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The Effect of Intermittent Fasting Diet and Light-Intensity Physical Activity on Serum Irisin Levels in Elderly Individuals

Aralıklı Açlık ve Hafif Yoğunluklu Fiziksel Aktivitenin Yaşlı Bireylerde Serum İrisin Düzeylerine Etkisi

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ÖZ

Amaç: Bu çalışmanın amacı, yaşlı bireylerde egzersiz ve aralıklı açlık diyetinin bazı antropometrik ölçümler ve dolaşımdaki irisin konsantrasyonu üzerindeki etkilerini değerlendirmek ve irisin ile vücut yağ yüzdesi arasındaki ilişkiyi araştırmaktı.
Araçlar ve Yöntem: Yaş ortalaması 69±9 olan 44 yaşlı gönüllü (21 erkek ve 23 kadın) rastgele 4 gruba ayrıldı; Kontrol (n=8), Bocce grubu (n=12), Aralıklı açlık grubu (n=12), Bocce ve Aralıklı açlık grubu (n=12). Kontrol grubundakiler günlük rutinlerine devam etti. Bocce grubundakiler haftanın 5 günü 2 saat boyunca Bocce Oyunu oynadı. Aralıklı açlık grubundakilere ardışık olmayan haftanın iki günü 16 saatlik besin kısıtlaması programı uygulandı. Bocce ve Aralıklı açlık grubundakilere Bocce Oyununa ilaveten besin kısıtlaması programı uygulandı. Uygulamalara 12 hafta devam edildi.
Bulgular: Uygulama öncesi ve sonrası aynı gruplar karşılaştırıldığında serum irisin değerleri arasında anlamlı bir fark bulunmadı ($p>0.05$). Vücut yağ yüzdesi, kontrol grubundaki artış dışında diğer tüm gruplarda anlamlı olarak azaldı ($p<0.05$). Vücut ağırlığı Bo ve IF gruplarında önemli ölçüde azaldı ($p<0.05$). Uygulama sonrası gruplar kontrol grubu ile karşılaştırıldığında, IF grubunun vücut yağ yüzdesinde anlamlı azalma ($p<0.05$) görülmesine rağmen, irisin seviyelerinde gözlenen benzer anlamlı farklılık muhtemelen deneysel uygulamanın sonucu olmayıp, gruplar arasındaki yaş yönünden gelişen kaçınılmaz heterojen dağılımdan kaynaklanmaktaydı. Vücut yağ yüzdesi ve vücut ağırlığı değişimi ile dolaşımdaki irisin seviyeleri arasında korelasyon bulunmadı (sırasıyla $r=0.116$, $p=0.437$; $r=-0.145$, $p=0.649$).
Sonuç: Aralıklı açlık ve Bocce müdahalesi yaşlı bireylerde vücut yağ yüzdesi ve ağırlığında azalmaya sebep olurken, serum irisin değerlerinde anlamlı bir değişikliğe yol açmadı. Bu durum, yaşlı bireylerde irisine verilen cevap süresinin daha yavaş olmasından ve/veya egzersizin süre ve yoğunluğundan kaynaklanıyor olabilir.

Anahtar Kelimeler: aralıklı açlık; bocce oyunu; irisin; yaşlı

ABSTRACT

Purpose: The aim of this study was to evaluate the effects of exercise and intermittent fasting diet on some anthropometric measurements and circulating irisin concentration and to investigate the relationship between irisin and body fat percentage in elderly subjects.
Materials and Methods: Forty-four elderly volunteers (21 men and 23 women) with a mean age of 69±9 years were randomly divided into 4 groups; Control (n=8), Bocce group (n=12), Intermittent fasting group (n=12), Bocce and Intermittent fasting group (n=12). Those in the control group continued with their normal activities. The Bocce group played Bocce for two hours five days a week. Those in the intermittent fasting group followed a 16-hour food restriction schedule on two non-consecutive days of the week. In addition to the Bocce Game, participants in the Intermittent Fasting and Bocce groups were given a food restriction regimen. The interventions were sustained for 12 weeks.
Results: There was no significant difference in serum irisin levels between the same groups before and after treatment ($p>0.05$). Body fat percentage decreased significantly in all groups except the increase in the control group ($p<0.05$). Body weight decreased significantly in Bo and IF groups ($p<0.05$). Although there was a significant decrease ($p<0.05$) in body fat percentage in the IF group compared to the control group, the similar significant difference observed in irisin levels was probably not the result of the experimental treatment, but was probably due to the inevitable heterogeneous distribution in terms of age between the groups. There was no correlation between body fat percentage and body weight change and circulating irisin levels ($r=0.116$, $p=0.437$; $r=-0.145$, $p=0.649$, respectively).
Conclusion: Intermittent fasting and Bocce intervention resulted in a decrease in body fat percentage and weight in elderly subjects, but not in serum irisin levels. This may be due to the slower response time to irisin in elderly individuals and/or the duration and intensity of exercise.

Keywords: aged; bocce game; irisin; intermittent fasting

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INTRODUCTION

In the 20th century, there has been an unprecedented increase in the average human lifespan in many countries of the world. In Türkiye, the proportion of the elderly population is increasing every year. With the increase in the elderly population, the incidence of chronic and metabolic diseases has also increased.[1] Aging is associated with several biological changes that result in a progressive decline in cognitive and physical function and consequent loss of independence and an increased risk of death. These changes are accelerated by a lifestyle characterized by low levels of physical activity, and/or excessive caloric intake and excess body weight. Therefore, lifestyle changes such as physical activity and dietary modifications that improve body composition (reducing body fat and/or increasing muscle mass) can slow the development of age-related diseases and mitigate the loss of cognitive and physical function.[2]

Inactivity can lead to many chronic diseases hence accelerating the secondary aging process and leading to premature death.[3] Regular exercise protects against the development of aging-related pathologies by increasing insulin sensitivity.[2] Therefore, physical activity and exercise are protective factors for non-communicable chronic diseases such as cardiovascular diseases, stroke, metabolic diseases such as diabetes, cancer, lung diseases, immune disorders, musculoskeletal system diseases, etc.[3]

Adipose tissue is a dynamic tissue that plays an important physiological role in maintaining health and homeostasis. White adipose tissue and brown adipose tissue are considered key endocrine organs; however, they differ functionally and morphologically. The browning of white adipose tissue produces beige adipocytes. Physical exercise leads to adipose tissue browning by increasing the levels of specific molecules such as beta- aminoisobutyric acid, irisin, and fibroblast growth factor 21 (FGF21). The central roles played by hormones in the process of browning adipose tissue highlight the importance of individual lifestyle, including circadian rhythm and diet. In contrast to the pro-inflammatory and adipose tissue-impairing effects of the Western diet, certain foodstuffs, including capsaicin and n-3 polyunsaturated fatty acids, dietary interventions such as calorie restriction and intermittent fasting promote browning and metabolic activity of white adipose tissue.[4]

Intermittent fasting is a non-pharmacological dietary intervention that slows aging. Intermittent fasting is reported to increase insulin sensitivity and reduce inflammation-related diseases and oxidative stress in the cell.[5] Today, one of the most popular types of intermittent fasting diets is the 16:8 time-restricted eating model in two days, which involves total or partial restriction of food intake during the 16 hours of the day while allowing food intake in the remaining 8 hours for two non-consecutive days of the week. This model, which does not include calorie restriction, has the potential to prevent metabolic diseases.[6]

Irisin is a peptide myokine consisting of 112 amino acids. The transmembrane protein is produced from Fibronectin type III domain 5 (FNDC5) protein.[7] Irisin is secreted mainly in skeletal muscle, especially from the nuclear parts of the perimysium and endomysium.[8] Irisin was initially identified by its ability to brown white adipose tissue.[7] It has also been shown that irisin has many other positive effects on metabolism such as increased mitochondrial biogenesis, reduction of bone loss and stimulation of bone formation, reduction of inflammation, and improved glucose tolerance.[9,10]

It is reported that circulating irisin levels in older people gradually decrease as muscle tissue mass decreases each year after the age of 50.[11] As a result, keeping irisin levels stable in the elderly is critical for controlling aging-related diseases.

It is reported that exercise has different effects on irisin levels, depending on the type and intensity of exercise.[12-14] Nutrition is another factor that influences the secretion of irisin. Unfortunately, the impact of intermittent fasting on the amounts of circulating irisin has not been definitively proven. There has been a multitude of contradictory outcomes concerning these relationships. For example, while it was reported that applying the 16:8 model, which is one of the time-restricted diets, for 12 weeks caused fluctuations in serum irisin levels,[15] another study reported that Ramadan fasting reduced irisin values.[16]

The objective of this study was to assess the impact of Bocce and intermittent fasting for two days per week on the serum irisin levels and anthropometric measurements of sedantery elderly individuals. In addition, correlations between serum irisin levels and whole-body fat composition, waist circumference measurements, and waist-hip ratio in the elderly were evaluated.

MATERIALS and METHODS

The study included 44 people, 21 men and 23 women, whose mean age was 69±9, who did not have a disease that prevented their inclusion and had voluntarily agreed to participate in the study. Based on the power analysis, it is recommended that each application group consist of twelve individuals. As a result, volunteers were divided into four groups at random. The participants in the control group proceeded with their regular daily activities (n=8). The Bocce group (Bo) where volunteers played a game of-Bocce for one hour 2 times a day, 5 days a week (n=12). The Intermittent fasting group (IF) implemented a two-day food restriction practice (16 hours on Mondays and Thursdays from 18:00 in the evening to 10:00 the next day) (n=12). The Bocce and Intermittent Fasting group (BoIF) combined the Bocce game with a food restriction program, without implementing any water restriction. The applications lasted for 12 weeks. Approval for this studywas received from AYBÜ Yeni Mahalle Training andResearch Hospital Clinical Research Ethics Committee (dated 17.02.2020 and numbered 2021-02/05).

Bocce

A special Bocce module developed for the elderly was used in the study.

The field dimensions for the elderly are arranged as 3m-2m-4.25m-4.25m-2m-3m and the ground is an artificial surface. Each team in this competitive game consists of five players, with two of them serving as substitutes. Each of the three athletes participating in the game has two balls. The balls are 7-8 cm in diameter and weigh 650gr -800gr. The target ball (pallino) made of wood is 2.5 cm and the athletes try to bring the shots close to the target ball.

Measurement of Serum Irisin Levels

In both pre- and post-application, a total of 5 ml of venous blood samples were collected from the participants, and subsequently, their serums were separated.The concentrations of serum irisin were measured using assay (ELISA) kits (Bioassay Technology Laboratory) following the instructions provided by the manufacturer.Optical density measurements of the samples were read by the standard microplate reader at a 450 nm (Heales MB580 brand ELISA reader).

Body Analysis

The body weights and body fat percentages of the subjects were measured using a body analyzer both before and after the applications (Tanita BC 730).

Statistical Analysis

Results were expressed as mean ± standard deviation. SPSS (version 22.0, IBM Corp., Armonk, NY, USA) package program was used for statistical analysis of the data. Accordingly, the One Way Anova-Tukey test was used to compare the groups, and the Paired Sample T-test was used to measure the within-group variation over time. Spearman Correlation Test was used for correlation analysis.

RESULTS

Comparison of the post-application groups with the pre-application groups showed no statistically significant difference in terms of serum irisin levels ($p>0.05$, Table 1). Comparison of the serum irisin values of the post-treatment groups with the control group showed a statistically significant increase in the IF group ($p=0.014$, Table 1). No statistically significant difference in serum irisin values was found between gender groups ($p=0.212$).

It was determined that the body fat percentage decreased statistically in the Bo, IF, and BoIF groups in the post-application measurements compared to the pre-application measurements, while it increased significantly in the control group ($p=0.013$, $p=0.001$, $p=0.024$, $p=0.007$, Table 1), respectively. In addition, the body fat percentage of the

post-treatment groups was found to be statistically significantly lower in the IF group when compared to the control group (p=0.012, Table 1).

Table 1. Comparison of group data before and after application and control group (Mean ± Standard Deviation).

	Before				After			
	Control	**Bo**	**IF**	**BoIF**	**Control**	**Bo**	**IF**	**BoIF**
n	**8**	**12**	**12**	**12**				
Age (years)	75±9	70±8.9	66±6	67.3±9				
Height (cm)	160.4±12.6	159.6±10.4	164.3±8.4	163.6±9.8				
Body weight (kg)	80±17.4	79.7±10.2	82±18.5	80.8±14.9	82±17.5	74.9±12.2*	76±19*	78±13.8
Fat percentage (%)	30.6±3	37.6±4.6	31.6±6	32.1±3.7	35.6±5*	31.9±5.3**	28.4±6.1$^{*\#}$	30.5±2.9*
Waist circumference (cm)	105.8±22.6	95.1±8.1	92.3±10.8	97.5±10.7	104±21.6	94.1±9.7	94.3±8	94.3±9.3
Hip circumference (cm)	115±17.8	109.5±13.8	102.3±12.4	107.2±9.4	110.4±17.6	109.9±10.3	103.7±10.6	102.6±14
Waist-Hip Ratio	0.92±0.13	0.91±0.11	0.9±0.1	0.92±0.1	0.94±0.09	0.86±0.09	0.9±0.1	0.92±0.1
Serum irisin level (ng/ml)	3.86±1.83	6.51±2.12	6.64±2.32	5.73±1.43	3.18±1.87	5.41±1.62	6.39±1.84$^{\#}$	4.86±2.83

The One Way Anova-Tukey test was used to compare the groups, and the Paired Sample T-test was used to measure the within-group variation over time. $^{*}p<0.05$, $^{**}p<0.001$: Comparison before and after application. $^{\#}p<0.05$: Comparison with the control group. (Bo: Bocce; IF: Intermittent fasting; BoIF: Bocce+Intermittent fasting).

Body weight decreased statistically significantly in the Bo and IF groups in the post-application measurements compared to the pre-application measurements (p=0.005, p=0.016 Table 1), respectively.

The alternation of circulating irisin level was not correlated with change in body fat percentage and body weight (r=0.116, p=0.437; r=-0.145, p=0.649, Figures 1 and 2), respectively

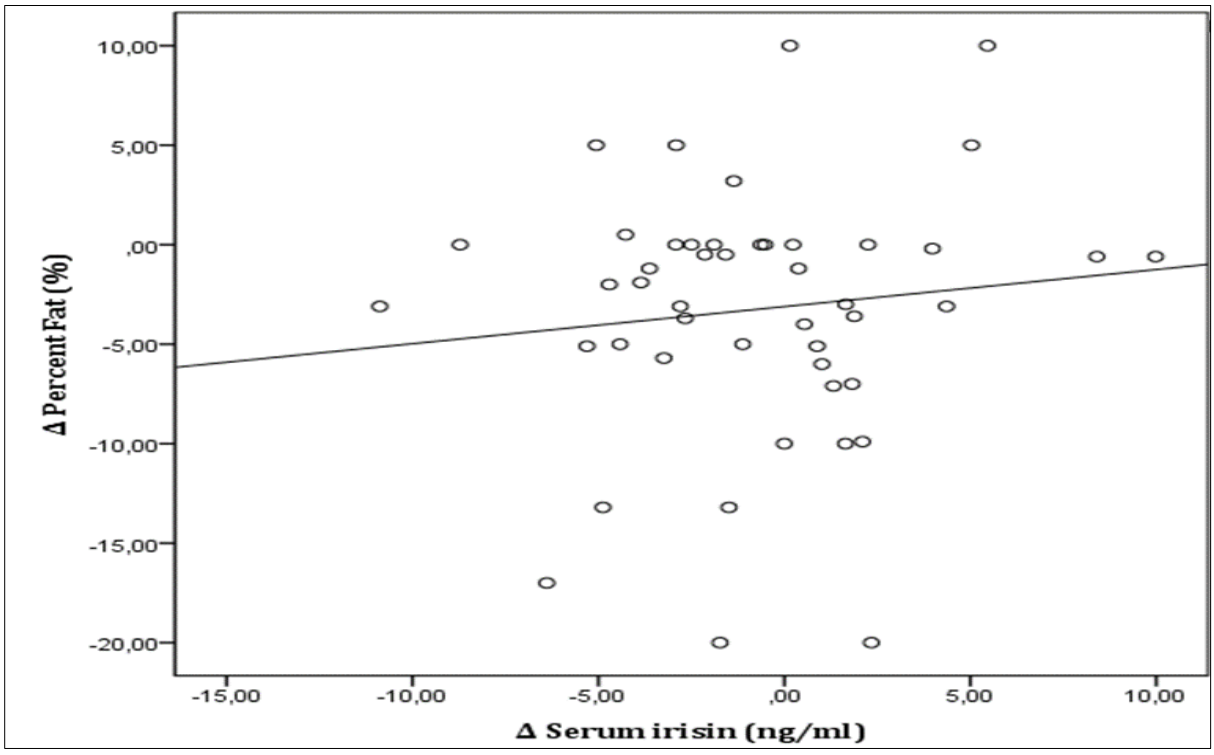

Figure 1. The relationship between circulating irisin and body fat percentage. Spearman's r=0.116, p=0.437.

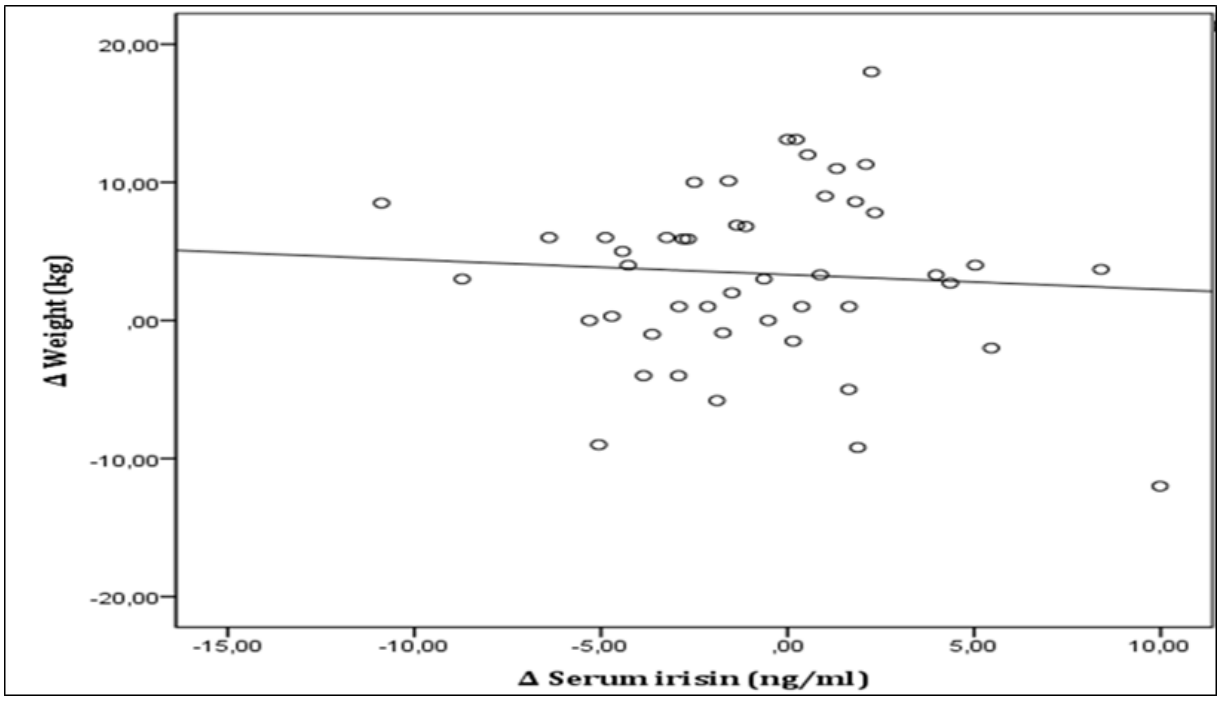

Figure 2. The relationship between circulating irisin and body weight. Spearman's r=-0.145, P=0.649.

There were no statistically significant differences seen in waist and hip circumference, as well as waist-to-hip ratio, between the groups before and after the application. Additionally, no significant differences were found between the control group and the Bo and BoIF groups after the application ($p>0.05$).

DISCUSSION

In this study, the effect of intermittent fasting and Bocce on serum irisin levels in the elderly was examined. There was no significant statistical difference observed in the irisin levels of the groups before and after treatment. It was observed that intermittent fasting and the Bocce caused a significant decrease in body fat percentage and body weight, and it was determined that the body fat percentage was significantly lower in the IF group than in the control group. No significant correlation was found between serum irisin and body fat percentages.

Despite the significant impact of diet on metabolic risk factors and the strong correlation between irisin and metabolic health, prior investigations into the potential of dietary treatments to regulate circulating irisin levels have yielded in conflicting results. A study investigating the impact of a diet's macronutrient composition on the levels of FNDC5 and irisin in mouse skeletal muscle found that a diet rich in fat and carbohydrates downregulated FNDC5 expression and resulted in a significant reduction in skeletal muscle irisin levels.[17]

A clinical study conducted on 163 patients with metabolic syndrome found a positive correlation between vegetable protein and saturated fat, and irisin levels.[18] Another study examining the effect of diet quality and diet style on irisin level found a positive correlation between the DASH (Dietary Approaches for the Prevention of Hypertension) score and irisin level. Fruit consumption has been shown to have a positive impact on the irisin levels while meat consumption is associated with a negative effect.[19] A study by Alzoughool et al. to investigate the effect of intermittent fasting on serum irisin levels reported that Ramadan fasting reduced serum irisin levels.[16] In a study by Spyridon et al., the effects of Orthodox fasting and a time-restricted diet (16:8) on irisin levels, in which daily consumption of animal foods such as meat, dairy products, and eggs are avoided during the fasting period and fish and olive oil are not consumed on certain days of the week, were examined. Orthodox fasting was reported to cause more significant increases in irisin levels than time-restricted feeding.[15]

In the present study, no significant change was observed in serum irisin values in the pre-and post-application intermittent fasting groups in the elderly, while serum irisin

values were found to be statistically higher in the post-application intermittent fasting group compared to the control group. However, it was not suggested that this difference was caused only by the intervention. The relationship between diet and irisin is influenced by various factors, including differences in diet composition, adherence to the diet, and duration of the study. The participants were given the same meals for this study to provide more conclusive evidence on the effectiveness of intermittent fasting. However, it was not recorded how much food was consumed by the participants. This particular circumstance represents one of the limitations present in the research.

Chronic exercise may cause increased circulating iris by contracting skeletal muscles[7,20] and may even offset decreases in muscle mass and strength in older adults.[21] White adipose tissue browning is an extremely dynamic process influenced by a variety of factors, including temperature, physical exercise, thyroid hormones, circadian rhythm, food components, and dietary regimens. The involvement of adipose tissue variability in the organism's metabolic health and inflammatory processes indicates that this process has a promising therapeutic effect for reducing the risk associated with many chronic diseases. It has been shown that brown and beige fat can regulate lipid metabolism with irisin in rats and humans.[22] There have been reports indicating a negative correlation between the decrease in whole body fat percentage in older persons who engage in 12 weeks of resistance exercise and the increase in serum irisin level.[23]

Due to the lower physiological serum irisin levels in older persons (>60 years), circulating irisin levels tend to rise more rapidly after training sessions compared to younger adults, particularly after intense training.24 Although exercise frequency is favorably associated with increased irisin blood levels,[25] it has been found that groups that exercise regularly do not gain equally from training.[24,26] For example, some in vivo studies using different physical exercise protocols failed to detect an association between irisin or PGC1α levels and exercise. It was observed that FNDC5 mRNA levels in the diaphragm muscles of obese Zucker rats and lean Zucker rats did not change even after 9 weeks of aerobic training on a motorized treadmill.[27]

In humans, mRNA PPARGC1A and FNDC5 levels in skeletal muscle significantly increased after 12 weeks of training. However, it was found that circulating irisin levels paradoxically decreased from 160 to 143 ng /ml.[28] In another study, it was reported that the expression of FNDC5 in human muscles did not change after an 8-week endurance training program.[29] In contrast, Morelli et al. showed higher serum irisin concentrations in individuals performing high-intensity physical activity compared to physically inactive subjects.[13] High-intensity exercise was associated with greater irisin response than low-intensity exercise at similar energy expenditure.[14] The Bocce game applied in this study did not cause significant changes in the irisin values of the subjects after the application compared to the pre-application. In the post-application values, serum irisin levels of the group playing the Bocce game were found to be higher than the control group, although not at a significant level. This could be attributed to Bocce being a low-intensity form of exercise, resulting in a slower development of the body's response to exercise in the elderly. Alternatively, it could be due to the exercise frequency not being sufficient to increase irisin levels. A study reported that irisin levels increased significantly after an 8-week resistance-training program but were not affected by aerobic training.[12] This indicates that the intensity and type of physical activity affect irisin concentrations. Therefore, to determine the impact of intermittent fasting and exercise on serum irisin levels in elderly individuals, it is important to conduct comprehensive investigations that consist of varying exercise durations based on intensity, a more limited age distribution among participants, gender-specific analysis, and a larger sample size.

The current study has a number of limitations. First, the groups formed as a result of randomization did not have a uniform age distribution because the ages of the older people in the research sample ranged widely. Furthermore, the observed disparity in irisin levels could potentially be attributed to the heterogeneous variations in daily individual activity among the groups and the differences in the mean ages of the groups, which arose as a consequence of randomization during the formation of the groups. For this reason, the after treatment values of the groups were compared with the post treatment values of the control group and the before treatment values of the same groups.

Conclusion

Lifestyle changes such as physical activity and dietary interventions in the elderly have the potential to slow the rate of development of age-related diseases by improving body composition (reducing body fat and/or increasing muscle mass). Despite the well-known benefits of physical activity, the vast majority of older adults do not engage in the minimum levels of physical activity required to stay healthy. At this time, it is critical to urge the elderly to engage in exercises other than light-intensity physical activities in order to achieve effective physiological levels.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Approval for this study was received from AYBÜ Yeni Mahalle Training and Research Hospital Clinical Research Ethics Committee (dated 17.02.2020 and numbered 2021-02/05).

Authors' Contributions

Concept/Design: HBS, SBD, FB, MSK. Data Collection and/or Pro-cessing: HBS, SBD, SN. Data analysis and interpretation: HBS, MSK, FB. Literature Search: HBS, SBD, SN, MSK, FB. Drafting manuscript: HBS, SBD, SN. Critical revision of manuscript: MSK, FB. Supervisor: MSK, FB.

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