REVIEW PAPERS

Why does body weight often increase again after initial loss? The role of metabolic adaptation

Dlaczego po schudnięciu masa ciała często ponownie wzrasta? Znaczenie adaptacji metabolicznej

*Jarosław Kozakowski[1], Piotr Dudek[1]**

[1] *Department of Endocrinology Medical Center of Postgraduate Education Bielański Hospital, Warsaw, Poland*

KEYWORDS:

- obesity
- weight loss
- metabolic adaptation
- energy balance
- weight regain

ABSTRACT

Obesity, often referred to as the tsunami of the 21st century", is a chronic, incurable disease prone to relapses. The crucial intervention aimed at reducing body weight for health benefits is lifestyle modification, but unfortunately, in most cases after the initial period of weight loss, a recurrence of overweight or obesity is observed. A similar process occurs in patients after bariatric surgery. It should be understood that the reason for this phenomenon not necessarily must be associated with the lack of the patient adherence, but is a consequence of the activation of a strong objective mechanism – metabolic adaptation, i.e. changes in energy homeostasis to counteract losing of energy. The article briefly describes the most important mechanisms of metabolic adaptation and presents the ways to counteract them.

SŁOWA KLUCZOWE:

- otyłość
- redukcja masy ciała
- adaptacja metaboliczna
- równowaga energetyczna
- nawrót otyłości

STRESZCZENIE

Otyłość, określana często jako „tsunami XXI" wieku to przewlekła, nieuleczalna choroba przebiegająca ze skłonnością do nawrotów. Podstawą postępowania mającego na celu redukcję masy ciała dla uzyskania korzyści zdrowotnych jest modyfikacja stylu życia, jednak często po początkowym okresie chudnięcia obserwowany jest nawrót nadwagi lub otyłości. Podobny proces ma miejsce po operacjach bariatrycznych. Należy mieć świadomość, że powodem tego zjawiska niekoniecznie musi być brak zaangażowania ze strony pacjenta, lecz włączenie się silnego obiektywnego mechanizmu – adaptacji metabolicznej, a więc zmian homeostazy energetycznej mających przeciwdziałać utracie energii. W artykule opisane są w skrócie najważniejsze mechanizmy adaptacji metabolicznej oraz sposoby jej przeciwdziałania.

Introduction

Obesity is the most common chronic disease in the present-day world, and it is a major contributor to morbidity, mortality and health care systems expense. It is defined as a chronic, multifactorial, incurable disease prone to relapse (1). Despite the fact that significant progress in understanding of the etiopathology of this disease has been observed in recent decades, and new methods of effective weight reduction were worked out, the recurrence of overweight and obesity after initial success, already signaled in the definition is still a problem. In such cases the responsibility for this process are very often placed on the patient. He is allegedly not consistent enough in implementing recommendations, has insufficient motivation or is even considered as a lazy and in the end is "to blame for himself". However, this approach is simplified and unjustified, because is based on the assume that the regulation of energy balance and, as a result, body weight are completely under our control. Now it is well known that the commonly observed phenomenon of weight regain and

*Address for correspondence: *Piotr Dudek, Department of Endocrinology, Medical Center of Postgraduate Education, Bielański Hospital, Cegłowska 80 street; 01-809 Warsaw, Poland, e-mail:* pldudek@wp.pl

Published and financed by Centre of Postgraduate Medical Education; https://doi.org/10.36553/wm.184.

obesity relapse after initially successful treatment is due to powerful biological mechanisms called metabolic adaptation.

Regulation of the energy balance

Preserving of an appropriate energy balance is a prerequisite to maintain optimal metabolism. In short, energy balance may be described as the difference between the amount of energy absorbed with the consumed food, and energy expended to maintain metabolic and physiological functions as well as to support physical activity. Energy is absorbed from food as a result of feeling hunger, lack of satiety, and increased appetite. Sense of increased hunger appears in hypothalamus. Neurons localized in the arcuate nucleus sense signals from the peripheral organs indicating the energy stores in the body. Through distinct projections, arcuate nucleus neurons communicate with second-order neurons, which are mostly localized in the paraventricular nucleus and in the lateral hypothalamus. The signals are then proceed further to neurons that generate complex responses aimed at maintaining whole-body energy homeostasis. Among the most important transmitters of information from the peripheral body to the regulatory centers are insulin, considered as the "satiety hormone", and ghrelin – the most powerful orexigenic hormone derived from the gastrointestinal tract, mainly from stomach. Ghrelin secretion increases in energy deficiency, and is called the "hunger hormone". Other important factors that participate in energy balance regulation include peptides of a gastrointestinal origin, e.g. glucagon-like polypeptide (GLP-1), cholecystokinin (CCK), peptide YY (PYY), amylin or oxyntomodulin. Between hormones derived from adipose tissue the most important is leptin – protein acting in opposition to ghrelin, the second, next to insulin "satiety hormone". Production of leptin increases with the expansion of fat mass. Other hormones secreted from adipose tissue include adiponectin and resistin. Orexigenic signals increase the expression of neurons secreting neurotransmitters responsible for feeling hunger – neuropeptide Y and AGRP (agouti-related peptide) and inhibit the expression of neurons that produce POMC (proopiomelanocortin) and CART (cocaine- and amphetamine-regulated transcript). Anti-orexigenic stimuli have an opposite effect, suppressing hunger and increasing the feeling of satiety (2-4).

In addition to the regulation of feeling hunger/satiety in the hypothalamus, the phenomenon of appetite, i.e. the desire to eat a specific kind of food (e.g., sweets) not due to replenish energy, but in order to feel pleasure (hedonistic reaction), is considered to be of great importance in the development of excessive body weight (5). The specific regions located in insular and limbic cortex are responsible for this mechanism. Dopamine and serotonin have been recognized as neuromediators that participate in this action (6).

As far as daily energy expenditure (EE) is concern it is believed, that it consists of two major components, that determine individual EE – resting energy expenditure (REE) and non-resting energy expenditure (non-REE). The first one, refers to the basal metabolic rate (BMR), defines the energy that is necessary for the basic life processes, such as breathing, brain activity, heart function, leisure time, etc. It is a largest constituent of total daily EE, with an average contribution of 70% to total daily EE. The second component can be further divided into three parts: physical activity-related thermogenesis, non-food thermic effect (NEAT), and food-related thermic effect, which includes energy loss associated with eating, digesting, absorbing, and metabolizing food. (TEF, thermic effect of food) (7).

Weight regain following initially successful weight loss

Weight recurrence after initially effective calorie-restriction even it is accompanied by pharmacotherapy therapy is common because obesity is a chronic and complex disease.

Although, a considerable increase in the utilization of the overweight/obesity-decreasing medications, particularly in GLP-1 receptor agonists has been observed the lack of available data regarding their medium- to long-term efficiency remains a salient concern. For example, in the one study patients treated with the GLP-1 agonist semaglutide for 68 weeks for obesity have lost 17% of their body weight. But one year after treatment was discontinued they have regained about 2/3 of the lost weight (8). In the other trial that has included 428 patients with overweight or obesity a weight regain of 6.5% (SD 7.4%) compared to the nadir of weight loss after 2.5 to 5.5 years of pharmacotherapy with FDA-approved and off-label medications has occurred. However, weight regain was found in half of the patients (9). In the recently published analysis a rapid regain of weight after cessation of therapy, regardless of the duration of the treatment with GLP-1 receptor or GIP/GLP-1 receptors agonists has been shown. Authors concluded, that this rebound has been likely to substantially mitigate the metabolic benefits attained through weight loss. Then, it may be essential for future research to focus on elucidating the optimal duration of these treatments or identifying techniques or schemes that involve a reduction in dosages to prevent weight regain (10).

Although this phenomenon is commonly observed after calorie restriction as a element of lifestyle modification procedure and after cessation of pharmacotherapy it also frequently occurs after bariatric surgery (11). The divergent data reported on this topic result from the lack of the standard definition for successful weight loss maintenance and weight regain. Probably the most commonly used definition assuming that weight gain by 10% in relation to the nadir of the decrease may be considered as weight regain. For example, in a study of 300 patients who underwent gastric bypass (RYGB), excessive weight regain, defined as ≥25 % of total lost weight, occurred in 37 % of participants (12). A systematic review showed that 76% patients after sleeve gastrectomy (SG) experienced a significant increase in body weight over 6 years of follow-up (13). In a large study of 1406 subjects after RYGB surgery, the increase in body weight compared to the nadir value was 5.7% after one year, 10.1% after two years, 12.9% after three years, 14.2% after four years, and 15% after five years. In this study, an increase in body weight of at least 10% compared to nadir at the same time intervals was observed in 23%, 51%, 64%, 69%, and 72% of the treated subjects, respectively (14). Thus, weight regain occurs no matter how the weight loss is achieved, by lifestyle changes including behavioral therapy, pharmacotherapy, or bariatric surgery. Many patients with weight recurrence feel frustrated and embarrassed and may experience recurrence of cardiometabolic disorders and other complications of obesity that they had suffer before treatment.

Now it is well known that the diminishing of body weight may be associated with significantly reduced energy expenditure as a result of changes in energy homeostasis, referred to as metabolic adaptation. In patients treated surgically changes in the anatomy of the gastrointestinal tract should be considered as additional factor contributing to weight gain.

Metabolic adaptation

The term metabolic adaptation refers to the phenomenon of a decrease in resting energy expenditure (REE) that is greater than would be naturally expected due to a decrease in fat free mass (FFM) and fat mass (FM) (15). As it was mentioned above, metabolic adaptation is frequently observed in obese individuals advised to reduce weight with the implementation of lifestyle modification program (16), as well as in patients using other treatment methods (17, 18). The conservation of energy ("hibernation mode") in response to weight loss (somehow in accordance with the "thrifty genotype" hypothesis) has significant clinical consequences. The severity of metabolic changes depends on the degree of energy deficit and significantly contributes to the effects of therapy.

Based on the results of many observations, a model describing changes in the energy balance during the intervention causing calorie restriction has been developed. According to this model in the first phase, immediately after beginning of calorie restrictions, the amount of energy expended exceeds the amount of the energy absorbed, hence the balance is negative and body weight is going down. During this time patients usually agreeably follow dietary recommendations. In the second phase, which usually begins after 3-6 months, the amount of energy expended is further reducing, although slowly, adequately to the decreasing body weight. This is a period of relative energy balance (energy absorbed is equal to energy loss). In the third phase, which begins after about 12 months, energy expenditure begins to decrease to a lesser extent than it would result from weight reduction. The energy balance becomes relatively positive, metabolic adaptation develops, and patients hardly adherence to recommendations referred to nutrition and physical activity. It has been shown, that metabolic adaptation measured in rest in calorie restriction studies, induced by low calorie diet or bariatric surgery ranges from 3% to 20% depending on the kind of a weight loss intervention (19). Interestingly, metabolic adaptation evaluated by resting metabolic rate was reduced more by traditional calorie restriction procedures, then by alternate day fasting (meals every other day), despite similar reduction in energy acquired and a comparable decrease in fat free mass and fat mass (20, 21).

Several mechanisms responsible for the metabolic adaptation are considered. Lifestyle modification with calorie restrictions, aimed at achieving a negative energy balance leads to significant changes in neurohormonal regulation of appetite. "Energy-exhausted" adipocytes produce less leptin, the most important anti-orexigenic hormone. The secretion of ghrelin – a potent factor responsible for sense of hunger increases. Moreover, secretion of other hormones in the gastrointestinal tract involved in hunger and satiety regulation changes significantly: e.g., levels of GLP-1 increases, while levels of gastric inhibitory polypeptide (GIP), peptide YY (PYY), cholecystokinin (CCK) or amylin decreases. Reduced secretion of thyroid stimulating hormone (TSH) in the pituitary gland results in lower triiodothyronine and thyroxine production, and in consequence, serum levels of the thyroid hormones. As far as autonomic nervous system is concerned decrease in sympathetic tone and increase in parasympathetic tone is observed. Changes in secretion of main hormones that participate in energy homeostasis regulation are shown in Table 1.

Table 1. Effect of weight loss on secretion of hormones involved in energy homeostasis regulation.

Hormone	Change	Clinical relevance
Ghrelin	increase	increased hunger
PP	increase	increased hunger
Leptin	decrease	anti-orexigenic effect
GLP-1	decrease	increased hunger
PYY	decrease	increased hunger
CCK	decrease	increased hunger
Amylin	decrease	increased hunger
TSH	decrease	decrease of T3, T4

PP – pancreatic polypeptide; **GLP-1** – glucagon-like peptide 1; **PYY** – peptide YY3-36; **CCK** – cholecystokinin; **TSH** – thyroid stimulating hormone (22, 23)

Mentioned above mechanisms lead to meaningful changes in absorption of the energy. Individuals consumed a calorie-restricted diet over time begin to feel less satiated. Resistance to stimuli encouraging to eat decreases. The perception of the amount of food to consumption changes – the portion of meal seems to be smaller than it actually is. Additionally, a decrease in the amount of energy expenditure both at rest and activity is observed. It is associated with lower physical activity as well as with higher skeletal muscles work efficiency. This increase in muscles efficiency occurs as a result of profound changes in their structure: the predominance of myosin heavy chains type I (MHC I) over type II (MHC II) and a decrease in the efficiency of the sarco-endoplasmic calcium reticulum (SERCA) responsible for the transport of calcium ions from the cytosol to the sarcoplasmic reticulum after muscle contraction (24). As a result of the described changes in the regulation of energy homeostasis, daily energy expenditure decreases by 300-400 kcal (25).

The loss of fat free mass which in 50% consists of skeletal muscles leads to condition called sarcopenia (the Greek sárx, "flesh" and pení¯a "poverty"). Sarcopenia contributes negatively to energy homeostasis regulation by directly reducing resting energy expenditure as skeletal muscles create a metabolically active tissue, and indirectly by decreasing non-exercise activity thermogenesis and overall physical activity. This reduced total energy expenditure, coupled with potential fat mass increase, shifts the energy balance towards a positive balance, promoting fat storage and afresh increasing the risk of obesity and related metabolic diseases (26, 27).

Management of the metabolic adaptation

It is believed that the best way to counteract the effects of metabolic adaptation is to keep or even increase physical activity, along with consistent follow dietary recommendations. Such procedure may help to maintain a favorable protein balance (less protein oxidation relative to intake) and slow down loss of fat free mass (28). Prolonged caloric restriction induces muscle proteolysis rather than inhibiting muscle protein synthesis. Taking into account unfavorable effects of sarcopenia, protein consumption beyond the levels recommended for healthy individuals is a crucial approach for diminishing fat free mass loss during weight loss. Adequate protein intake varies widely across guidelines, ranging from 0.8 g/kg body weight per day for healthy individuals to 1.2-1.5 g/kg for elderly. Nonetheless, recently published studies indicate that overweight/obesity patients who consume higher protein diets (1.3 g/kg per day) during weight loss retain more muscle mass compared to those without enhanced protein intake (29). Although, some studies suggest that high protein intake (1.2 g/kg per day) during weight loss may attenuate improvements in insulin sensitivity (30) and may counteract the positive effects of exercise on glucose homeostasis (31).

Regular training program for increases in muscle mass and strength is of vital importance. Age, gender, genetic predisposition, prior training status, and general health are the factors that influence the optimal load. Two times/week training may be best for increasing muscle size, strength, ease of locomotion, and non-food thermic effect. It is important particularly in older adults (32).

Moreover, according to the position of the Polish Society for the Treatment of Obesity (PTLO), "pharmacotherapy is a method of obesity treatment in patients in whom dietary and behavioral management has not resulted in significant weight reduction and therapeutic goals have not been achieved" (33). Thus, although the basis for optimizing health, including body weight, is lifestyle modification, in many cases start with weight reducing drugs may be necessary. Medications approved (by Food and Drug Administration or European Medicines Agency) for treatment have also shown effectiveness in cases of not successful weight loss or weight recurrence after bariatric surgery. In such cases, GLP-1 or GLP-1/GIP receptors agonists seem to be the most effective in comparison with other anti-obesity drugs (34, 35). However, combine pharmacologic therapy in some patients may be also necessary (36).

Interestingly, there are increasing evidence of the role of gut microbiota in the regulation of host appetite and feeding behavior. Gut bacteria-derived proteins interact with host satiety signaling via stimulating the release of intestinal hormones such as GLP-1 and PYY, and may also activate anorexigenic pathways in hypothalamic and brainstem nuclei. Hence, the use of probiotics to achieve anti-obesity effects has been proposed. For example, it has been shown, that a 12-week treatment with the probiotic strain Hafnia alvei significantly improves weight loss, feeling of fullness and reduction of hip circumference in overweight subjects following moderate hypocaloric diet (37). These data suggest, that the use of probiotics in the global management of excess weight could be reasonable.

Decline in muscle mass associated with body weight reduction negatively affects metabolism regulation. The gut microbiota is a new found important contributor involved in the onset of obesity and related disorders. It was recently demonstrated in a 12-week, double-blind, placebo-controlled clinical trial involving 100 individuals aged 60 and above, that oral administration of pasteurized postbiotic *Akkermansia muciniphila* could mitigate muscle wasting, can enhance muscle strength and functionality, even in elderly individuals (38). These outcomes suggest that postbiotics like *A. muciniphila* may be probably a valuable intervention for enhancing muscle performance and then counteracting metabolic adaptation.

Conclusion

Weight regain after lifestyle modification as well as after implementation other methods of obesity treatment, including bariatric surgery is often a reason for disappointment and frustration in patients. Moreover, it may be associated with recurrence of obesity-associated metabolic changes and diseases. In such situations, patients are often given generalized lifestyle recommendations that were ineffective prior to treatment. This is due to the lack of knowledge of the strong biological mechanisms responsible for the recurrence of obesity, referred to as metabolic adaptation, and about the ways to counteract it. Given the complex etiopathology of obesity, in real-world practice lifestyle modification albeit necessary is alone rarely sufficiently effective, and most often pharmacological treatment is also required.

References

(1) Olszaniecka-Glinianowicz M, Mazur A, Chudek J, et al. Obesity in Adults: Position Statement of Polish Association for the Study on Obesity, Polish Association of Endocrinology, Polish Association of Cardiodiabetology, Polish Psychiatric Association, Section of Metabolic and Bariatric Surgery of the Association of Polish Surgeons, and the College of Family Physicians in Poland. Nutrients 2023; 15:1641. doi.org/10.3390/nu15071641.

(2) Badman MK, Flier JS. The gut and energy balance: visceral allies in the obesity wars. Science 2005; 307(5717):1909-14. DOI:10.1126/science.1109951.

(3) Theilade S, Christensen MB, Vilsbøll T, et al. An overview of obesity mechanisms in humans: Endocrine regulation of food intake, eating behavior and common determinants of body weight. Diabetes Obes Metab 2021; 23(Supp.1):17-35. DOI:10.1111/dom.14270.

(4) Martinez JA. Body-weight regulation: causes of obesity. Proc Nutr Soc 2000; 59(3):337-45. DOI:10.1017/s0029665100000380.

(5) Gainetdinov RR. Mesolimbic dopamine in obesity and diabetes. Am J Physiol Regul Integr Comp Physiol 2007; 293(2):R601-2. DOI:10.1152/ajpregu.00450.2007.

(6) Naef L, Pitman KA, Borgland SL. Mesolimbic dopamine and its neuromodulators in obesity and binge eating. CNS Spectr 2015; 20(6):574-83. DOI:10.1017/S1092852915000693.

(7) Martínez-Gómez MG, Roberts BM. Metabolic Adaptations to Weight Loss: A Brief Review. J Strength Cond Res 2022; 36(10):2970-2981. DOI:10.1519/JSC.0000000000003991.

(8) Wilding JPH, Batterham RL, Davies M, et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: the STEP 1 trial extension. Diabetes Obes Metab 2022; 24 (8):1553-64.

(9) Weintraub MA, D'Angelo D, Tchang BG, et. al. Five-year weight loss maintenance with obesity pharmacotherapy. J Clin Endocrinol Metab 2023; 108(9):e832-41.

(10) Quarenghi M, Capelli S, Galligani G, et al. Weight Regain After Liraglutide, Semaglutide or Tirzepatide Interruption: A Narrative Review of Randomized Studies. J Clin Med 2025; 14(11):3791. DOI:10.3390/jcm14113791.
(11) Noria SF, Shelby RD, Atkins KD, et al. Weight Regain After Bariatric Surgery: Scope of the Problem, Causes, Prevention, and Treatment. Curr Diab Rep 2023; 23(3):31-42. DOI:10.1007/s11892-023-01498-z.
(12) Cooper TC, Simmons EB, Webb K, et al. Trends in weight regain following Roux-en-Y gastric bypass(RYGB) bariatric surgery. Obes Surg 2015; 25(8):1474-81. doi.org/10. 1007/s11695- 014- 1560-z.
(13) Lauti M, Kularatna M, Hill AG, et al. Weight regain following sleeve gastrectomy-a systematic review. Obes Surg 2016; 26(6):1326-34. doi.org/10.1007/s11695-016-2152-x.
(14) King WC, Hinerman AS, Belle SH, et al. Comparison of the performance of common measures of weight regain after bariatric surgery for association with clinical outcomes. JAMA 2018; 320(15):1560-9. https:/doi.org/10.1001/.
(15) Müller MJ, Enderle J, Pourhassan M, et al. Metabolic adaptation to caloric restriction and subsequent refeeding: the Minnesota Starvation Experiment revisited. Am J Clin Nutr 2015; 102(4):807-19. DOI:10.3945/ajcn.115.109173.
(16) Dabas J, Shunmukha Priya S, Alawani A, et al. What could be the reasons for not losing weight even after following a weight loss program? J Health Popul Nutr 2024; 43(1):37. DOI:10.1186/s41043-024-00516-4.
(17) Schwartz A, Doucet E. Relative changes in resting energy expenditure during weight loss: a systematic review. Obes Rev 2010; 11(7):531-47. DOI:10.1111/j.1467-789X.2009.00654.x.
(18) McInnis K, Brown JL, Finlayson G, et al. Appetite Changes in Weight Regain and Weight Maintenance After Roux-en-Y Gastric Bypass. Obes Surg 2022; 32(7):1-12. DOI:10.1007/s11695-022-06061-5.
(19) Most J, Redman LM. Impact of calorie restriction on energy metabolism in humans. Exp Gerontol 2020; 133:110875. DOI:10.1016/j.exger.2020.110875.
(20) Catenacci VA, Pan Z, Ostendorf D, et al. A randomized pilot study comparing zero-calorie alternate-day fasting to daily caloric restriction in adults with obesity. Obesity (Silver Spring) 2016; 24(9):1874-83. DOI:10.1002/oby.21581.
(21) Stekovic S, Hofer SJ, Tripolt N, et al. Alternate Day Fasting Improves Physiological and Molecular Markers of Aging in Healthy, Non-obese Humans. Cell Metab 2019; 30(3):462-476.e6. DOI:10.1016/j.cmet.2019.07.016.
(22) Busetto L, Bettini S, Makaronidis J, et al. Mechanisms of weight gain. Eur J Int Med 2021; 93:3-7.
(23) Aronne LJ, Hall KD, Jakicic MJ, et al. Describing the Weight-Reduced State: Physiology, Behavior, and Interventions. Obesity (Silver Spring) 2021; 29(Supp. 1):S9-S24. DOI:10.1002/oby.23086.
(24) Rosenbaum M, Goldsmith RL, Haddad F, et al. Triiodothyronine and leptin repletion in humans similarly reverse weight-loss-induced changes in skeletal muscle. Am J Physiol Endocrinol Metab 2018; 315(5):E771-E779. DOI:10.1152/ajpendo.00116.2018.
(25) Löffler MC, Betz MJ, Blondin DP, et al. Challenges in tackling energy expenditure as obesity therapy: From preclinical models to clinical application. Mol Metab 2021; 51:101237. DOI:10.1016/j.molmet.2021.101237.
(26) Bilski J, Pierzchalski P, Szczepanik M, et al. Multifactorial Mechanism of Sarcopenia and Sarcopenic Obesity. Role of Physical Exercise, Microbiota and Myokines. Cells 2022; 11:160. doi.org/10.3390/cells11010160.
(27) Hunter GR, Singh H, Carter SJ, et al. Sarcopenia and Its Implications for Metabolic Health. J Obes 2019; 8031705. DOI:10.1155/2019/8031705.
(28) Caturano A, Amaro A, Berra CC, et al. Sarcopenic obesity and weight loss-induced muscle mass loss. Curr Opin Clin Nutr Metab Care 2025; 28:339-350. DOI:10.1097/MCO.0000000000001131.
(29) Kokura Y, Ueshima J, Saino Y, Maeda K. Enhanced protein intake on maintaining muscle mass, strength, and physical function in adults with overweight/obesity: a systematic review and meta-analysis. Clin Nutr ESPEN 2024; 63:417-426.
(30) Smith GI, Yoshino J, Kelly SC, et al. High-protein intake during weight loss therapy eliminates the weight-loss-induced improvement in insulin action in obese postmenopausal women. Cell Rep 2016; 17:849-861.
(31) Batsis JA, Batchek DJ, Petersen CL, et al. Protein supplementation may dampen positive effects of exercise on glucose homeostasis: a pilot weight loss intervention. Nutrients 2023; 15(23):4947. DOI:10.3390/nu15234947.
(32) Hunter GR, Bickel CS, Fisher G, et al. Combined aerobic/strength training and energy expenditure in older women. Med Sci Sports Exerc 2013; 45(7):1386-93. DOI:10.1249/MSS.0b013e3182860099.
(33) Bąk-Sosnowska M, Białkowska M, Bogdański P, i wsp. Zalecenia kliniczne dotyczące postępowania u chorych na otyłość 2024. Stanowisko Polskiego Towarzystwa Leczenia Otyłości. Medycyna Praktyczna. Wydanie specjalne, Wrzesień 2024.
(34) Mousavi A, Shojaei S, Azarboo A, et al. The role of glucagon-like peptide-1 receptor agonists in weight regain treatment or prevention after bariatric surgery: a systematic review and meta-analysis. Eat Weight Disord 2025; 30(1):70. DOI:10.1007/s40519-025-01770-z.
(35) Çalık Başaran N, Dotan I, Dicker D. Post metabolic bariatric surgery weight regain: the importance of GLP-1 levels. Int J Obes (Lond) 2025; 49(3):412-417. DOI:10.1038/s41366-024-01461-2.
(36) Wharton S, Yin P, Burrows M, et al. Extended-release naltrexone/bupropion is safe and effective among subjects with type 2 diabetes already taking incretin agents: a post-hoc analysis of the LIGHT trial. Int J Obes (Lond) 2021; 45(8):1687-1695. DOI:10.1038/s41366-021-00831-4.
(37) Dechelotte P, Breton J, Trotin-Picolo C, et al. The Probiotic Strain H. alvei HA4597® Improves Weight Loss in Overweight Subjects under Moderate Hypocaloric Diet: A Proof-of-Concept, Multicenter Randomized, Double-Blind Placebo-Controlled Study. Nutrients 2021; 13:1902. doi.org/10.3390/nu13061902.
(38) Kang CH, Jung ES, Jung SJ, et al. Pasteurized Akkermansia muciniphila HB05 (HB05P) Improves Muscle Strength and Function: A 12-Week, Randomized, Double-Blind, Placebo-Controlled Clinical Trial. Nutrients 2024; 16:4037. doi.org/10.3390/nu16234037.