ORIGINAL ARTICLE

CONTENTS

# Gut microbiota as an efficacy marker of surgical treatment of obesity

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## ABSTRACT

**Aim:** To study the impact of bariatric interventions on changes in the parameters of the intestinal microbiome.

**Materials and Methods:** The research method is a prospective observational cohort monocentric study. 112 patients were included in the study. All patients had indications for surgical obesity treatment due to IFSO criteria. All patients were offered surgical treatment. 53 patients who consented to the operation formed the study group. 59 patients who refused surgical treatment formed the control group. The result of the study was evaluated one year after the start of treatment. The studied group of patients underwent bariatric interventions. The control group consisted of 59 obese patients who were treated conservatively.

**Results:** evaluating criteria was: %EWL (percentage of excess weight loss), comorbidity regression, life quality improvement. Overwhelming majority of surgically treated patients with gut microbiome composition improvement reached %EWL≥50. Patients who didn't have improvements in gut microbiota composition had insufficient efficacy of surgical treatment.

**Conclusions:** 1) Surgical treatment of obesity leads to the positive changes in the gut microbiota.

2) Operated patients, who had positive dynamics in changes of gut microbiota demonstrated sufficient efficacy of surgical treatment due to %EWL.

3) Firmicutes/Bacteriodetes ratio and Bacterioidetes/Faecalibacterium ratio can be one of the criteria of the efficacy of surgical treatment of obesity.

4) Patients of the control group, had positive dynamics of changes in gut microbiota much rarely than operated patients and the effectiveness of obesity treatment was insufficient.

**KEY WORDS:** treatment, gut microbiota, surgical treatment, obesity, %EWL

Wiad Lek. 2024;77(7):1464-1469. doi: 10.36740/WLek202407122 DOI

## INTRODUCTION

The set of microorganisms that colonize the gastrointestinal tract - the intestinal microbiota - its pattern, the ratio of different families of microorganisms is one of the influencing factors in the metabolism of fats and carbohydrates in the intestinal lumen, the degree of their absorption into the bloodstream, and as a result - the development of metabolic syndrome and obesity. According to the literature, the human body is colonized by about 38 trillion microbial organisms, of which about 90% colonize the gastrointestinal tract [1]. More than 35,000 bacterial families have been classified in the colon, among which *Firmicutes* (which includes Gram-positive species), *Bacteroides* (which includes Gram-negative species), *Proteobacteria*, *Actinobacteria*, *Fusobacteria*, and *Verrucomicrobia* are the most common. The indicated families, groups and species represent approximately 90% of the entire microbiome of the large intestine. The most widespread representatives of the microbiota are obligate anaerobes from the species *Bacteroides, Eubacterium, Clostridium, Ruminococcus, Peptococcus, Peptostreptococcus, Bifidobacterium,* and *Fusobacterium* and facultative anaerobes such as *Escherichia, Enterobacter, Enterococcus, Klebsiella, Lactobacillus*, and *Proteus* [2]. *Firmicutes*/*Bacteriodetes* ratio and *Bacterioidetes*/*Faecalibacterium* ratio are indicators that represent the ratio of the predominant number of microorganisms that are present in the colon. It was established that these ratios are an indicator of the physiological status of the intestinal microbiome, and change in response to changes in eating behavior and the occurrence of methabolic disorders and obesity in the studied individuals. However, the relationship between the changes in the intestinal microbiota and the surgical treatment of obesity and its effectiveness is still being studied, so the analyzis of the changes in the intestinal microbiome after bariatric surgery is extremely relevant [3].

Bariatric surgery is increasingly used in most countries of the world as an effective and safe method of obesity

treatment. According to the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) 8th Global registry report, in 2023, 480,970 bariatric operations were performed in the world. The most common metabolic interventions are sleeve gastrectomy - 290,505 operations (60.4%), Roux-en-Y gastric bypass - 141,886 operations (29.5%), mini gastric bypass - 20,681 operations (4.3%) and other surgeries in the amount of 27,896 (5.8%) such as Single anastomosis duodenoileal bypass (SADI), biliopancreatic diversion, gastric banding and endoscopic installation of an intragastric balloon. Among these operations, 93.47% were performed initially, and 4.11% were provided as revision interventions. Bariatric interventions are performed more in obese women: 82.2% of all interventions than in men - 17.8% [4].

In some scientific publications, changes in the intestinal microbiota were evaluated depending on the body weight of the subjects, and changes in the intestinal microbiota after bariatric interventions [5], but the effectiveness of surgical treatment of obesity depending on the changes in the intestinal microbiota in response to the performed bariatric intervention has not yet been investigated. Therefore, the aim of the study was to study the effectiveness of surgical treatment of obesity due to changes in the intestinal microbiota.

## AIM

The purpose of the study was to study the impact of bariatric interventions on changes in the parameters of the intestinal microbiota.

## MATERIALS AND METHODS

The research method is a prospective observational cohort monocentric study, which was conducted on the basis of the Department of General Surgery No. 2 of the O.O. Bogomolets National Medical University.

112 patients were included in the study (clinical characteristics of the patients are presented in Table 1). All patients had indications for surgical treatment due to IFSO criteria, namely BMI ≥ 35 kg/m2 regardless of the presence and severity of comorbid diseases, patients with BMI 30-34.99 kg/m2 and existing comorbid conditions [6]. All patients included in the study were offered surgical treatment. 53 patients who consented to the bariatric procedure were included in the study group. 59 patients who refused surgical treatment and underwent conservative treatment formed the control group. The result of the study was evaluated one year after the start of treatment. The studied group of patients underwent the following bariatric interventions: laparoscopic gastric bypass – 20 patients (37.7%), laparoscopic sleeve gastrectomy – 17 patients (32.2%), and 16 patients (30.1%) with superobesity (BMI≥50 kg\m$^2$) who underwent two-stage surgical treatment [7]: the installation of an intragastric balloon for a period of 6 months as the first stage of the two-stage treatment, followed by gastric bypass within 14 days after the removal of the balloon and the assessment of the final result 12 months after the start of the two-stage treatment [8]. The control group consisted of 59 obese patients who were treated conservatively: individual diet prescription, psychological support sessions, lifestyle correction, and dosed physical activity.

In both groups, at the beginning of the treatment and 12 months after the treatment, the following studies were performed - anthropometric examinations, routine general clinical examinations and stool analysis by the PCR method to determine the quantitative and qualitative indicators of the intestinal microbiome.

The following criteria were used to assess the effectiveness of treatment.

%EWL – percentage of excess body weight loss. The American Society for Metabolic and Bariatric Surgery considers a %EWL (Excess Weight Loss) of at least 50% in the 12-month postoperative period as an indicator of effective surgical treatment of obesity [9].

Positive changes (positive changes are taken to be the return of the specified microbial ratios to the reference values) of the intestinal microbiota [10]. The main studied parameters of changes in the intestinal microbiota are *Firmicutes*/*Bacteriodetes* ratio and *Bacterioidetes*/*Faecalibacterium* ratio - the ratio of the predominant number of representatives of the families of microorganisms that colonize the intestinal mucosa. Average European normal indicators of the indicated colonies are 1-5 for *Firmicutes*/*Bacteriodetes* ratio and 0.01-100 for *Bacterioidetes*/*Faecalibacterium* [11, 12].

Regression of comorbid conditions was considered a return to the reference values of indicators of carbohydrate metabolism (blood glucose level, glycosylated hemoglobin), fat metabolism (LDL, LDL), blood pressure indicators and cardiac function parameters [13].

## RESULTS

The average BMI of patients in the study group before surgery was 48.6 ± 20.1 kg/m2, among patients in the control group the average BMI before treatment was 41.6 ± 16.0 kg/m2. After the treatment, the average BMI of the studied BMI decreased to the level of 29.5 ± 5.4 kg/m2, in patients of the control group it was 40.2 ± 13.8 kg/m2 (Table 2).

In the patients of the study group, the average %EWL after 12 months of observation was 59.21% ± 23%. The

**Table 1.** Clinical characteristics of obese patients included in the study

| | All patients included in the study, n=112 | Study group, n=53 | Control group, n=59 | p* |
|---|---|---|---|---|
| Age, years | 48,2±9,2 (27 - 68) | 47,7±9,1 (23 - 68) | 48,9±9,5 (29 - 67) | 0,286** |
| Body mass, kg | 144,8±15,7 (110,14 – 210,22) | 148,03±18,38 (110,14 - 210,22) | 141,8±12,2 (117,2-172,2) | 0,085** |
| Height, sm | 165,62 ± 12,6 (150 – 188) | 165,27±11,7 (152 - 188) | 165,91±13,3 (150 -185) | 0,818 |
| Initial BMI, kg/m$^2$ | 45,1±6,1 (35,2 - 75,3) | 48,6±7,4 (35,2 - 75,3) | 41,6±3,1 (35,5 - 50,5) | 0,256** |
| Ideal body mass, kg | 62,2±7,2 (51,5 – 74,5) | 62,6±7,1 (52,8 – 73,3) | 61,2±6,8 (51,1 – 74,5) | 0,362** |
| Excess weight, kg | 100,2 ± 19,0 (65,9 - 144,6) | 101,5 ± 22,3 (70,5 - 144,6) | 99,8 ± 18,5 (62,3 - 132,7) | 0,321** |

* - comparison of data in the studied and control groups

** - in one or both groups, the distribution of data was different from normal, the analysis was performed using the Wilcoxon T-criteria.

**Table 2.** BMI dynamics in patients of both groups depending on the type of treatment

| Type of treatment | BMI, kg/m$^2$ | | p* |
|---|---|---|---|
| | Before treatment | After treatment | |
| Gastric bypass | 47,8 ± 10,1 (35,2 – 75,3) | 28,5±6,2 (26,2 – 30,1) | <0,001 |
| Sleeve gastrectomy | 42,2±7,4 (35,4 – 48,6) | 30,1±5,5 (29,2 – 31,0) | <0,001 |
| Intragastric balloon+gastric bypass** | 52,2±6,4 (50,1 – 54,4) | 28,3±6,0 (26,1 – 30,5) | <0,001 |
| Average in study group | 48,6 ± 20,1 (35,2 – 75,3) | 29,5 ± 5,4 (26,1 – 31,0) | <0,001 |
| Conservative tratment | 43,6 ± 16,2 (35,5 – 50,5) | 40,2 ± 13,8 (33,4 – 47,0) | 0,06 |

*comparison was made between patients of the study and control groups;

**intragastric baloon+gastric bypass – installation of an intragastric balloon as the first stage of treatment of superobese patients and performing gastric bypass 6 months after the start of treatment [7].

highest rate of %EWL of patients in the study group was 77.2%, the lowest was 49.9%. In patients of the control group, the average %EWL was at a significantly lower level – 9.92% ± 7.25%. The interval between the highest and lowest %EWL in the control group is 19.45% and 2.2%, respectively.

The average %EWL in patients who underwent bariatric surgery varies depending on different surgical techniques. Patients who underwent gastric bypass method showed the highest %EWL – 69.71% ± 20.0%, patients who underwent sleeve gastrectomy had an %EWL – 51.57% ± 5.9%, and patients after two-stage surgical treatment - average %EWL 51.7% ± 7.92%.

During the analysis of the quantitative changes in the gut microbiota composition, significant differences were found in response to the treatment in both groups. Thus, when analyzing the *Firmicutes*/*Bacteriodetes* ratio (FBR) and *Bacterioidetes*/*Faecalibacterium* ratio (BFaR) in the studied group, it was established that the average FBR before surgical treatment was 94.5. FBR before treatment was within the reference values only in three patients of this group (5.67%). The average BFaR in the studied group was 1708.5 (there is a significant range of minimum and maximum indicators in the group), 50000 and 0.0003, respectively. BFaR before surgical treatment was within the reference values in two patients (3.77% of the group).

During the analysis of the changes that occurred in the intestinal microbiota patterns of the patients, 12 months after the surgery, the following changes were found. The average FBR after the surgical treatment of obesity was 2.84 ± 6.4, the interval of the maximum and minimum values was 7.19 and 0.79, respectively. Gut microbiota of 50 patients (94.33% of the group) reached reference values. Three patients (5.67%), who did not have positive changes in FBR indicators, had insufficient effectiveness of surgical treatment in terms of % EWL - an average of 49.52%±0.6. The average BFaR

**Table 3.** Gut microbiota changes in relation with the type of treatment.

| Treatment type | Firmicutes/Bacteriodetes ratio | | p* | Bacterioidetes/Faecalibacterium ratio | | p* |
|---|---|---|---|---|---|---|
| | Before treatment, % of referent values | After treatment, % of referent values | | Before treatment, % of referent values | After treatment, % of referent values | |
| Gastric bypass | 5,00 | 95,00 | <0,001 # | 10,00 | 95,00 | <0,001 # |
| Sleeve gastrectomy | 0,00 | 94,22 | <0,001 # | 5,82 | 94,28 | <0,001 # |
| Intragastric balloon+gastric bypass ** | 6,25 | 87,50 | <0,001 # | 0,00 | 81,25 | <0,001 # |
| Study group (average) | 5,67 | 94,33 | <0,001 # | 3,77 | 92,40 | <0,001 # |
| Control group | 3,38 | 16,90 | 0,06 | 0 | 18,60 | 0,07 # |

# in one or both groups, the distribution of data differs from normal, the comparison was carried out using the Wilcoxon T-criteria;
* comparison was made between patients of the study and control groups;
**intragastric baloon+gastric bypass – installation of an intragastric balloon as the first stage of treatment for superobese patients and performing gastric bypass 6 months after the start of treatment [7].

in operated patients after 12 months was 58.4, with a range of the highest and lowest indicators – 121 and 0.256, respectively. In 49 patients (92.4% of the group), microbiota reached reference values. Four patients (7.6%) did not have intestinal microbiota indicators return to reference values and had insufficient effectiveness of surgical treatment in % EWL - the average indicator was 49.33%±1.1.

In patients of the control group, the intestinal microbiota changed in response to the start of treatment in a different way. The mean FBR before treatment was 52.5 ± 91.1. In two patients of this group (3.38%), the average FBR fluctuated within the reference values before the start of treatment. The mean BFaR before treatment in the control group was 579.1. BFaR reference values before treatment were not found in the control group.

After treatment in the control group, the average FBR was 6.1 ± 22.2 (range 0.2 - 22.4). Ten patients of the control group (16.9%) demonstrated results within the reference values from the start of treatment. In turn, the average BFaR in patients who underwent a course of treatment were 130.2; this parameter reached reference values in eleven patients (18.6%) (Table 3).

In the course of the statistical analysis of the obtained data, the linear correlation method confirmed the existence of a strong positive correlation between the surgical treatment of obesity and the effectiveness of the treatment according to %EWL, r=0.969 at p≥0.001, and the absence of a correlation between the choice of conservative methods of obesity treatment and treatment efficiency according to %EWL, r=0.172 at p≥0.01. A strong negative rank correlation was also found between the value of BMI (degree of obesity) and the frequency of detection of reference indicators of intestinal microbiota in the sample, r=0.798 at p≥0.05. Only 2.67% of patients had a pattern of intestinal microbiota close to the reference values before the start of treatment. In turn, in the postoperative period of patients in the study group, in 93.3% of cases there were changes in the patterns of the intestinal microbiome and their return to the reference values, which correlates with the degree of reduction in BMI r=0.717 (p≥0.05), and %EWL r=0.633 (p≥0.001). There is a correlation between the choice of surgical method of obesity treatment and the return to normal FBR and BFaR indicators r=0.628 and r=0.642 (p≥0.05). During the analysis of the data of patients of the control group, no relation was found between the effectiveness of the treatment according to %EWL and the normalization of intestinal microbiota indicators r=0.077 (p≥0.05) of the control group 17.7% of patients of the control group had positive changes in the patterns of intestinal microbiota , however, the correlation with the effectiveness of the treatment was not found r=0.112 (p≥0.05).

## DISCUSSION

During the research, a number of regularities and tendentions were revealed.

Intestinal microbiota is a variable functional unit of intestinal work and metabolism as a whole. Changes in the composition of intestinal microbiota occur in response to changes in diet and eating behavior [1-3]. Christopher L. Gentile, Tiffany L. Weir and others. in

their study of the functioning of the intestinal microbiota, they found that a change in the nature of the diet, especially an increase in the amount of fat, causes changes in the composition of the intestinal microbiota and a number of metabolic disorders, even before the appearance of overweight and obesity [1]. Gomes AC, Hoffmann C, et al. in their study indicate that changes in the pattern of intestinal microbiota mediated by a diet with a high content of fats and carbohydrates cause a pro-inflammatory response in the lymphoid tissue of the large intestine, which leads to a violation of the mechanisms of nutrient absorption, a violation of the hunger-satiety regulation system, and leads to changes in eating behavior, namely overeating [3].

Bariatric surgery is also an important factor affecting changes in intestinal microbiota patterns. The operated patients included in the study in the vast majority of cases demonstrated positive dynamics of changes in the composition of the intestinal microbiota in the postoperative period, in comparison with indicators of functioning of the microbiota before surgical treatment of obesity. According to the study of Gutiérrez-Repiso, C., Moreno-Indias et al. intestinal microbiota after sleeve gastrectomy and gastric bypass according to the Roux method, changes during the study period and in comparison with the preoperative pattern of intestinal microbiota. In their study, the authors are looking for the possibility of identifying a specific composition of the intestinal microbiota that could predict remission of type 2 diabetes or unsuccessful weight loss after bariatric surgery [5].

Bariatric interventions are more effective than conservative methods and have a greater impact on the intestinal microbiota. Silvia Palmisano, Giuseppina Campisciano and others. in their study evaluated the relationship between gastric bypass and changes in the intestinal microbiota and concluded that bariatric interventions have a greater clinical effect in cases accompanied by positive dynamics in the composition of the intestinal microbiota, compared to patients who did not have the indicated changes [14] .

Changes in the composition of the intestinal microbiota after surgical treatment of obesity are interrelated and play a role both in the functioning of the intestine after the intervention and in the metabolism of nutrients, so they can be attributed to the factors affecting the effectiveness of surgical treatment.

## CONCLUSIONS

1) Effective surgical treatment of obesity leads to the positive changes in the intestinal microbiota in 93.3% of cases ($p \leq 0.001$), in contrast to the control group, where microbiota approached the reference values only in 17.7% of cases ($p \geq 0.06$).
2) Patients of the studied group, who had positive dynamics in changes of gut microbiota in 98.1% of cases, had the effectiveness of obesity treatment due to %EWL at the level of 59.21% ($r=0.717$; $p \leq 0.001$). %EWL ≤ 50% was observed in patients who did not have positive changes in intestinal microbiota after surgical treatment.
3) *Firmicutes*/*Bacteriodetes* ratio and *Bacterioidetes*/*Faecalibacterium* ratio can be one of the criteria for evaluating the efficacy of surgical treatment of obesity.
4) In patients of the control group, positive dynamics of changes in gut microbiota composition occurred in 17.7% of cases and the average effectiveness of obesity treatment by %EWL was 9.92% ($r=0.077$; $p=0.06$).

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## CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

**RECEIVED:** 09.02.2024
**ACCEPTED:** 27.06.2024