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Marietta Bracha[1,B-D], **Małgorzata Szady-Grad**[2,F]

SELECTED BLOOD PARAMETERS WITH POTENTIAL DIAGNOSTIC APPLICATION IN THE COURSE OF INFLAMMATION IN CHRONICALLY OBESE INDIVIDUALS UNDERGOING BARIATRIC SURGERY

Wybrane parametry krwi o potencjalnie diagnostycznym zastosowaniu w przebiegu stanu zapalnego u osób przewlekle otyłych poddanych operacji bariatrycznej

[1] Katedra Geriatrii, Zakład Biochemii i Biogerontologii, Uniwersytet Mikołaja Kopernika w Toruniu, Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy, Polska
[2] Katedra Higieny, Epidemiologii i Ergonomii i Kształcenia Podyplomowego, Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy, Polska

A - Koncepcja i projekt badania, B - Gromadzenie i/lub zestawianie danych, C - Analiza i interpretacja danych, D - Napisanie artykułu, E - Krytyczne zrecenzowanie artykułu, F - Zatwierdzenie ostatecznej wersji artykułu

Marietta Bracha - 0000-0002-0553-8200
Małgorzata Szady-Grad - 0000-0003-4336-2311

Abstract (in Polish):
Chirurgia bariatryczna została uznana za najskuteczniejszą długoterminową metodę leczenia otyłości. Prowadzi do radykalnej i trwałej utraty wagi, poprawy jakości życia oraz zmniejszenia ryzyka wystąpienia chorób metabolicznych. Poszukiwanie potencjalnego mechanizmu odpowiedzialnego za patogenezę

chorób związanych z otyłością ujawniło ścisły związek między nadmiarem składników odżywczych a rozwojem stanu zapalnego. Coraz większa ilość badań dotyczących wpływu chirurgii bariatrycznej na poziom parametrów stanu zapalnego we krwi dowodzi zmniejszenia ogólnoustrojowego stanu zapalnego.

Abstract (in English):
Bariatric surgery has been recognized as the most effective long-term treatment for obesity. It leads to radical and permanent weight loss, improved quality of life and reduced risk of metabolic diseases. The search for a potential mechanism responsible for the pathogenesis of obesity-related diseases has revealed a close relationship between excess nutrients and the development of inflammation. An increasing number of studies on the impact of bariatric surgery on the level of inflammatory parameters in the blood proves a decrease in systemic inflammation.

Keywords (in Polish): otyłość, stan zapalny, operacja bariatryczna.

Keywords (in English): obesity, inflammation, bariatric surgery.

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Short title
Parametry stanu zapalnego u osób po operacji bariatrycznej

Corresponding author
Marietta Bracha
Katedra Geriatrii, Zakład Biochemii i Biogerontologii, Uniwersytet Mikołaja Kopernika w Toruniu, Collegium Medicum im. Ludwika Rydygiera w Bydgoszczy, Polska; email: marietta.bracha@cm.umk.pl

Authors (short)
M. Bracha, M. Szady-Grad

Introduction

Obesity is a rapidly growing public health problem, occurring both in highly industrialized and developing countries. The majority of the world's population lives in countries where overweight and obesity result in more deaths than undernutrition [1]. According to a report published by the WHO in May 2022, more than one billion people worldwide are obese – 650 million adults, 340 million adolescents and 39 million children. In Europe, 60% of the population is overweight or obese, and this figure is still growing [2]. This is due to excessive energy intake from food consumption coupled with reduced energy expenditure, leading to an increase in body fat mass. This leads to the development of low-grade inflammation, called metabolic inflammation or meta-inflammation [3].

Significant weight loss occurring after bariatric surgery gives the opportunity to learn about the mechanisms underlying the development of comorbidities in obesity [4]. Current research results allow us to assume that after bariatric surgery, the level of inflammatory parameters in the blood will gradually decrease.

The aim of the study was to present current knowledge on selected parameters of blood inflammation in chronically obese people undergoing bariatric surgery.

According to the WHO, overweight and obesity are defined as abnormal or excessive accumulation of body fat, which affects the deterioration of health. The main indicator for diagnosing abnormal body weight in adults is body mass index (BMI). BMI above 25 kg / m2 indicates overweight, while above 30 kg/m2 indicates obesity [1]. Obesity is a disease that affects most body systems - the heart, liver, kidneys, joints and reproductive system. It leads to a number of non-communicable diseases (NCDs), such as type 2 diabetes, cardiovascular diseases, respiratory diseases, different kind of cancers, as well as neurodegenerative diseases and mental health problems [5].

The search for a potential mechanism responsible for the pathogenesis of obesity-related diseases revealed a close relationship between excess nutrients and the development of inflammation [3]. Adipose tissue is mainly made of adipocytes, but other cells are also involved in its growth and functioning, including preadipocytes, lymphocytes, macrophages, fibroblasts and vascular cells. Currently, adipose tissue is considered to be an active endocrine organ synthesizing numerous, biologically active peptides called adipokines, which act within adipose tissue and on distant organs and tissues that can cause increased inflammation. Obesity can lead to significant changes in the cellular composition of adipose tissue and also modulate the phenotype of the cells present there [6]. Many factors are involved in the development of meta-inflammation, which include hypoxia and adipocyte death, oxidative stress, endoplasmic reticulum stress, activation of inflammasomes, activation of TLR receptors and disorders of the composition of the natural intestinal flora [7, 8, 9].

Although diet, lifestyle modification, and pharmacological therapy are common treatment options for obesity, current evidence indicates that these interventions do not show long-term weight reduction in cases of morbid obesity [10, 11, 12]. Bariatric surgery is currently the most effective treatment for patients with obesity whose BMI exceeds 40 kg/m2 or 35 kg/m2 with current obesity complications. Surgery leads to radical and permanent weight loss, improved quality of life and reduced risk of obesity-related disorders [13]. Among bariatric treatments, we distinguish three main types of surgeries: restrictive, exclusionary and restrictive-exclusionary. Among the restrictive methods, we distinguish adjustable gastric banding (AGB), vertical gastric banding (VGB), laparoscopic sleeve gastrectomy (LSG). Exclusionary surgeries significantly reduce the absorption of energy from food consumption by excluding part of the digestive tract from digestion and absorption. These include biliopancreatic diversion (BPD). Restrictive-exclusionary methods include: Roux-Y-gastric bypass (RYGB), mini-gastric bypass (OAGB, MGB), biliopancreatic diversion with duodenal switch (BPD-DS) [14 , 15]. RYGB and LSG together account for more than 80 % of bariatric surgery performed worldwide [16].

Weight reduction interventions in obese patients are associated with improvements in systemic inflammation [17]. Inflammation in people with obesity can be measured by quantifying inflammatory parameters such as pro-inflammatory cytokines (e.g. tumor necrosis factor (TNF-α), interleukin 1 (IL-1), interleukin 6 (IL-6), interleukin 8 (IL-8), leukocyte counts, adipokines, C-reactive proteins (CRPs), high sensitivity CRP (hs-CRP) [5, 18]. An increasing number of studies indicate that bariatric surgery (BS) lowers inflammatory parameters in the blood [19].

A meta-analysis of 95 studies involving a total of 6232 patients undergoing bariatric surgery showed a significant decrease in leptin, ghrelin, CRP, hs-CRP, IL-6, TNF-α, IL-1β levels and an increase in adiponectin, GLP-1 and YY peptide (PYY) levels [20]. El-Zawawy et al. in their study showed a decrease in hs-CRP levels after just 3 months after BS [21]. This is accordance with the results of Lautenbach et al., which showed a significant reduction in hs-CRP after 6 months, 2 years and 4 years from BS respectively [19]. Furthemore, Oliveras et al. in their studies showed a significant reduction in hs-CRP after 1 year from BS [22]. The aim of the study of Lautenbach et al. was a long-term evaluation of the effect of BS on inflammatory markers. The results of a four-year study involving 163 patients showed that patients with optimal weight loss exhibited a significant decrease in leukocytes, CRP throughout the follow-up period. The most significant decrease in inflammatory state parameters was observed in the first 6 months after surgery. The reduction in inflammation was statistically significantly associated with a decrease in BMI and remission of type 2 diabetes [19]. In the research of Netto et al. the impact of RYGB surgery on pro-inflammatory, prothrombotic parameters and selected metabolic syndrome parameters was assessed. After 6 months from surgery, a statistically significant decrease was observed in PAI-1, CRP, intercellular adhesion molecules 1 (ICAM-1), leptin, resistin and TNF-α. Moreover, a decrease in the leptin/adiponectin ratio was also observed. Levels of anti-inflammatory IL-10 and adiponectin were elevated [23]. In addition, the ratio of adiponectin to leptin can be considered as a better parameter of inflammation than adipokines alone, since this ratio is characterized by high sensitivity and specificity for metabolic parameters, regardless of BMI values [24]. In the studies of Sachan et al. the profile of inflammatory adipocytokines: IL-6, IL-8, CRP, TNF-α and adiponectin and resistin in blood serum was evaluated. The tests were performed first immediately after BS (on the day of discharge from the hospital) and then 6 months after surgery. Postoperative evaluation of serum cytokines showed a significant reduction in serum TNF-α concentrations while lowering IL-8 levels. On the other hand, an increase in CRP and IL-6 was found. CRP is an acute phase protein, so its concentration in the immediate postoperative period may have been higher. After 6 months, the levels of CRP, MCP-1, IL-8 decreased, while the level of adiponectin increased significantly compared to its initial level. The study noted that IL-6 levels began to increase in the immediate postoperative period, while TNF-α levels decreased. Over time after surgery and during follow-up evaluation at 6 months, TNF-α showed an upward trend with an accompanying increase in IL-6 levels. The authors of the study point out that the interaction of cytokines can be much more complex [25]. In a meta-analysis of 116 studies examining the impact of bariatric surgery on the levels of IL-6, TNF-α, and CRP in blood serum, a statistically significant reduction in their concentrations was observed [18]. Also, studies conducted on a group of 126 LSG patients showed a statistically significant decrease in serum concentration of IL-1β, IL-6 and IFNγ during the 12-month observation period [26]. The results obtained by Carmona-Maurici et al. in a study of 62 OAGB patients reported a significant decrease in hs-CRP and IL-6 levels within 12 months after surgery. In terms of postoperative adipocytokine changes, serum adiponectin levels increased significantly, while leptin and resistin levels decreased. However, no significant changes were observed in the serum concentrations of IL-8 and TNF-α 12 months after surgery [27]. The study conducted by Schmatz et al. focused on inflammatory markers and oxidative stress markers in patients after RYGB surgery. The study demonstrated a significant decrease in the concentration of lipid peroxidation products, carbonyl groups of proteins, and non-protein thiol groups (NPSH). Additionally, there was an increase in the activity of superoxide dismutase (SOD) and catalase (CAT). Furthermore, the decrease in resistin levels was accompanied

by a reduction in inflammatory markers IL-1, IL-6, and TNF-α, as well as an increase in the anti-inflammatory adiponectin [28].

Conclusions

Low-grade chronic inflammation plays a crucial role in the development of metabolic diseases in individuals with chronic obesity. This condition results from the increased release of pro-inflammatory factors in response to an increased number of adipocytes and immune cells in adipose tissue [29]. Bariatric surgery has been recognized as the most effective long-term treatment for obesity. In addition, long-term studies have proven that it is effective in the treatment of diabetes and cardiovascular diseases [30] An increasing number of studies on the impact of bariatric surgery on the level of inflammatory parameters in the blood prove a reduction in systemic inflammation due to fat loss. Recent studies show a decrease in the level of the following parameters: CRP, IL-1β, IL-6, Il-8, IFNγ, PAI-1, ICAM-1, leptin, resistin, ghrelin and an increase in the concentration of adiponectin, GLP-1 and PYY concentrations. Results may differ slightly, which may be attributed to differences in the type of bariatric surgery, patients' initial body weight, or the duration of observation (19). With the increasing use of bariatric surgery in the treatment of obesity, it is crucial to elucidate the underlying mechanisms responsible for improving the health status of individuals with chronic obesity [4].

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