Niğde Ömer Halisdemir Üniversitesi
Spor Bilimleri Fakültesi
BEDEN EĞİTİMİ VE SPOR BİLİMLERİ DERGİSİ

Araştırma Makalesi

ACTN3 RS1815739, PPARA RS4253778 VE IL6 RS1800795 GEN POLİMORFİZMLERİNİN VOLEYBOLCULARDA AEROBİK DAYANIKLILIK ÜZERİNE ETKİLERİNİN İNCELENMESİ

INVESTIGATION OF THE EFFECTS OF ACTN3 RS1815739, PPARA RS4253778 AND IL6 RS1800795 GENE POLYMORPHISM ON AEROBIC ENDURANCE IN VOLLEYBALL PLAYERS

Gönderilen Tarih: 28/08/2024
Kabul Edilen Tarih: 15/03/2025

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Actn3 Rs1815739, Ppara Rs4253778 ve Il6 Rs1800795 Gen Polimorfizmlerinin Voleybolcularda Aerobik Dayanıklılık Üzerine Etkilerinin İncelenmesi

ÖZ

Bu çalışmada voleybolcularda aerobik dayanıklılık ile ACTN3 rs1815739, PPARA rs4253778 ve IL-6 rs1800795 polimorfizmlerini karşılaştırmayı amaçladık. Çalışmaya, 22 voleybol sporcusu (yaş: 21.59 ± 2.70 yıl; boy: 1.87 ± 7.92 m; vücut ağırlığı: 80.99 ± 8.14 kg; vücut yağı: 12.05 ± 5.78%) gönüllü olarak katıldı. Bukkal epitel hücrelerinden DNA ekstraksiyonu ticari bir kit ile sağlandı. Genotipleme için Real-Time PCR yapıldı. Test sonuçlarının istatistiksel analizi SPSS 23 (SPSS Inc., Chicago, IL, ABD) paket programı kullanılarak yapıldı. Varyans homojenliği Levenne testi ile analiz edildi ve normal dağılım Shapiro-Wilk testi ile analiz edildi. Tüm parametreleri analiz etmek için One Way ANOVA Testi kullanıldı. Anlamlılık p<0,05'te belirlendi. ACTN3 rs1815739, PPARA rs4253778 ve IL6 rs1800795 polimorfizmleri ile aerobik performans parametreleri arasında istatistiksel olarak anlamlı bir fark tespit edilmedi (p>0,05). Bulgularda, Kohortumuzda ilgili polimorfizmler ile aerobik performans parametreleri arasında istatistiksel olarak anlamlı bir fark tespit edilmedi. Sonuç olarak, ACTN3 rs1815739, PPARA rs4253778 ve IL6 rs1800795 genleri voleybol oyuncularında aerobik dayanıklılıkta herhangi bir fark yaratmadı. Sonuçlarımızın daha ileri çalışmalarla doğrulanması gerekiyor.

Anahtar Kelimeler: Sporcu, güç, polimorfizm, voleybol

Investıgation of the Effects of Actn3 Rs1815739, Ppara Rs4253778 and Il6 Rs1800795 Gene Polymorphısm on Aerobic Endurance in Volleyball Players

ABSTRACT

In this study, we aimed to compare ACTN3 rs1815739, PPARA rs4253778 and IL-6 rs1800795 polymorphisms with aerobic endurance in volleyball players. Twenty-two volleyball players (age: 21.59 ± 2.70 years; height: 1.87 ± 7.92 m; body weight: 80.99 ± 8.14 kg; body fat: 12.05 ± 5.78%) participated in the study voluntarily. DNA extraction from buccal epithelial cells was provided by a commercial kit. Real-Time PCR was performed for genotyping. Statistical analysis of the test results was performed using SPSS 23 (SPSS Inc., Chicago, IL, USA) package program. Homogeneity of variance was analyzed by Levenne test and normal distribution was analyzed by Shapiro-Wilk test. One Way ANOVA Test was used to analyze all parameters. Significance was determined at p<0.05. No statistically significant difference was detected between ACTN3 rs1815739, PPARA rs4253778 and IL6 rs1800795 polymorphisms and aerobic performance parameters (p>0.05). In the findings, no statistically significant difference was detected between the relevant polymorphisms and aerobic performance parameters in our cohort. In conclusion, ACTN3 rs1815739, PPARA rs4253778 and IL6 rs1800795 genes did not create any difference in aerobic endurance in volleyball players. Our results need to be confirmed by further studies.

Keywords: Athlete, power, polymorphism, volleyball

INTRODUCTION

The era of sports genetics started in the early 2000s after the deciphering of human DNA structure and the discovery of the first DNA polymorphisms associated with athletic performance[1-3]. Recently, studies examining the relationship between endurance and genes in sports genetics studies have been put forward and more than 200 genetic regions related to sports genetics have been identified[4]. In addition, Alpha-Actinin-3 (*ACTN3*), Interleukin 6 (*IL*-6), Peroxisome Proliferator-Activated Receptor Alpha (*PPARA*) genes have been associated with cardiovascular endurance[5-10].

In type II muscle fibers, the alpha-actinin-3 protein is encoded by the ACTN3 gene. This protein is a structural and functional protein found in the Z-lines of muscles, in the contracting units called sarcomers. There have been a number of reviews focusing on the association of the C allele and CC genotype of the rs1815739 polymorphism of the gene with the strength phenotype. The results of those studies suggest that this polymorphism may affect many different traits such as exercise strength, injury risk, and training adaptation[11,12].

The short arm of chromosome 7 (7p15.3) is the location of *IL6*. The gene codes for IL6 protein, which is a cytokine protein for pro-inflammatory effect and myokine for anti-inflammatory effect of the muscles[13]. The molecular function of this protein makes the protein and the gene coding the protein a target biomarker for sports genetics studies. rs1800795 polymorphism within the gene affects the plasma amounts of the protein. Recent research has shown that individuals with the G allele of the rs1800795 polymorphism tend to have elevated IL6 plasma levels, which is believed to offer advantages in strength-oriented sports. Conversely, individuals carrying the C allele of the same polymorphism tend to have lower IL6 plasma levels, which is thought to be advantageous in endurance sports[14].

PPARA gene encodes a transcription factor crucial for regulating lipid, glucose, and energy homeostasis, while also governing body weight and vascular inflammation. Its expression is notably high in tissues specialized in fatty acid catabolism, such as the liver, skeletal, and cardiac muscles, albeit lower in others like the pancreas[15]. Notably, PPARA expression predominates in type I (slow-twitch) muscle fibers over type II (fast-twitch) fibers. Endurance training enhances fatty acid utilization and potentially boosts skeletal muscle oxidative capacity through PPARA-mediated gene regulation[16]. PPARA also modulates the expression of critical muscle enzymes involved in fatty acid oxidation[17]. These findings underscore PPARA's significance in adapting to endurance training, translating physiological cues from exercise into the expression of nuclear genes that encode enzymes for skeletal muscle mitochondrial fatty acid oxidation.

Given that carbohydrate and fatty acid catabolism chiefly fuel working skeletal muscles, substrate selection primarily hinges on exercise intensity and gene variants governing muscle metabolism. The G>C transversion within intron 7 of the *PPARA* gene (rs4253778; g.46630634G>C) is identified as a pivotal factor influencing response to physical activity, along with pertinent gene-environment interactions[18]. Performance in volleyball based on many characteristics such as technique, tactics as well as physical and physiological parameters. In a single volleyball competition or

training, athletes use agility to jump vertically, many times, in spikes and blocks. They perform sudden changes of direction in order to take position to the ball and position to the hit, sprint in order to meet the ball in the right place on the court, and endurance in order to adapt to these activities. Therefore, athletes need to have a good level and capacity in those and many other characteristics in order to perform much more better[19]. These physical characteristics require aerobic and anaerobic activities most of which are determined by the genetic endowment of the athletes. To have the most suitable personal training or adaptation to training, athletes must have the required genetic background.

Regarding to the literature, genetic polymorphisms effect on volleyball, which includes many skills such as speed, power and endurance[20] is a subject of research. In addition, it has been reported that the effect of muscle fiber types and the resulting explosive power on volleyball performance is 40% and 67%, respectively[21, 22]. Therefore, the aim of this study was to compare *ACTN3* rs1815739, *PPARA* rs4253778 and *IL6* rs1800795 polymorphisms with the test results of aerobic endurance in volleyball athletes.

This study may provide important information for personalized training programs to optimize the participation of athletes by examining the genetic characteristics of aerobic endurance of volleyball players. It also contributes to the sports science literature of genetic research and helps athletes make basic biologically based decisions.

MATERIAL AND METHODS

Participants

22 female volleyball players were enrolled for the study. Üsküdar University, Ethical Committee approved the study protocol (2021/14-61351342), and the study is conducted in accordance with the principles of the Declaration of Helsinki II. Written informed consent that explains the study stages and aims was signed by all participants. This work was supported by Gümüşhane University Scientific Research Organization (GÜBAP2902-21.A0310.02.01).

Sample Collection and Genotyping

DNA isolation from buccal cells was performed with a commercially available PureLink DNA isolation kit (Invitrogen, Thermo Fisher Scientific, Inc.). Genotyping of *ACTN3* rs1815739, *PPARA* rs4253778, and *IL6* rs1800795 polymorphisms was performed with specific primers using StepOnePlus (Thermo Fisher Scientific, Inc.) Real-Time PCR device and Taqman Genotyping Mater Mix genotyping kits according to manufacturers' protocols (Thermo Fisher Scientific, Inc.). In summary, 5 µl Master Mix (Applied Biosystems, Foster City, CA), 3.5 µl nuclease-free H_2O (Thermofisher, USA), 0.5 µl gene region specific assays and finally 1 µl DNA were added for a total reaction volume of 10 µl.

Yo-Yo IRT 1

A sound system and funnel were used for Yo-Yo IRT1 of volleyball athletes, athletes were asked to run as far as they could run in a distance of 20 metres, athletes who did

not reach the finish points in the desired time were given an error warning, the test was terminated in the second error. The runs were performed in a sports hall[23].

Statistical Analysis

SPSS 23 (SPSS Inc., Chicago, IL, USA) package program was used for statistical analysis of the findings. The homogeneity of variance of the data was analyzed by Levence Test and normal distribution was analyzed by Shapiro-Wilk Test. One Way ANOVA test was used to analyze all parameters. Statistical significance was tested as $p<0.05$.

RESULTS

TT genotype of the *ACTN3* rs1815719, CC genotype of the *PPARA* rs4253778, and the GG genotype of the *IL6* rs1800795 were detected as dominant genotypes in our cohort. When we count the alleles, T allele for *ACTN3* rs1815719, C allele for *PPARA* rs4253778 and G allele for *IL6* rs1800795 polymorphisms were higher than the other alleles. Table 1 lists the genotype and allele numbers and percentages of the polymorphisms.

Tablo 1. Genotype and Allele Distrubition of the Volleyball Players (n=22)

	ACTN3 rs1815739 Polymorphism				
	Genotype			Allelic Frequency	
	CT	TT	TT	C	T
Volleyball players	5	5	12	15	29
Percentage	22.7%	22.7%	54.5%	36.09%	65.91%
	PPARA rs4253778 Polymorphism				
	Genotype			Allelic Frequency	
	GG	CG	CC	G	C
Volleyball players	0	6	16	6	38
Percentage	0%	27.3%	72.7%	13.64%	86.36%
	IL6 rs1800795 Polymorphism				
	Genotype			Allelic Frequency	
	GG	CG	CC	G	C
Volleyball players	12	8	2	32	12
Percentage	54.5%	36.4%	9.1%	72.73%	27.27%

Table 2. The Average Yo-Yo IRT 1 (M), Standart Deviation (Sd), f And p Values of Volleyball Players for *ACTN3* Rs1815739 Polymorphism

	n	$\bar{x}$	sd	f	p
YoYo IRT 1(m)	CC	608.00	142.54	0.18	0.83
	CT	640.00	135.64		
	TT	646.66	107.64		

*Significant at $p<0.05$ level $\bar{x}$: arithmetic mean sd: standard deviation.

Table 3. The Avarage Yo-Yo IRT 1(M), Standart Deviation (Sd), f and p Values of Volleyball Players for *PPARA* Rs4253778 Polymorphism

	n	$\bar{x}$	sd	f	p
Yo-Yo IRT 1 (m)	GG	0.00	0.00	0.06	0.80
	CG	646.66	96.05		
	CC	632.50	126.67		

*Significant at $p<0.05$ level $\bar{x}$: arithmetic mean sd: standard deviation.

Table 4. The Avarage Yo-Yo IRT 1 (M), Standart Deviation (Sd), f and p Values o Volleyball Players for *IL6* Rs1800795 Polymorphism

	n	$\bar{x}$	sd	f	p
Yo-Yo IRT 1 (m)	GG	626.66	136.80	0.16	0.84
	CG	640.00	95.61		
	CC	680.00	113.13		

*Significant at p<0.05 level $\bar{x}$: arithmetic mean sd: standard deviation.

DISCUSSION

The aim of this study is to determine the effects of *ACTN3* rs1815739, *PPARA* rs4253778, and *IL6* rs1800795 polymorphisms on aerobic endurance in volleyball players.

Upon examining the initial findings of the study, no significant difference was found between the aerobic performance of volleyball players and *ACTN3* rs1815739 polymorphisms (Table 2). Eken et al., (2021)[24] reported that the TT genotype is only associated with endurance in some sports, which supports our findings[24]. Additionally, this protein seems to be involved in regulating muscle metabolism[25]. TT genotype carriers lack α-actinin-3 and are associated with oxidative type I fiber dominance. Statistical analysis of the study shows that the TT allele is more prevalent in the *ACTN3* rs1815739 gene. This characteristic of the *ACTN3* TT genotype seems to confer a predisposition. Ruiz et al. (2011)[21] recently gathered genotypic data from the top 66 male and female volleyball players, juxtaposing them with the outcomes of strength and power assessments (SJ and CMJ) [21]. Similar investigations by other authors have suggested that ACTN3 expression doesn't directly influence the strength and power metrics of volleyball players. Jumping prowess holds paramount importance in volleyball performance, intricately woven into defensive maneuvers (such as blocking), offensive strategies, and serves. Given that a strong jumping ability is a cornerstone of success for most volleyball players, training regimes often prioritize its enhancement. Consequently, the genetic predisposition may not yield discernible differences in this critical phenotype for volleyball, particularly when assessing jumping capability. Furthermore, prior studies have failed to establish a significant correlation between the *ACTN3* rs1815739 polymorphism and sprint/power or endurance performance[26,27].

Studies conducted using animal models[28,29] have shown that mice lacking α-actinin-3, as seen in the *ACTN3* knockout model, exhibit decreased activity in the anaerobic glycolytic pathway while demonstrating increased activity in the aerobic oxidative pathway.

Although the results of the *ACTN3* gene did not reach statistical significance in Yo-Yo distances, reaching the TT level has shown to be effective aerobically. Studies in the literature showing significant results in anaerobic parameters are thought to reflect the effectiveness of anaerobic parameters in volleyball.

Upon examining the second finding of the study, statistically significant results in both negative and positive directions could not be reached between *PPARA* rs4253778 polymorphisms and aerobic performance (Table 3). When examining the literature, no study related to *PPARA* rs4253778 in volleyball players was encountered.

There is compelling evidence suggesting that the *PPARA* gene G/C polymorphism correlates with endurance performance in sports[30]. Specifically, the G allele is linked with elevated fatty acid oxidation within skeletal muscles and a higher proportion of type I slow-twitch muscle fibers[31].

Petr et al. (2019)[32] stated that carrying *PPARA* alleles may provide partial benefit to achieve elite sports status, but if they are absent, they will not prevent reaching elite status. On the other hand, they stated that the G allele of *PPARA* rs4253778 supports success in endurance athletes[32].

In their investigation exploring the connection between the *PPARA* gene G/C polymorphism and endurance sports, Lopez-Leon et al. (2016)[30] analyzed data from 760 endurance athletes alongside 1792 control subjects. Their findings revealed that proficient endurance athletes exhibited a greater frequency of the GG genotype and G allele compared to the control group[30].

PPARα intron 7 G/C and *PPARGC1A* Gly482Ser polymorphisms have been found to be associated with aerobic activities. The low frequency of the *PPARGC1A* Ser482 allele and the high frequency of the *PPARα* GG genotype have been shown to be associated with endurance activation exercises[33].

Statistically significant results could not be achieved in the *PPARA* gene Yo-Yo distances, and when examining the literature, the lack of the GG genotype in volleyball players strengthens the idea that the sport is more anaerobic.

Akkoç et al. (2020)[10] associated *IL6* polymorphisms with athletic performance[10], while Keller et al. (2005)[34] stated that exercise increases *IL6* receptor production in human skeletal muscle[34]. It is believed that *IL6* plays a crucial role as a key mediator in the inflammatory response necessary for exercise-associated muscle damage repair.

The final finding of the study revealed no statistically significant difference in aerobic performance between *IL6* rs1800795 polymorphisms in both negative and positive directions (Table 4). The influence of a singular measurement on anabolic/catabolic hormones and inflammatory cytokines has predominantly been scrutinized within individualized endurance-based sports. Consequently, our study delved into athletes engaged in team sports, with a particular emphasis on elite volleyball players. Volleyball stands out as a widely embraced team sport for both males and females, encompassing a blend of strength, aerobic, and anaerobic attributes.

Tuna et al. (2022)[35] investigated the impact of the *IL6* rs1800795 polymorphism among Turkish swimmers, contrasting their findings with those of sedentary individuals. Their study involved 75 participants, comprising 45 professional swimmers and 30 healthy sedentary individuals forming the control group. Results unveiled a heightened prevalence of the GG genotype and G allele in both swimmers and the control cohort. Nonetheless, no statistically significant variance emerged in the *IL6* rs1800795 polymorphism between swimmers and controls. Additionally, no significant difference was found when comparing swimming styles, distances, and genotypes[35]. Upon reviewing the literature, Keller et al. (2005)[34] found that infusion of *IL6* increases the production of IL6 receptor protein, suggesting that *IL6* may enhance IL6 receptor production at a post-transcriptional level[34]. Eliakim et al. (2013)[36] investigated the effect

of training on hormonal and inflammatory response to a single volleyball practice session in elite female volleyball players. They found that along with improvements in strength and anaerobic and aerobic characteristics, training reduced the exercise-induced catabolic and inflammatory response[36].

Upon evaluating the data in our study, there was no statistically significant difference ($p>0.05$) in aerobic endurance between *ACTN3* rs1815739, *PPARA* rs4253778, and *IL6* rs1800795 gene polymorphisms.

CONCLUSION

Consequently, in our study, the above genes did not cause differentiation in aerobic endurance in volleyball sports. When reviewing the literature, it is thought that the relationship between *ACTN3* rs1815739, *PPARA* rs4253778, and *IL6* rs1800795 polymorphisms and aerobic performance in volleyball players has not been conclusively clarified.

However, the inconsistency between the present research findings and those mentioned above could be a result of the variability in the types of tests used, the levels of athlete performance, and participant characteristics ranging from athletes to sedentary individuals. The different training levels of athletes indicate that higher capacities can be identified. In the future, it is recommended that studies like this be conducted with larger sample groups.

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