An integrated approach to manage class 3 obesity: A case study

Babak Esmealy¹, Leyla Esmealy²

¹ Department of Sport Physiology, Tabriz University, Tabriz, Iran

² Department of Cardiology, Tabriz University of Medical Sciences, Tabriz, Iran

Abstract

Obesity is a chronic health problem with alarmingly increasing prevalence. It can lead to the most critical healthcare challenges in a near future. The case of this study was a 38 year-old women with a body mass index (BMI) of almost 45 kg/m², severe class 3 obesity, and several obesity-related complications. Obesity is a multifactorial problem and hence, multi-component interventions (consisted of cognitive-behavioral therapy, physical activity, calorie restriction, and Rosa canina seed extract supplementation) are necessary for its effective management. The multi-component intervention of this study reduced the patient's weight by 44 kg and improved her metabolic parameters. The integrated multi-component intervention of this study is effective in managing obesity and reducing BMI, body fat mass, and heart disease risk factors.

Keywords: Obesity, Weight loss, Lifestyle modification, Rosa canina.

INTRODUCTION

Obesity, defined as a body mass index (BMI) of more than 30 kg/m², is a major public health issue that its prevalence is alarmingly increasing [1]. It is a significant predictor of early death in adulthood. Moreover, it increases the risk of chronic non-communicable diseases such as type 2 diabetes mellitus, coronary artery disease, stroke, cancer, asthma, and chronic obstructive pulmonary disease [2,3]. It is probable that in the next decade, more than 50% of adults will face obesity which will impose the heavy financial burden of 4.32 trillion dollars on the world [4].

Unhealthy lifestyle, reduced physical activity, and unhealthy eating, such as the consumption of high-carbohydrate foods, are the main causes of the current obesity epidemic [5]. There are different strategies for obesity management, including restricted calorie intake, physical activity, lifestyle modification, medication therapy, and surgery [6]. The successful long-term management of obesity also depends on the effective management of the psychosocial variables that have significant relationship with obesity, including self-esteem, quality of life, and stressful life events. Therefore, obesity management guidelines state that obesity management approaches should be interdisciplinary [7,8]. These programs should include psychological interventions such as psychoeducation, cognitive-behavioral therapy (CBT), interpersonal interventions, systemic-strategic therapy, and psychodynamics [9,10]. A study also highlighted the necessity of long-term and combined interventions for weight management [11]. Combined obesity management interventions are also associated with closer patient adherence [8].

Complementary therapies such as herbal nutrients may also be helpful in obesity management. Rosa canina seed extract is a herbal product with high levels of antioxidants, vitamins, minerals, polyphenols, amino acids, and fatty acids [12]. It contains tiliroside that stimulates the oxidation of fatty acids and inhibits lipid accumulation in adipose cells and hence, helps effectively prevent weight gain [13,14]. It also induces the browning of white adipose tissues and increases the phosphorylation of adenosine monophosphate-activated protein kinase and hence, facilitates the anti-obesity effects of dietary plans [15]. Therefore, the inclusion of Rosa canina seed extract in obesity management programs can help improve adherence to weight management interventions and improve the effects of the other components of these programs [16].

*Corresponding author:
Leyla Esmealy
Department of Cardiology, Tabriz University of Medical Sciences, Tabriz, Iran
Email:
leylaesmealy@gmail.com

A study showed that aerobic exercises combined with Rosa canina seed extract supplementation can reduce weight and risk of obesity by promoting the regulation of irisin and adipolin [17]. However, we could not find any study into the effects of an integrated approach containing Rosa canina seed extract on weight management. Therefore, the present study was conducted to assess the effects of an integrated approach (consisted of CBT, physical activity, calorie restriction, and Rosa canina seed extract supplementation) on the management of class 3 obesity.

CASE PRESENTATION

This case study was conducted from March 2022 to March 2023 in Tabriz, Iran. The case was a 38 year-old woman with a BMI of almost 45 kg/m². Her medical history, physical examinations, and laboratory tests showed that she had hypothyroidism, iron deficiency anemia, and a history of one pregnancy complicated with deep vein thrombosis in the lower limb that required the daily intake of subcutaneous enoxaparin sodium 40 mg for six months. The patient also mentioned the history of affliction by hypertension for five years, the history of psoriasis, and no history of substance abuse and smoking. She used captopril 25 mg twice daily for hypertension management and levothyroxine 0.1 mg once daily for hypothyroidism management. She was from a low-income family and had strong social support. She had referred to several specialists for obesity management but had abandoned her obesity management programs after a while. She referred to a gym, where the second author worked in, to reduce her weight and improve her health. At the beginning, a three-day dietary reminder was given to her and then, a dietary plan with restricted calorie intake (1500 calorie per day) was given for two weeks. After two weeks, she lost two kg and seemed to have good adherence to the plan. Then, the main intervention was implemented for her.

Intervention

The main intervention of the study was an integrated multi-component approach to manage class 3 obesity that consisted of CBT, physical activity, restricted calorie intake, and Rosa canina seed extract supplementation (Figure 1). Initially, the patient consent was obtained, primary examinations were performed, weight, height, and waist circumference were measured, waist-hip ratio was calculated, and body composition analysis and blood tests were performed (Table 1).

Table 1: The outcomes of the study before, six months, and twelve months after the intervention onset

| Outcomes	Before	6 month after	12 month after
Wight (Kg)	127	102	83
Height (cm)	168	—	—
BMI (Kg/m²)	45	36	28
Waist circumference (cm)	118	100	86
Waist-hip ratio (cm)	1.7	0.96	0.77
Total fat mass (kg)	68.58	49.83	26.07
Body fat percentage	54	49	33
Total lean body mass (kg)	58.40	52.17	56.93
Systolic blood pressure (mm Hg)	162	148	125
Diastolic blood pressure (mm Hg)	91	89	77
Heart rate (beats/min)	95	78	75
Total cholesterol (mg/dL)	230	194	168
Low-density lipoprotein (mg/dL)	170	120	109
High-density lipoprotein (mg/dL)	31	42	54
Triglycerides (mg/dL)	187	165	130
Glucose (mg/dL)	122	112	91
Erythrocyte sedimentation rate (mm/hr)	22	19	12
C-reactive protein (mg/L)	2/13	1/7	0/57
Irisin (µg/ml)	114	122	148
Adipolin (µg/ml)	401	414	509
Thyroid stimulating hormone (mIu/L)	4.10	4.19	4.26
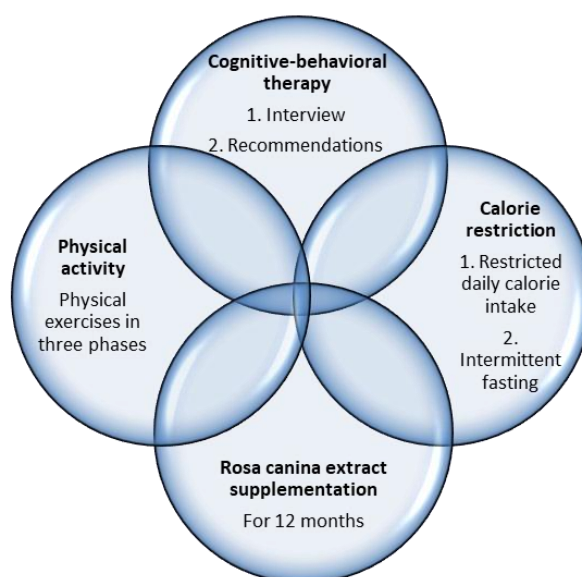
Figure 1: The schematic model of the study intervention

CBT

Initially, a home visit was made to introduce the members of the research team and the intervention to the patient and perform initial assessment of her diet. Then, biweekly thirty-minute home visits were made. During the visits, the patient's eating and behavioral habits were assessed through questions such as, "Where do you usually eat your food?", "What foods do you prefer to eat?", "How much time does it take for you to eat your meal?", "Do you allocate a certain time to eating?", "Does any thought hit your mind during eating?", "Do you consider yourself an angry, alone, anxious, impatient, or depressed person?", "Do you have any motivation for weight loss?", "Do you know the importance of weight loss?", and "Do you feel this plan would be helpful to reduce your weight?" Then, recommendations about lifestyle modification, healthy eating, physical activity, and consumption of fruits and vegetables as well as explanations about the risks and the complications of obesity and her BMI and obesity class were provided to the patient. She was also informed about the results of her body composition analysis to increase her awareness of her body fat and fat-free body mass. Then, the Rosa canina seed extract supplement was introduced and daily prescribed since the first day of the intervention. Finally, she was provided with the opportunity to ask her questions and was ensured of the voluntariness of her participation in the study, confidentiality of her data, free of cost intervention of the study, and her easy 24-hour access to the members of the research team through telephone contact or short message service.

Physical activity

The physical activity component of the study intervention included usual aerobic exercises (such as walking on a treadmill) and resistance exercises, during which heart rate was continuously monitored using a portable heart rate monitoring system. The intensity of the exercises was determined based on the patient's personal skills and her score on the Rate of Perceived Exertion scale. The rest time interval between exercises was 60–90 seconds. Energy consumption during physical activity was calculated as follows,

Energy consumption (kilocalorie per minute) = 0.0175×Weight (kg)×METs (Metabolic equivalent task)

Accordingly, energy consumption varied from 500 to 1000 kilocalorie per day. The patient performed all exercises under the supervision of a qualified trainer. The intensity of the exercises was gradually increased according to the personal data and characteristics of the patient.

The physical exercise program consisted of three main phases. The first phase was for the first and the second three months and consisted of 12000–100000 steps per day. The second phase was for the third three months and included aerobic exercises up to 50% of the maximum age-adjusted heart rate (HRmax = 220–Age) in three five-minute sets for four days per week. The third phase was for the fourth three months and included a ten-minute warm up exercise to reach 50% of the maximum heart rate, 35-minute resistance and aerobic exercises, and four-minute cool down exercises for five days per week. The patient performed aerobic exercises through running on a home treadmill (GX 902) and performed resistance exercises through the dumbbell-free barbell squat for the lower extremities and one-kilogram dumbbells for the upper extremities (i.e., the biceps, pectorlis, deltoid, and triceps muscles). The aim of these exercises was to maintain muscle mass and reduce fat mass.

Restricted calorie intake

Primarily, the patient completed the three-day dietary reminder. Then, a moderate calorie restriction based on her target weight was determined through multiplying the target weight by thirty kilocalories per weight. Her target weight was calculated based on her BMI. From the end of the second week to the end of the intervention, she had a 1800-kilocalorie diet for five nonconsecutive days and a 1200-kilocalorie diet for two nonconsecutive days per week. The diet was designed so that 40%–55% of the calorie was obtained from carbohydrates, 15%–20% from proteins, and 20%–30% from fats. The taken calorie was 30% in the breakfast meal, 40% in the launch meal, and 30% in the dinner meal. The patient took the prescribed calorie at three main time points in a twelve-hour period, i.e., at 08:00–08:30, 12:00–13:00, and 19:00–20:00 [18].

Rosa canina seed extract supplementation

The patient received a daily drink consisted of 150 ml water and 750 mg Rosa canina seed extract. She received the drink fifteen minutes after physical exercises and received nothing else per month from two hours before to two hours after physical exercises. The drink was produced by LonierHerb Company and had the approval of the Food and Drug Administration of Iran.

Study outcomes

The primary outcomes of the study were weight, BMI, body fat mass, waist circumference, and waist-hip ratio. Secondary outcomes were body composition, heart disease risk factors, biomarkers of inflammation, irisin, and adipolin.

Outcome measurement

BMI was calculated according to the standards of the Centers for Disease Control and Prevention. Height was measured using a stadiometer with a precision of 0.5 cm (Seca, Germany), while weight was measured using a weight scale with a precision of 0.1 kg (Seca, Germany) and with the minimum possible clothes and no shoes. Body fat mass and fat-free body mass were measured using a bioelectrical impedance analysis (Tanita Body Composition Analyzer, BC-418, Korea). Waist and hip circumferences were measured using a non-elastic tape measure at the middle of the rib arc and the iliac crest. For blood testing, the patient was asked to avoid eating, drinking, smoking, and doing intense physical exercise since 22:00 and then, five ml of venous blood was taken at sitting position from the brachial vein next day at 07:00–08:00.

Heart disease risk factors were measured using the spectrophotometry method and a LipidPro analyzer with a blood sample of 5 μl. In the analyzer, the blood sample was influenced by an enzyme which led to a color change. The analyzer turned the color change into electrical signal, measured the signal, and provided the results. More saturated colors implied higher levels of lipid.

C-Reactive protein (CRP) was measured using a kit with an intra-assay CV of 1.95% and an inter-assay CV of 6.3% (Bionik company). Erythrocyte sedimentation rate (ESR) was measured using the Westergren method, in which a venous blood sample was kept at 0°C for sixty hours and then, was added to tubes with a blood-sodium citrate ratio of 0:0 and finally was evaluated.

Irisin and adipolin levels were also measured using the enzyme-linked immunosorbent assay and EASTBIOPHARMA and ZB-13231C-H9648 kits with a sensitivity of 0.023 mg/ml and a precision of less than 10%. Moreover, heart rate and blood pressure were measured using a portable heart monitoring system (Tajhiz Salamat Nikan Company, Iran). Blood pressure was measured from the right arm. All study variables were measured three times, namely before, six months, and twelve months after the intervention onset.

Ethical considerations

Current study is exempted from ethnical approval. Informed consent was obtained from the participant for participation and for reporting the findings.

Findings

Physical examination

At admission, patient's height, weight, and BMI were 168 cm, 127 kg, and 45 kg/m2 (Table 1), and she seemed obese. Her blood pressure was 162.91 mm Hg and her other vital signs were in normal range. Other physical examinations showed no abnormal findings.

Laboratory tests

At admission, the blood levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and glucose were 230, 170, 31, 187, and 122 mg/dL, respectively. ESR was 22 mm/hr, CRP was 2.13 mg/L, irisin was 114 μg/ml, adipolin was 401 μg/ml, and thyroid stimulating hormone (TSH) was 4.10 mIU/L (Table 1).

The patient lost two kg of her weight in the first two weeks of the intervention and continued to lose weight throughout the study. She also reported no increase in her blood pressure throughout the intervention. She also highlighted that although adherence to weight loss programs was difficult for her, the diverse components of the study intervention and their synergistic effects increased her motivation to adhere to the intervention.

Her weight decreased by 25 kg six months after the study intervention onset and she moved from class 3 obesity to class 2 obesity. Twelve months after the study intervention onset, her weight loss was 44 kg and she lost 90% of her fat mass. The fat mass in her body was 33% and her BMI was 28 kg/m2. Heart disease risk factors and inflammatory biomarkers also decreased. Moreover, the blood levels of her total cholesterol, LDL, HDL, triglycerides, and glucose were 168, 109, 54, 130, and 91 mg/dL, respectively. ESR was 12 mm/hr, CRP was 0.57 mg/L, irisin was 148 μg/ml, adipolin was 509 μg/ml, and TSH was 4.26 mIU/L (Table 1).

DISCUSSION

To the best of our knowledge, this was the first case study into the effects of an integrated four-component intervention on class 3 obesity. Findings revealed that our twelve-month intervention considerably reduced body weight and BMI. Previous studies showed that lifestyle modification and other weight loss interventions such as low-calorie diets were effective in reducing weight only for short periods of time and most of their participants regained the lost weight due to the difficulty of adherence to the interventions. However, multi-component interventions like our intervention can be effective for the long-term management of obesity. In agreement with our findings, a study showed that a three-component intervention consisted of CBT, physical exercise, and nutritional therapy significantly reduced weight among women with polycystic ovary syndrome [19]. CBT may improve adherence to weight loss interventions through improving individuals' knowledge about healthy weight-related behaviors and facilitating behavioral modification. Contrary to our findings, a study found that CBT had no significant effects on weight loss. This contradiction may be due to the fact that our intervention had different components including CBT, while the intervention of that study was only CBT. The Rosa canina seed extract supplementation component of our intervention might also have improved the effects of CBT. Flavonoids in Rosa canina seed extract can promote learning, memory function, and cognition, and stimulate neurogenesis in the dentate gyrus of the hippocampus. Neurogenesis is a process that has significant relationship with cognitive function. Besides, flavonoids influence the different parts of the brain, particularly the hippocampus, through inducing the expression of the brain-derived neurotrophic factor and hence, balance cognitive-behavioral functions. The antioxidant effects of Rosa canina seed extract may also influence a specific part of the

brain that is supposed to have significant role in motivation improvement and thereby, the extract enhances the effects of CBT and improves motivation for closer adherence to obesity management programs [20,21].

We also found that the integrated approach for obesity management positively improved body composition indices namely weight, BMI, waist circumference, and waist-hip ratio. This is in agreement with the findings of a study which showed the greater effectiveness of a multi-component intervention compared with dietary modification or physical exercise in effectively managing obesity-related parameters. Similarly, another study reported that moderate-intensity aerobic and resistance exercises can reduce body weight and waist circumference in individuals with overweight and obesity. The significant decrease in abdominal obesity (measured through waist circumference and waist-hip ratio) implies that the effective management of general obesity (measured through BMI) is associated with significant decrease in visceral fat. Regular resistance exercises modify body composition through stimulating muscular hypertrophy and reducing fat mass [22,23]. Aerobic exercises also increase metabolism through stimulating oxidation in muscular mitochondria to produce high amounts of adenosine triphosphate because they need high amounts of it. Moreover, these exercises inhibit biosynthetic and anabolic pathways (i.e., the synthesis of glycogen and protein) and stimulate catabolic pathways and thereby, increase glucose transfer and lipid metabolism and maintain adenosine triphosphate.

The present study provides evidence that reducing body weight and fat mass can correct lipid profile which is in line with the findings of a previous study [24]. A meta-analysis also indicated that the combination of physical exercise and dietary modification can reduce total cholesterol, triglyceride, and LDL, and increase HDL [25]. Physical activity can facilitate the use of lipid during physical exercise through increasing muscular mitochondria and oxidation capacity and inhibiting the use of glycogen. Therefore, regular physical activity should be combined with dietary modification in order to improve lipid profile.

We also found that the study intervention had positive effects on blood pressure. Reduction of fat mass, particularly atopic fat, improves the endocrine function and reduces blood pressure [26]. A meta-analysis also indicated that dynamic resistance exercises significantly reduced systolic and diastolic blood pressures among patients with hypertension. Reduced vascular stress due to physical exercise also plays significant role in reducing blood pressure.

Another finding of the study was that the integrative obesity management intervention increased the levels of irisin and adipolin. A previous study also reported the same finding [17]. During physical exercise, the production of peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha is increased in the muscles which increases the production of fibronectin type III domain-containing protein 5 and thereby, increases irisin production. Irisin enters the blood and reaches adipose cells, where it turns white fat into brown fat. Besides, the induction of tumor necrotizing factor-alpha and endoplasmic reticulum stress in obese individuals reduces the expression of adipolin gene [27,28].

This study had some limitations. First, it was conducted on a single case and hence, studies with large samples are essential to produce firmer evidence respecting the effects of integrated interventions consisted of CBT, physical activity, dietary modification, and Rosa canina extract supplementation.

CONCLUSION

This study concludes that an integrated four-component approach, consisted of CBT, physical activity, calorie restriction, and Rosa canina seed extract supplementation, has significant positive effects on the

management of class 3 obesity. It also improves cognitive and physical self-control and adherence to the obesity management intervention and a healthy lifestyle.

Conflict of interest

The authors have declared no conflict of interest.

Financial Support

None declared.

ORCID ID

Leyla Esmealy: https://orcid.org/0000-0001-8152-8082

Babak Esmealy: https://orcid.org/0000-0001-6634-1404

REFERENCES

1. Hecker J, Freijer K, Hiligsmann M, Evers S. Burden of disease study of overweight and obesity; the societal impact in terms of cost-of-illness and health-related quality of life. BMC Public Health. 2022;22(1):1-13.
2. Tiwari A, Balasundaram P. Public health considerations regarding obesity. 2021.
3. Balasundaram P, Krishna S. Obesity effects on child health. 2021.
4. Mahase E. Global cost of overweight and obesity will hit $4.32 tn a year by 2035, report warns. British Medical Journal Publishing Group; 2023.
5. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. Elsevier; 2022. p. 155217.
6. Wen X, Zhang B, Wu B, Xiao H, Li Z, Li R, et al. Signaling pathways in obesity: mechanisms and therapeutic interventions. Signal Transduction and Targeted Therapy. 2022;7(1):298.
7. Chakhtoura M, Haber R, Ghezzawi M, Rhayem C, Tcheroyan R, Mantzoros CS. Pharmacotherapy of obesity: An update on the available medications and drugs under investigation. EClinicalMedicine. 2023;58.
8. Kim S-D. Complementary and Integrative Health Approaches for Weight Management in the Obese Population: The 2018 Korea National Health and Nutrition Examination Survey. International Journal of Environmental Research and Public Health. 2021;18(15):8161.
9. Castelnuovo G, Pietrabissa G, Manzoni GM, Corti S, Ceccarini M, Borrello M, et al. Chronic care management of globesity: promoting healthier lifestyles in traditional and mHealth based settings. Frontiers in psychology. 2015;6:1557.
10. Castelnuovo G, Pietrabissa G, Manzoni GM, Cattivelli R, Rossi A, Novelli M, et al. Cognitive behavioral therapy to aid weight loss in obese patients: current perspectives. Psychology research and behavior management. 2017:165-73.
11. Lee HS, Lee J. Effects of combined exercise and low carbohydrate ketogenic diet interventions on waist circumference and triglycerides in overweight and obese individuals: a systematic review and meta-analysis. International Journal of Environmental Research and Public Health. 2021;18(2):828.
12. Vlaicu PA, Untea AE, Turcu RP, Panaite TD, Saracila M. Rosehip (Rosa canina L.) Meal as a Natural Antioxidant on Lipid and Protein Quality and Shelf-Life of Polyunsaturated Fatty Acids Enriched Eggs. Antioxidants. 2022;11(10):1948.
13. Nagatomo A, Nishida N, Fukuhara I, Noro A, Kozai Y, Sato H, et al. Daily intake of rosehip extract decreases abdominal visceral fat in preobese subjects: a randomized, double-blind, placebo-controlled clinical trial. Diabetes, metabolic syndrome and obesity: targets and therapy. 2015:147-56.
14. Nagatomo A, Nishida N, Matsuura Y, Shibata N. Rosehip extract inhibits lipid accumulation in white adipose tissue by suppressing the expression of peroxisome proliferator-activated receptor gamma. Preventive nutrition and food science. 2013;18(2):85.
15. Cavalera M, Axling U, Berger K, Holm C. Rose hip supplementation increases energy expenditure and induces browning of white adipose tissue. Nutrition & metabolism. 2016;13(1):1-9.
16. Trujillo-Garrido N, Santi-Cano MJ. Motivation and limiting factors for adherence to weight loss interventions among patients with obesity in primary care. Nutrients. 2022;14(14):2928.
17. Taherzadeh S, Rasoulian B, Khaleghi M, Rashidipour M, Mogharnasi M, Kaeidi A. Anti-obesity effects of aerobic exercise along with Rosa canina seed extract supplementation in rats: The role of irisin and adipolin. Obesity Research & Clinical Practice. 2023.
18. Liu D, Huang Y, Huang C, Yang S, Wei X, Zhang P, et al. Calorie restriction with or without time-restricted eating in weight loss. New England Journal of Medicine. 2022;386(16):1495-504.
19. Jiskoot G, Timman R, Beerthuizen A, Dietz de Loos A, Busschbach J, Laven J. Weight reduction through a cognitive behavioral therapy lifestyle intervention in PCOS: the primary outcome of a randomized controlled trial. Obesity. 2020;28(11):2134-41.
20. Neshatdoust S, Saunders C, Castle SM, Vauzour D, Williams C, Butler L, et al. High-flavonoid intake induces cognitive improvements linked to changes in serum brain-derived neurotrophic factor: Two randomised, controlled trials. Nutrition and healthy aging. 2016;4(1):81-93.
21. Mármol I, Sánchez-de-Diego C, Jiménez-Moreno N, Ancín-Azpilicueta C, Rodríguez-Yoldi MJ. Therapeutic applications of rose hips from different Rosa species. International journal of molecular sciences. 2017;18(6):1137.
22. Gonzalez-Gil AM, Elizondo-Montemayor L. The role of exercise in the interplay between myokines, hepatokines, osteokines, adipokines, and modulation of inflammation for energy substrate redistribution and fat mass loss: a review. Nutrients. 2020;12(6):1899.
23. Koh J-H, Pataky MW, Dasari S, Klaus KA, Vuckovic I, Ruegsegger GN, et al. Enhancement of anaerobic glycolysis—a role of PGC-1α4 in resistance exercise. Nature communications. 2022;13(1):2324.
24. Carbajo MA, Jiménez JM, Luque-de-León E, Cao M-J, López M, García S, et al. Evaluation of weight loss indicators and laparoscopic one-anastomosis gastric bypass outcomes. Scientific reports. 2018;8(1):1961.
25. Khalafi M, Sakhaei MH, Kazeminasab F, Rosenkranz SK, Symonds ME. Exercise training, dietary intervention, or combined interventions and their effects on lipid profiles in adults with overweight and obesity: a systematic review and meta-analysis of randomized clinical trials. Nutrition, Metabolism and Cardiovascular Diseases. 2023.
26. MacDonald HV, Johnson BT, Huedo-Medina TB, Livingston J, Forsyth KC, Kraemer WJ, et al. Dynamic resistance training as stand-alone antihypertensive lifestyle therapy: a meta-analysis. Journal of the American Heart Association. 2016;5(10):e003231.
27. Rahim Pour R, Mehrabani J. The effect of treadmill aerobic training on adipolin, glucose and insulin in type 2 diabetic male rats. Journal of Applied Health Studies in Sport Physiology. 2018;5(1):93-105.

28. Islam MR, Valaris S, Young MF, Haley EB, Luo R, Bond SF, et al. Exercise hormone irisin is a critical regulator of cognitive function. Nature Metabolism. 2021;3(8):1058-70.