



# The effect of a period of high-intensity interval swimming training on plasma levels of myonectin, insulin-like growth factor-1 (IGF-1), and lipid profile in overweight men

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## Abstract

Myonectin is a novel myokine whose expression is influenced by both physical activity and nutrition. This study examined the effect of high-intensity interval swimming training on plasma myonectin levels, insulin-like growth factor (IGF-1), and lipid profile in overweight men. Twenty-four overweight men between 19 and 26 were randomly divided into two groups, experimental (n=12) and control (n=12). The experimental group's 8-week training program included high-intensity interval swimming three times a week. Blood samples were drawn to determine serum myonectin, IGF-1, and lipid profiles before and after the intervention. In addition, paired t-test and covariance analysis at a  $p < 0.05$  were used to analyze the data statistically. Data analysis revealed that the training protocol significantly increased serum levels of myonectin and IGF-1, while TG, TC, and HDL were significantly reduced in the experimental group compared to the control group ( $P < 0.05$ ). Evaluating the intra-group changes in myonectin, IGF-1, and BMI in the experimental group exhibited a significant difference between the mean before and after training ( $P < 0.05$ ). According to the findings, high-intensity interval swimming can affect overweight and obesity-related anthropometric indices and effectively reduce the potential risk of obesity-related diseases by influencing myonectin and IGF-1 levels.

**Keywords:** Myokine, myonectin, IGF-1, obesity and overweight, lipid profile

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## 1. Introduction

The prevalence of overweight and obesity is increasing significantly in both developed and developing countries and is regarded as the most significant threat to global health [1]. The results indicate that childhood obesity is a reliable predictor of adult obesity. Being overweight or obese increases the risk of coronary heart disease, type 2 diabetes, strokes, dyslipidemia, and several types of cancer. Lean body and muscle mass are the primary metabolic regulators [2]. Through the secretion of myokine, skeletal muscles communicate with other tissues. Among these hormones are interleukins, irisin, myostatin, myonectin, and insulin-like growth factor 1 (IGF-1). Myonectin causes insulin sensitivity, reduces weight, increases oxygen consumption, and improves glucose homeostasis [3]. Myonectin, also known as C1q/Tnf-Related Protein Isoform 15 (CTRP15), is a recently discovered myokine whose expression is influenced by physical activity and nutrition, increasing the extraction of plasma-free fatty acids by adipose tissue and liver by increasing the expression of fatty acids transporters [4]. Myonectin also mediates between skeletal muscle and other metabolic organs, such as adipose tissue and liver, and regulates and coordinates the

body's metabolism [5]. Most studies have demonstrated a correlation between elevated levels of myonectin, increased extraction of free fatty acids, and increased expression of lipid-transfer proteins in lipocytes [6]. Furthermore, increased cyclic adenosine monophosphate (cAMP) and intracellular calcium are additional factors influencing myonectin expression changes. Plasma myonectin levels are typically low in the fasting state and rise two hours after consuming glucose or fat. The findings indicate that myonectin levels are negatively correlated with obesity. By phosphorylating AMP-activated protein kinase (AMPK) and calling the glucose carrier, myonectin increases glucose uptake and stimulates fatty acid oxidation [7]. Free radical production is increased when the production and function of myonectin are disrupted. The imbalance of oxidants and antioxidants can activate the P38-MAPK pathway. This mechanism deactivates insulin receptors and heightens insulin resistance [8]. According to the results of several studies, increased intracellular calcium ion levels following exercise may increase myonectin expression in the muscles [9]. In other studies, sedentary people have been found to exhibit decreased myonectin levels, whereas sports can increase myonectin levels in these individuals [6]. Insulin-like growth factor (IGF-1) is regarded as an additional

factor promoting muscle growth. Along with growth hormone, insulin-like growth factor (IGF-1) is the most significant anabolic hormone known to cause the natural growth of bones and tissues. In response to growth hormone stimulation, the liver, skeletal muscles, and many other tissues secrete IGF-1. A substantial amount of IGF-1 in the blood is bound to its carrier proteins, and the interaction between IGF-1 and these carrier proteins determines its physiological effects. IGF-1 participates in cell division, differentiation, and apoptosis [10]. Following binding to insulin receptors, this hormone phosphorylates Phosphatidylinositol 3-kinase (PI3K) and Akt. Akt also activates the crucial protein mammalian target of rapamycin (mTOR), and the continuation of this crucial pathway ultimately results in the synthesis of new proteins in the ribosome [11]. Physical activity-induced muscle contraction (spasm) increases the gene expression of myonectin and stimulates the hypothalamus to secrete growth hormone. The liver and muscles produce Insulin-like growth factor (IGF-1) when growth hormone is secreted [12]. In addition to regulating glucose metabolism and lipid and energy balance, myonectin helps regulate insulin sensitivity effectively. After four weeks of resistance exercise, Shahidi et al. found no significant changes in serum myonectin levels or IGF-1; however, myonectin levels increased significantly after six weeks [5]. In contrast, Moein Farsani et al. [13] concluded that an 8-week resistance exercise regimen decreases myonectin levels. Safarzadeh et al. also reported that resistance training led to a significant increase in plasma myonectin levels, which in turn led to a significant decrease in weight, BMI, body fat percentage, and plasma total cholesterol levels [14].

High-intensity interval training (HIIT), comprising very high-intensity interval activities and active rest periods of low intensity, is one of the most important protocols in sports. HIIT is a highly efficient form of exercise that stimulates numerous metabolic adaptations resulting from regular and endurance training [15]. According to the obtained results, changes in myonectin gene expression following a period of physical activity are inconsistent with previous research. HIIT, on the other hand, activates the aerobic and anaerobic systems, increasing metabolite extraction and enhancing the state of the metabolism. In addition, myonectin contributes to improving metabolic homeostasis, as indicated by research. The combination of these two factors appears to improve obesity and overweight conditions. Thus, this study aimed to evaluate the changes in plasma myonectin levels, IGF-1 levels, and lipid profiles of overweight men following a high-intensity interval swimming training period.

## 2. Materials and methods

The current study was semi-experimental with pre-and post-tests, a control group, and field and laboratory research. This study's statistical population consisted of non-athletic male students aged 19 to 26 randomly selected based on the inclusion criteria. The objectives and conditions of the study were explained to the participants, who then signed the consent form before participation. Eventually, they were referred to a specialist, and permission was granted for their participation in the study. Using the Cochran formula, 24 of Rezaeimanesh et al., 2022

42 eligible volunteers were selected to participate in regular exercise programs and randomly divided into experimental (n=12) and control (n=12) groups. The inclusion criteria included swimming proficiency, a body mass index (BMI) of more than 25kg/m<sup>2</sup>, a lack of regular sports activity during the previous six months, good health, no history of taking drugs affecting the variables, absence of smoking, absence of sleep disorders, cardiovascular, liver, kidney, and respiratory diseases. The exclusion criteria were absence from more than two sessions, illness, and lack of consent to continue cooperation. We measured height, weight (with a stadiometer and scales), and body mass index (BMI) by dividing weight in kilograms by the square of height in meters. All study participants were instructed to maintain their normal diet until the conclusion of the research. All medical ethics and surveillance arrangements were made with the coordination of the specialist and the patient's consent.

### 2.1. The training protocol

The participants attended the swimming pool where the training protocol was implemented one week before the start of the protocol to learn how to implement that protocol. The training program included eight weeks of high-intensity interval swimming training, comprising three sessions per week on alternate days. Each session began with a warm-up, followed by specific exercises, and concluded with a cool-down. During the warm-up phase, the participants stretched and swam slowly for 10 minutes. Specific training included 30-second high-speed swimming repetitions with a 2-minute active rest in between. The number of repetitions increased to 6 in the first and second weeks and 8 in weeks 3, 4, and 5; however, the number of repetitions increased to 10 in weeks 6, 7, and 8. Stretching movements and slow swimming were performed for 10 minutes at the end of each session to cool down and return to the initial state [16]. During the study, the control group did not engage in any regular sports activity.

### 2.2. Measurement of biochemical variables

Blood samples were collected in the laboratory before the beginning of the first training session, 48 hours after the conclusion of the last session, and after 12 hours of fasting. A specialist drew 10 ccs of blood from the antecubital vein of the forearm of each group's forearm following the hygiene procedure. An expert in the laboratory was responsible for isolating and transferring serum samples. Myonectin and IGF-1 levels were measured using an enzyme-linked immunosorbent assay (ELISA) and two ELISA kits (BT Lab, China & Diasorin, Italy). Moreover, a Pars Azmoun kit was used to measure lipid profile indices.

### 2.3. Statistical method

The Shapiro-Wilk test was used to determine whether or not the data distribution was normal, and the Levon test was used to investigate the equivalence of variance. After assuring that the data were normal, the statistical test of covariance (ANCOVA) and t-pair were used at P<0.05 level. Data analysis was performed via SPSS software version 23.

## 3. Results and Discussions

As shown in Table 1, there was no statistically significant difference ( $P>0.05$ ) between the subjects' height, weight, and BMI variables in the experimental and control groups at the pre-test. After eight weeks of high-intensity interval swimming training, there was a statistically significant difference ( $P<0.05$ ) in resting myonectin levels (Figure 1). According to the intragroup changes, there was a significant difference between the experimental group's mean before and after training ( $P<0.05$ ). Moreover, the evaluation of IGF-1-related data revealed a significant increase after exercise intervention ( $P<0.05$ ) (Figure 2). Based on the intragroup comparisons, there was a significant difference ( $P<0.05$ ) between the experimental group's mean before and after exercise.

There was a significant difference in TG, TC, and HDL indices change between the two groups following the exercise intervention ( $P<0.05$ ). However, there was no significant difference between the LDL index of the two groups ( $P>0.05$ ). According to intragroup changes, all indices related to lipid profile (TG, TC, LDL, and HDL) show a significant difference between the mean values before and after training ( $P<0.05$ ) (Table 3). Based on the results, after eight weeks of HIIT, plasma myonectin levels and IGF-1 increased in overweight men. This increase led to a substantial decrease in body weight and body composition. The levels of triglyceride (TG), total cholesterol (TC), and high-density lipoprotein (HDL) also markedly decreased. However, there was no significant decrease in low-density lipoprotein (LDL). This study's findings regarding variations in plasma myonectin levels are consistent with those of Shaidi et al. [5], Safarzadeh et al. [14], and Seldin et al. [4]. Other studies, meanwhile, have reported a decrease in myonectin serum levels. Peterson et al. demonstrated that myonectin gene expression decreased in Zucker rats after nine weeks of sports activity [6]. Lim et al. also reported an increase in myonectin serum levels in young and older females after ten weeks of sports training [17].

Most of a normal-weight person's body comprises skeletal muscles [4]. Muscles, as endocrine tissue, are involved in the secretion of myokines and other physiological processes in response to physical activity; however, their underlying mechanisms remain unclear. Calcium and cAMP increase due to muscle contraction during physical activities. Increased calcium and cAMP secretion appear to increase myonectin levels; however, additional research is required to clarify its mechanism. By increasing plasma myonectin levels during physical activity, AMPK phosphorylation also increases. This method enhances the use of GLUT4 on the cell membrane surface, improves glucose absorption, and stimulates the oxidation of free fatty acids [18]. In fact, myonectin functions similarly to insulin, except that insulin levels rise immediately after a meal, whereas myonectin levels rise two hours after glucose or lipid consumption. Myonectin delays the extraction of fatty acids and glucose [7]. Several researchers demonstrated that myonectin is nutrient-sensitive as a myokine and that its activation of the

P13K/AKA/mTOR pathway is essential for developing energy intake and storage in the liver [19].

After a period of high-intensity interval swimming training, there was a significant increase in IGF-1 serum levels, as indicated by the results of the present study. This finding is consistent with the research conducted by Ansari Kalachahi et al. [20] and Amirsasan et al. [21] on IGF-1 levels. Amirsasan et al. evaluated the effect of HIIT on the fitness factor IGF-1. After eight weeks of HIIT, their results revealed a significant increase in IGF-1 levels in teenage boys [21]. Ansari Kalachahi et al. examined the impact of TRX training on IGF-1 levels in physically active women. After training, their results demonstrated an increase in IGF-1 levels [20]. Changes in the extracellular concentration of IGF-1 stimulate muscle protein synthesis via autocrine and paracrine signaling pathways. Based on an evaluation of the signaling pathways involved in the hypertrophic function of IGF-1, the enzymes AKT and P13K are regarded as key enzymes. These two enzymes regulate cell growth and proliferation and the translation of mRNAs involved in protein synthesis, which is essential for muscle hypertrophy. IGF-1 is therefore regarded as an essential mitogen and differentiation factor for skeletal muscle cells [22]. Increased IGF-1 levels in response to various sports protocols indicate its role in promoting muscle hypertrophy. The response of IGF-1 to physical activity is influenced by the type of training protocol and measuring the duration of the resting levels. Results indicate that the hypertrophy protocol stimulates IGF-1 synthesis more than the strength protocol [23]. Accordingly, it appears that high-intensity interval training (HIIT) increases the positive growth regulators (IGF-1) and decreases the negative growth regulators, thereby promoting muscle growth. A thorough analysis of all the mechanisms involved in the muscle hypertrophy pathways is required to reach a definitive conclusion.

Another affecting factor achieved through sports training, including high-intensity interval training, is the impact on body weight and BMI, which decreased significantly following high-intensity interval swimming training in the current study. This can be viewed as a method for enhancing muscle protein synthesis. Numerous studies demonstrate that exercise can improve body composition by reducing body fat and weight [24]. Various studies, both directly and indirectly, have evaluated the effect of sports activity on lipid profiles in a variety of individuals and populations, and the results of most of these studies suggest the effect of training on lipid profiles, particularly the reduction of cholesterol levels [25]. Following these findings, in the experimental group of the present study, there was a significant decrease in total cholesterol and triglyceride and an increase in HDL, but no significant reduction in LDL-C. The results indicate that increasing training volume by increasing rounds and repetitions affects the lipid profile more than increasing training intensity [26].

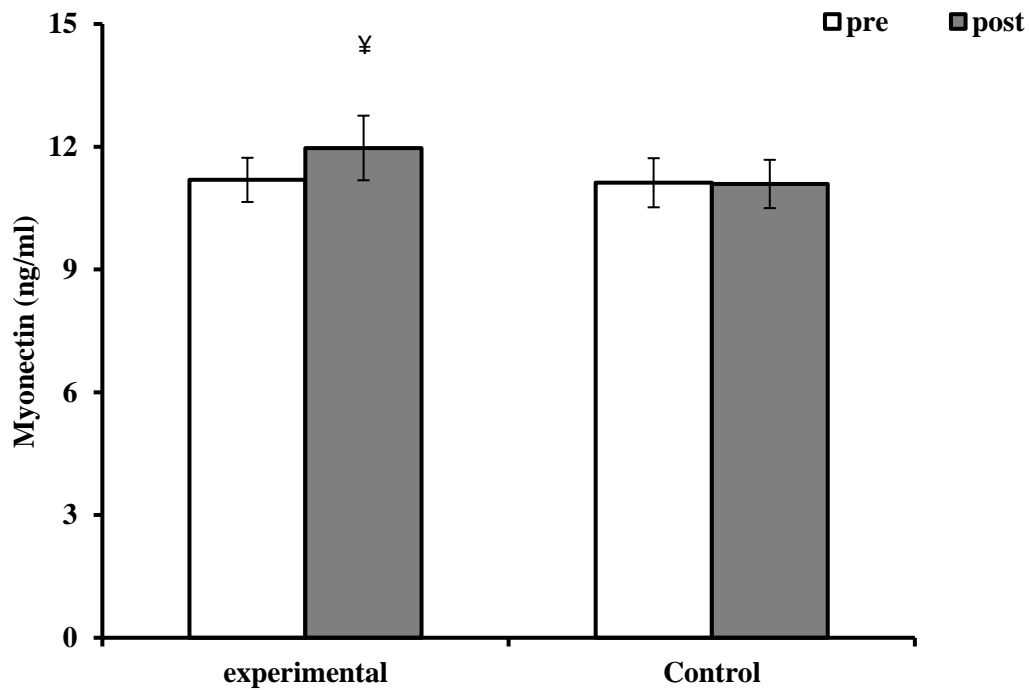
**Table 1:** Anthropometric characteristics of the subjects in pre-test.

Variables	Pre-test experimental	Pre-test control	t P	
High (cm)	178.4±6.4	176.4±5.4	0.863	0.407
Weight (kg)	87.2±10.27	85.3±6.87	1.36	0.203
BMI (kg/m <sup>2</sup> )	27.33±1.99	26.6±27.3	0.053	0.959

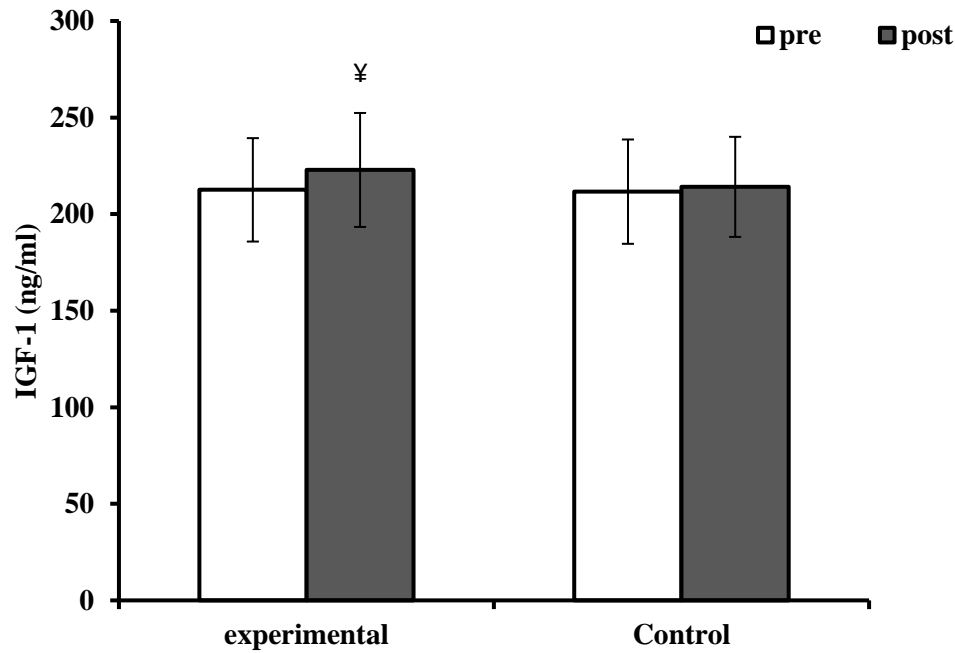
**Table 2:** Investigation of inter- and intra-group changes in general characteristics in two groups.

Variables	Group	Pre-test Mean and SD	Post-test Mean and SD	In-group t P	Intergroup F P
Weight (kg)	experimental	87.21±10.27	82.95±8.98	5.39 *0.0001	20.41 ¥0.0001
	control	85.31±6.87	85.27±6.99	0.063 0.951	
BMI (kg/m <sup>2</sup> )	experimental	27.33±1.99	26.02±1.94	5.9 *0.0001	23.29 ¥0.0001
	control	27.3±2.6	27.28±2.49	0.148 0.885	

\*In-group Statistical significance; ¥ intergroup Statistical significance



**Figure 1:** Mean (±Standard error) of Myonectin before and after training in groups. ¥ intergroup Statistical significance.



**Figure 2:** Mean ( $\pm$ Standard error) of IGF-1 before and after training in groups. ¥ intergroup Statistical significance.

**Table 3:** Investigation of inter- and intra-group changes in Physiological Indices in two groups.

Variables	Group	Pre-test Mean and SD	Post-test Mean and SD	In-group		Intergroup	
				t	P	F	P
Myonectin (ng/mL)	experimental	11.19 $\pm$ 0.54	11.97 $\pm$ 0.79	4.41	*0.001	20.07	¥0.0001
	control	11.12 $\pm$ 0.6	11.09 $\pm$ 0.59	1.41	0.189		
IGF-1 (ng/mL)	experimental	212.57 $\pm$ 26.77	222.87 $\pm$ 29.5	4.27	*0.001	7.89	¥0.011
	control	211.63 $\pm$ 27.01	214.11 $\pm$ 25.91	1.97	0.074		
TG (mg/dl)	experimental	132.1 $\pm$ 15.9	126.2 $\pm$ 13.8	4.69	*0.001	15.05	¥0.001
	control	133.1 $\pm$ 15.5	132.1 $\pm$ 15.9	2.65	*0.023		
TC (mg/dl)	experimental	161.2 $\pm$ 18.1	154.4 $\pm$ 16.2	4.75	*0.001	12.92	¥0.002
	control	162.9 $\pm$ 20	161.2 $\pm$ 17.3	1.59	0.139		
LDL (mg/dl)	experimental	70.7 $\pm$ 17.9	64.8 $\pm$ 15.2	3.59	*0.004	3.8	0.065
	control	71.8 $\pm$ 19.3	69.9 $\pm$ 18.9	1.21	0.253		
HDL (mg/dl)	experimental	35.8 $\pm$ 4.5	40.7 $\pm$ 8.3	2.46	*0.031	7.32	¥0.013
	control	36.7 $\pm$ 5.3	35.9 $\pm$ 4.7	1.75	0.107		

\*In-group Statistical significance; ¥ intergroup Statistical significance

concluded that high-intensity interval swimming training reduces body weight in overweight individuals by increasing myonectin serum levels, and ultimately contributes to weight control and improvement of body composition indices in overweight and obese individuals.

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**4. Conclusions**

According to the findings, a period of high-intensity interval swimming training effectively increased plasma myonectin and IGF-1 and decreased overweight men's lipid profile, weight, and BMI. The current study provides practical and novel information regarding changes in levels of this myokine as a result of high-intensity interval swimming training in overweight individuals; thus, it can be

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