметрів експресії генів зазначених груп мікроорганізмів у різні періоди після операції.

З огляду на збільшення кількості бариатричних втручань у світі актуальним є вивчення патофізіологічних механізмів взаємозв'язків між мікроорганізмами для поліпшення результатів хірургічного лікування ожиріння та розробки методики їх прогнозування.

**Ключові слова:** ожиріння, пацієнти з ожирінням, шлункове шунтування по методиці Roux-en-Y, дослідження, індекс маси тіла, кишковий мікробіом, зниження ваги.

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