Sadi Ön [1, *]
Ibrahim Can[2]
Serdar Bayrakdaroğlu[3]
Mehmet Onur Sever[3]
Gürkan Diker[4]
Hüseyin Özkamçi[5]
Raif Zileli[6,7]
Mehmet Söyler[8]
Özlem Özge Yilmaz[9]
Tolga Polat[9]
Beste Tacal Aslan[9]
Korkut Ulucan[9,10]

ACTN3, IL-6 AND PPARA GENE POLYMORPHISMS AND ANAEROBIC PERFORMANCE IN VOLLEYBALL PLAYERS

POLIMORFIZMI GENOV ACTN3, IL-6 IN PPARA TER ANAEROBNA ZMOGLJIVOST PRI ODBOJKARJIH

ABSTRACT

The aim of this study is to determine the relationship between *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 gene polymorphisms and anaerobic test parameters among volleyball players. A total of 22 volleyball players voluntarily participated in the study. DNA isolation from buccal epithelial cell samples were performed using a PureLink DNA isolation kit, following the manufacturer's instructions. The genotyping of *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 gene polymorphisms were determined using the real-time polymerase chain reaction technique. Statistical analysis of the test results was performed using the SPSS 23 software package. Homogeneity of variance was assessed with the Levene test, and normal distribution was evaluated using the Shapiro-Wilk test. The One-Way ANOVA test was applied for the analysis of all parameters, and significance was set at $p < 0.05$. When the data were evaluated, no statistically significant differences were observed between *PPARA* rs4253778 and *ACTN3* rs1815739 gene polymorphisms and anaerobic performance parameters ($p>0.05$). Statistically significant differences were observed between the *IL-6* rs1800795 gene polymorphism and anaerobic performance parameters of back strength ($p> 0.05$). In conclusion, in volleyball, *PPARA* rs4253778 and *ACTN3* rs1815739 gene polymorphisms did not cause differentiation in anaerobic performance parameters. However, IL-6 gene polymorphism caused differentiation only in the back strength parameter. Additionally, the good performance of athletes with different prevalent level of genotypes in the studied performance criteria does not fully reveal which performance outcomes are influenced by the gene or genotype distributions. It is understood that further studies are needed to better determine the gene-performance relationship.

Keywords: Sport, polymorphism, gene

[1]Faculty of Sports Science, Ahi Evran University, Kırşehir, Turkey.
[2]School of Physical Education and Sport, Igdır University; Igdir, Turkey
[3]School of Physical Education and Sport, Gümüşhane University, Gümüşhane, Turkey
[4]Department of Physical Education and Sport, Faculty of Sports Science, Sivas Cumhuriyet University, Sivas, Turkey
[5]Departmant of Sport Management, Faculty of Sports Sciences, Sinop University, Sinop, Turkey
[6]Faculty of Health Science, Bilecik Şeyh Edebali University, Bilecik, Turkey.
[7]Biotechnology Application and Research Center, Bilecik Şeyh Edebali University, Bilecik, Turkey
[8]Yapraklı Vocational School, Çankırı Karatekin University, Çankırı, Turkey.
[9]Department of Medical Biology and Genetics, Marmara University, Faculty of Dentistry, Istanbul, Turkey
[10]Department of Molecular Biology and Genetics, Üsküdar University, Faculty of Engineering and Natural Sciences, Istanbul, Turkey

IZVLEČEK

Cilj te študije je bil ugotoviti povezavo med polimorfizmi genov ACTN3 rs1815739, IL-6 rs1800795 in PPARA rs4253778 ter parametri anaerobnih testov pri odbojkarjih. V raziskavi je prostovoljno sodelovalo 22 odbojkarjev. Izolacija DNK iz vzorcev bukalnih epitelijskih celic je bila izvedena s pomočjo kompleta PureLink za izolacijo DNK, v skladu z navodili proizvajalca. Genotipizacija polimorfizmov genov ACTN3 rs1815739, IL-6 rs1800795 in PPARA rs4253778 je bila določena z uporabo tehnike verižne reakcije s polimerazo v realnem času (real-time PCR). Statistična analiza rezultatov je bila izvedena s programskim paketom SPSS 23. Homogenost varianc je bila preverjena z Levenovim testom, normalnost porazdelitve pa z uporabo Shapiro–Wilkovega testa. Za analizo vseh parametrov je bil uporabljen enosmerni ANOVA test, statistična značilnost pa je bila določena pri $p < 0,05$. Rezultati so pokazali, da med polimorfizmoma genov PPARA rs4253778 in ACTN3 rs1815739 ter parametri anaerobne zmogljivosti niso bile ugotovljene statistično značilne razlike ($p > 0,05$). Statistično značilne razlike so bile ugotovljene med polimorfizmom gena IL-6 rs1800795 in parametrom anaerobne zmogljivosti hrbtne moči ($p < 0,05$). Torej, pri odbojki polimorfizma genov PPARA rs4253778 in ACTN3 rs1815739 nista povzročila razlik v parametrih anaerobne zmogljivosti. Vendar je polimorfizem gena IL-6 vplival na razlikovanje zgolj pri parametru hrbtne moči. Poleg tega dobra zmogljivost športnikov z različno zastopanimi genotipi pri proučevanih merilih ne razkriva popolnoma, katere dejavnike zmogljivosti dejansko določajo geni oziroma njihova porazdelitev. Jasno je, da so potrebne nadaljnje raziskave za natančnejšo opredelitev odnosa med geni in zmogljivostjo.

Ključne besede: šport, polimorfizem, gen

Corresponding author:* Sadi Ön

Kırşehir Ahi Evran University
E-mail: sadi.on@ahievran.edu.tr
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INTRODUCTION

Volleyball is defined as an intermittent and complex anaerobic team sport, characterized by short-duration high-intensity activities followed by low-intensity or passive recovery periods (Gabbett & Georgieff, 2007; Sheppard et al., 2009). In volleyball, high-intensity activities are typically brief, lasting between three and nine seconds, while the low-intensity or passive recovery periods between these activities range from approximately 10 to 20 seconds (Polglaze & Dawson, 1992).

A substantial proportion of points scored in volleyball are attributable to high-intensity actions (Voigt & Vetter, 2003). Despite the variability in actions among players, depending on the technical and tactical demands of their individual roles, common movements include acceleration and deceleration, jumping, striking the ball, and multidirectional movements (Sheppard et al., 2007). The importance of explosive power in volleyball is particularly evident during jumping and spiking actions (Marques et al., 2008), while speed and agility are integral to sudden changes in direction (Lidor & Ziv, 2010). During a volleyball match, athletes frequently perform numerous jumps and sprints over distances of up to 10 meters (Jastrzebski et al., 2014). It is widely acknowledged that vertical jump ability is a critical performance criterion in volleyball and other sports that demand explosive movements (Kraska et al., 2009).

The explosive power, speed, and agility of both upper and lower extremities are crucial criteria for athletes competing at an elite level in volleyball (Lidor & Ziv, 2010). Given the diverse directional changes, frequent sprints, and various jumping actions involved in the sport, physical performance is a critical determinant of success in volleyball (Kim & Park, 2016; Trajković et al., 2016). While the development of motor abilities is influenced by various factors, genetic predisposition accounts for 66% of the variance in sports performance (De Moor et al., 2007). It has been hypothesized that these variations in physical performance may be attributable to differences in the expression of specific genes (Puthucheary et al., 2011).

Researchers have reported that muscle fiber composition affects physical performance (Zawadowska et al., 2004) and that α-actinin plays a critical role in the formation of type II muscle fibers (Yang et al., 2003). The existence of disparities in the functional and structural adaptations of various systems, including but not limited to skeletal and cardiac muscle, bone, and lungs, suggests the potential for polymorphic variations in genes to influence the physical performance of athletes (Puthucheary et al., 2011). In sports disciplines that require a diverse

range of skills and abilities, athletes with gene variants such as *ACTN3*, *PPARA*, and *IL-6* have been reported to demonstrate superior performance (Ahmetov et al., 2016).

Researchers have noted that individuals with the RR homozygous genotype exhibit greater muscle mass, maximal strength (Erskine et al., 2014), peak power output (Kikuchi et al., 2013), and vertical jump performance (Pimenta et al., 2013) compared to XX homozygotes. For instance, Orysiak et al. (2015) conducted jump tests on young Polish athletes and found that those with the RR genotype demonstrated significantly higher jump heights and power output compared to XX homozygotes, highlighting a significant association between explosive leg muscle strength and the *ACTN3* polymorphism.

It is acknowledged that sports performance is contingent on a multitude of genetic factors that influence the athletic phenotype. Consequently, the polygenic inheritance model is regarded as a more suitable framework for elucidating athletic performance (Buxens et al., 2011). While adaptations occur in response to external physical loads, genetic architecture plays a critical role in the development and adaptation of motor abilities (Végh et al., 2022). For instance, a higher prevalence of alleles associated with aerobic metabolism has been linked to better responses to aerobic training (Gonzalez-Freire et al., 2009), whereas a greater number of alleles associated with endurance increases the likelihood of becoming a successful endurance athlete (Flueck et al., 2010).

A study of power-related traits in athletes identified *ACTN3*, *PPARA*, and *IL-6* genes as significant contributors (Naureen et al., 2020). Given that volleyball is a sport that demands high-speed movements and explosive power (Marques et al., 2009), it is influenced by genetic factors. The *ACTN3* gene, which has been identified as a key player in muscle strength and power (MacArthur & North, 2004), the *PPARA* gene, which plays a pivotal role in endurance adaptations (Lopez-Leon et al., 2016; Petr et al., 2018), and the *IL-6* gene, which regulates lipid and glucose metabolism (Prestes et al., 2008), are considered to be critical in explaining performance variations in volleyball (Ruiz et al., 2011).

The paucity of studies investigating these genes in volleyball players, coupled with the incomplete understanding of gene-performance relationships, has motivated this research. The objective of this study is to ascertain the disparities between *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 polymorphisms and anaerobic performance parameters in volleyball athletes. A comprehensive understanding of the impact of individual genetic variations on performance in sports requiring explosive power and agility, such as volleyball,

can facilitate the development of personalized training programs. Furthermore, by exploring the relationship between genetic polymorphisms and anaerobic performance in volleyball players, this study seeks to contribute to the creation of performance enhancement strategies based on individual genetic profiles.

METHODS

Participants:

A total of 22 female volleyball players who play in the professional volleyball league, have no injuries, and participate in 6-8 training sessions per week, (age: 21.59 ± 2.70 years; height: 1.87 ± 7.92 m; weight: 80.99 ± 8.14 kg; body fat: 12.05 ± 5.78%) participated in this study. The study protocol was approved by the Ethical Committee of Üsküdar University (2021/14-61351342) and conducted in accordance with the principles of the Declaration of Helsinki II. Written informed consent forms elucidating the study procedures and objectives were obtained from all participants. The present research was supported by the Scientific Research Organization of Gümüşhane University (GÜBAP2902-21.A0310.02.01).

Procedure:

Buccal epithelial cell samples were collected from the athletes in a room designated for volleyball players. Following sample collection, sprint tests were conducted in an outdoor setting on an artificial turf surface. Prior to the commencement of the test, the athletes underwent a standard warm-up routine, which was meticulously designed and overseen by the coach. This warm-up comprised five minutes of jogging, three minutes of dynamic stretching, and seven minutes of sport-specific drills (Diker et al., 2023).

Genotyping:

DNA isolation from buccal cells of athletes participating in the study were performed with the commercially available PureLink DNA extraction kit (Invitrogen, Thermo Fisher Scientific, Inc.). Genotyping of the *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 polymorphisms were performed using StepOnePlus Real-Time PCR (Thermo Fisher Scientific, Inc.) and Taqman Genotyping Mater Mix (catalog no. 4371355, Thermo Fisher Scientific, Inc.) genotyping kits following the manufacturers' protocols. A 10µl total reaction volume consisted of 5µl Genotyping Master Mix (Applied Biosystems, Foster City, CA), 3.5µl nuclease-free H_2O

(Thermofisher, the USA), 0.5µl genotyping assay (Applied Biosystems) and 1µl DNA. The TaqMan Probe sequences used for genotyping are shown in Figure 1.

		Sequencing 5'- 3'
ACTN3 **rs1815739**	**FAM/VIC**	CAAGGCAACACTGCCCGAGGCTGAC**[T/C]**GAGAGCGAGGT GCCATCATGGGCAT
IL-6 **rs1800795**	**FAM/VIC**	ACTTTTCCCCCTAGTTGTGTCTTGC**[C/G]**ATGCTAAAGGAC GTCACATTGCACA
PPARA **rs4253778**	**FAM/VIC**	ACACTTGAAGCTTGATATCTAGTTT**[G/C]**GATTCAAAAGCT TCATTTCCCATAT

Figure 1. Sequences of the TaqMan probe used for genotyping the *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 polymorphism.

Jumping and Sprinting Performance

The vertical jump test was conducted using a Newtest contact mat (Newtest 1000, OY, Oulu, Finland) with an accuracy of ± 2.0 mm for jump height measurement. Participants performed the test by bending their lower limbs (countermovement) and immediately executing a vertical jump. Each participant completed two trials of the jump test, aiming to jump as high as possible with their arms open. A one-minute rest interval was allotted between attempts.

Participants were also instructed to perform 10-meter and 30-meter sprints on two separate occasions. Verbal instructions were given to encourage them to cover the designated distances (10 m and 30 m) in the shortest possible time. Following a preliminary warm-up session, all participants completed maximum sprint runs over the designated distances of 10 meters and 30 meters within a one meter starting zone. The trials commenced with the participants adopting their natural starting position, with their front foot positioned just behind the designated starting line. The timing system was automatically triggered as the participant crossed the photocell at the starting line. The initiation of the sprint was at the discretion of the participant. Passive recovery intervals of three minutes were provided between each sprint. The split times for 10 metres and 30 metres were recorded using a photocell system (Newtest 1000, OY, Oulu, Finland). Photocells were positioned at the starting line, the 10-metre mark, and the 30-metre mark, with the photocells situated at a height of one meter. The timing accuracy of the system was determined to be ±0.001 seconds (Diker et al., 2022).

Right-Left Hand Grip Strength Test

The grip strength test was conducted using a Takei TKK 5401 hand dynamometer (Grip-D, Takei Scientific Instruments Co. Ltd., Tokyo, Japan) with a measurement range of 5.0–100 kgf, a minimum measurement increment of 0.1 kgf, and an accuracy of ±2.0 kgf. The athlete performed the measurement while standing, with the arm positioned at a 30º angle from the body, without bending the elbow or allowing the arm to touch the torso. Measurements were repeated twice for both the right and left hands, and the best values were recorded in kgf. A 30-second rest period was provided between trials (Halder et al., 2015).

Back and Leg Strength Test

The back and leg strength test were conducted using a Takei TKK 5402 dynamometer (Back-D, Takei Scientific Instruments Co. Ltd., Tokyo, Japan), with a measurement range of 20–300 kgf, a minimum measurement increment of 0.5 kgf, and an accuracy of ±0.6 kgf. The strength values were displayed on a three-digit LCD (digital) screen and recorded in kgf.

For the leg strength measurement, participants were instructed to maintain straight arms, a flat back, a slightly forward-leaning torso, and knees bent at 130–140 degrees. They were asked to grip the dynamometer bar firmly and pull it vertically upward with maximum effort using their legs. The test was repeated twice with a 30-second rest interval, and the best result was recorded (Halder et al., 2015). For the back strength measurement, participants were instructed to keep their arms straight, their back and knees fully extended, and their torso slightly leaning forward. They were asked to grip the dynamometer bar firmly and pull it vertically upward with maximum effort using their arms and back. This test was also repeated twice with a 30-second rest interval, and the best result was recorded (Halder et al., 2015).

T-Test

The T-test was used to measure agility and directional change speed (Semenick, 1990). The timing between the start and finish was recorded using a photocell system.

The athlete began at point A and sprinted straight to point B, touching the base of the marked cone with their hand. They then moved laterally to point C using side shuffle steps, touched the base of the cone with their hand, turned toward point D, and touched the cone at D. From there, they returned to point B using side shuffle steps, touched the cone, and sprinted back to point A to complete the test.

If the athlete crossed one foot over the other during lateral shuffles, failed to touch the cone's base with their hand, or did not face forward during the test, the trial was deemed invalid. In

such cases, the test was repeated after an appropriate rest interval. The measurement was performed using the Fusion Sports electronic gate system.

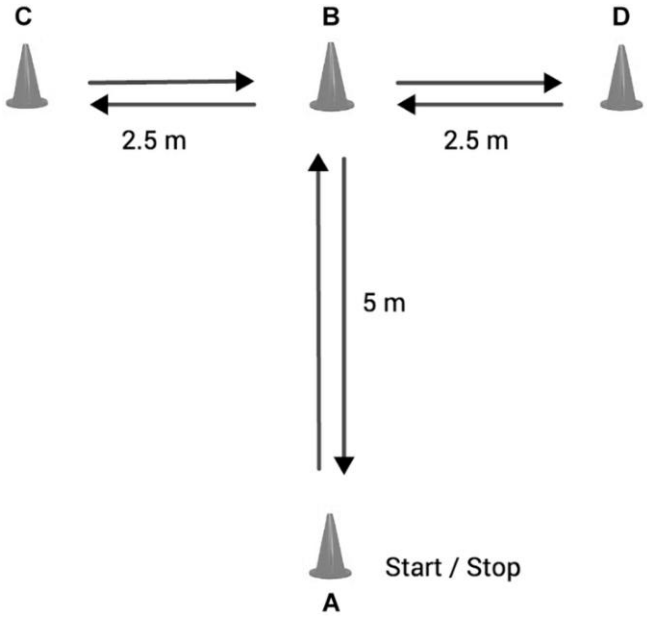

Figure 2. T-Test Agility Course.

Data Analysis

The statistical analysis of the test results was performed using the SPSS 23 software package (SPSS Inc., Chicago, IL, USA). Variance homogeneity was assessed using Levene's Test, and normal distribution analyses were conducted with the Shapiro-Wilk Test. The study examined three different genes and three different genotypes for each gene. The one-way ANOVA test was used to analyze whether there were differences between the genotypes. In cases where significant differences were found, the Bonferroni post-hoc test was applied. Statistical significance was set at $p < .05$.

RESULTS

The findings for *ACTN3* rs1815739, *IL-6* rs1800795, and *PPARA* rs4253778 in volleyball players are presented below.

Table 1. Descriptive Statistics of Participants.

	$\bar{x}$	SD
Age (years)	21.59	2.70
Height (cm)	187.77	7.93
Body Weight (kg)	80.99	8.15
Body Fat Percentage (%)	12.05	5.79
Muscle Mass (kg)	39.99	6.16

Table 2. Distribution of *ACTN3* rs1815739, *PPARA* rs4253778, and *IL-6* rs1800795 Genes in Volleyball Players.

	ACTN3			***PPARA***			***IL-6***		
		n	**%**		**n**	**%**		**n**	**%**
Genotype Distribution	**CC**	5	22.7	**GG**	0	0.00	**GG**	12	54.5
	CT	5	22.7	**CG**	6	27.3	**CG**	8	36.4
	TT	12	54.5	**CC**	16	72.7	**CC**	2	9.1

Notes. In volleyball players, the ACTN3 gene TT genotype (54.5%), the PPARA gene CC genotype (72.7%) and the IL6 gene GG genotype (54.5%) appear to be prevalent genotype in this cohort.

Table 3. Descriptive Statistics of Physical Performance Parameters.

	$\bar{x}$	SD
Vertical Jump (cm)	46.86	18.74
10 m Sprint (s)	1.70	0.12
30 m Sprint (s)	4.30	0.32
Right Hand Grip Strength (kg)	48.06	6.32
Left Hand Grip Strength (kg)	47.88	6.79
Back Strength (kg)	131.57	20.15
Leg Strength (Nm)	128.07	23.55
T-Test (s)	11.75	0.72

Notes. $\bar{x}$ - arithmetic mean; SD - standard deviation.

Table 4. Comparison of Physical Performance Parameters Across *ACTN3* rs1815739, *PPARA* rs4253778, *and IL-6* rs1800795 Genotypes.

	ACTN3				***PPARA***				***IL-6***			
	n	**x̄**	**SD**	**p**	**n**	**x̄**	**SD**	**p**	**n**	**x̄**	**SD**	**p**
Vertical Jump (cm)	CC	53.86	25.44		GG	0.00	0.00		GG	41.26	10.13	
	CT	39.82	8.84	0.51	CG	42.03	11.81	0.47	CG	55.81	26.12	0.24
	TT	46.87	19.02		CC	48.66	20.79		CC	44.60	21.07	
10 m Sprint (s)	CC	1.68	0.08		GG	0.00	0.00		GG	1.72	0.14	
	CT	1.68	0.11	0.93	CG	1.67	0.12	0.56	CG	1.65	0.08	0.47
	TT	1.70	0.14		CC	1.70	0.12		CC	1.71	0.14	
30 m Sprint (s)	CC	4.30	0.35		GG	0.00	0.00		GG	4.38	0.28	
	CT	4.21	0.39	0.79	CG	4.30	0.47	0.95	CG	4.18	0.39	0.43
	TT	4.33	0.30		CC	4.30	0.26		CC	4.28	0.07	
Right Hand Grip Strength (kg)	CC	47.44	4.78		GG	0.00	0.00		GG	46.01	9.09	
	CT	50.68	8.23	0.59	CG	45.56	7.89	0.26	CG	51.42	6.22	0.16
	TT	47.22	6.25		CC	48.99	5.62		CC	46.85	3.88	
Left Hand Grip Strength (kg)	CC	46.64	6.04		GG	0.00	0.00		GG	47.24	8.01	
	CT	52.14	8.45	0.29	CG	44.60	5.57	0.17	CG	50.32	4.38	0.27
	TT	46.61	6.15		CC	49.10	6.94		CC	41.90	1.41	
Back Strength (kg)	CC	129.90	25.55		GG	0.00	0.00		GG	123.04	14.79	
	CT	137.50	27.37	0.77	CG	130.41	26.43	0.87	CG**	145.56	22.63	**0.03***
	TT	129.79	15.62		CC	132.00	18.29		CC	126.75	6.71	
Leg Strength (Nm)	CC	127.60	32.00		GG	0.00	0.00		GG	120.08	16.35	
	CT	134.10	28.91	0.81	CG	119.83	31.05	0.32	CG	142.00	29.73	0.10
	TT	125.75	18.97		CC	133.12	20.43		CC	120.25	8.83	
T Test (s)	CC	11.76	0.39		GG	0.00	0.00		GG	11.97	0.80	
	CT	11.36	0.58	0.38	CG	11.45	0.54	0.24	CG	11.39	0.53	0.21
	TT	11.91	0.83		CC	11.86	0.75		CC	11.85	0.27	

Notes. *Significant at p<0.05 level - x̄: arithmetic mean - SD: standard deviation - **Different than GG genotyp

The distribution of the *ACTN3* gene polymorphism among volleyball players shows CC and CT genotypes at 22.7%, while the TT genotype is predominant at 54.5%. The TT genotype emerges as the prevalent genotype among volleyball players, indicating a limitation associated with the *ACTN3* gene. When analyzing the relationship between performance and genotype distribution, athletes with the CT genotype outperformed those with CC and TT genotypes in strength-based measurements (grip strength, back strength, and leg strength). This suggests that volleyball players with a higher CT genotype expression demonstrate superior strength performance under the constraints of the *ACTN3* gene. In terms of leg strength, volleyball players with the CT genotype exhibited better outputs compared to those with the CC and TT genotypes. However, in vertical jump performance, athletes with the CC genotype achieved greater jump heights compared to CT and TT genotypes. These contrasting results could be attributed to the roles of CC the prevalent genotype in this players, whose positions within the team are likely jump-based. For sprint performance, volleyball players with CC and CT genotypes showed better times in the 10m sprint compared to those with the TT genotype. However, as the sprint distance increased to 30m, players with the CT genotype outperformed those with CC and TT genotypes. This indicates that the CT genotype may be a key determinant of sprint performance in volleyball players, regardless of distance. Similarly, CT prevalent genotype in players also demonstrated better agility test performance compared to those with CC and TT genotypes. The distribution of the *PPARA* gene polymorphism in volleyball players shows no presence of the GG genotype, with CG and CC genotypes present in 27.3% and 72.7% of players, respectively. Under the constraints of the *PPARA* gene, the CC genotype emerges as the prevalent genotype among volleyball players. Athletes with the CC genotype exhibited higher strength values (grip strength, back strength, and leg strength) compared to those with the CG genotype. This suggests that CC the prevalent genotype in players can generate greater strength. Parallel to leg strength values, CC prevalent genotype in players also achieved higher vertical jump performance compared to those with the CG genotype. In 10m sprint performance, CG prevalent genotype in players outperformed those with the CC genotype, while no significant differences were observed between genotypes for the 30m sprint. In agility tests, CG prevalent genotype in players exhibited better performance than CC prevalent genotype in players, aligning with their superior leg strength.

The distribution of the *IL-6* gene polymorphism among volleyball players shows CC genotype at 9.1%, CG genotype at 36.4%, and GG genotype at 54.5%, making the GG genotype the prevalent genotype under the constraints of the *IL-6* gene. For strength measurements (grip

strength, back strength, and leg strength), athletes with the CG genotype demonstrated higher values compared to those with the GG and CC genotypes. Back strength, in particular, showed a statistically significant difference in favor of CG prevalent genotype in players ($p < 0.05$). In terms of vertical jump height, CG prevalent genotype in players performed better than those with GG and CC genotypes, parallel to their superior leg strength. Similarly, CG prevalent genotype in players achieved better times in both 10m and 30m sprints compared to those with GG and CC genotypes, with agility test results following the same trend. While it remains, unclear which genetic polymorphisms influence key volleyball movements such as short sprints, direction changes, and jumps, these movements are thought to be more influenced by training-based performance indicators. Another perspective is that professional volleyball players may not rely heavily on genetic polymorphisms impacting energy pathways due to the intermittent nature of the sport. Volleyball players are known to have longer rest periods compared to rally durations, relying on anaerobic energy systems during rally actions and aerobic energy systems for recovery. Studies have highlighted the complexity of athletic performance, which cannot be attributed to a single gene (Orysiak et al., 2015). Even in studies investigating multiple genes, identifying clear performance determinants is challenging. Epigenetic and environmental factors, along with complex gene-gene and gene-environment interactions, are critical determinants in sports genetics and must be considered (Orysiak et al., 2015). The presence of multiple polymorphisms can amplify the effects of those that fail to influence performance individually through genetic interactions. This implies that combinations of polymorphisms may have a more significant impact on overall sports phenotypes than single polymorphisms and should be considered when predicting sports performance and designing training regimes (Flueck et al., 2010; Williams & Folland, 2008).

DISCUSSION AND CONCLUSION

The aim of this study was to determine the relationship between the *ACTN3*, *PPARA*, and *IL-6* genes and their genotypes with anaerobic-based performance outputs, including jumping, sprinting, strength, and agility, in volleyball players. The findings of the study are discussed below under specific headings.

In the investigation of the relationship between the *ACTN3* gene and performance outcomes in anaerobic-based activities, no statistically significant association was found between the measured parameters and the *ACTN3* gene ($p > 0.05$) (Table 4). When examining performance

values based on intragroup genotype differences, it was observed that short-distance sprint performance (10 m) yielded similar favorable times for athletes with CC and CT genotypes. However, as the sprint distance increased (30 m), athletes with the CT genotype demonstrated better performance outcomes, showing a positive distinction. Although it was expected that leg strength and jumping performance would yield the best results for the same prevalent genotype in, the findings revealed differences between the prevalent genotypes in contributing to optimal leg strength and jumping performance. According to the data obtained, athletes with the CT genotype achieved the best leg strength performance, while those with the CC genotype excelled in jumping performance. This discrepancy could be attributed to the multifaceted nature of jumping as a multi-joint performance activity, involving the coordinated contribution of different joints (hip, knee, and ankle) through various angular movements (extension, flexion) and roles (agonist/synergist or antagonist contractions). Among the athletes participating in the study, although the TT genotype of the *ACTN3* gene was prevalent genotype in 12 athletes, five athletes with the CT genotype demonstrated positive contributions to performance indicators. This limitation of the *ACTN3* gene might explain the lack of statistically significant associations between performance and gene/genotype relationships.

Volleyball is a sport that requires high-speed movements and explosive power (Marques et al., 2009). Jumping is one of these activities and involves a multi-joint movement that requires the coordinated participation of most lower extremity muscles (Brown & Weir, 2001). Therefore, athletes need to perform specific jump training. α-Actinin-3 is a genetic factor that determines high power production and fast muscle contractions (MacArthur & North, 2004). This genetic potential does not show differences between sports disciplines in the evaluation of jumping ability (Pimenta et al., 2013). Although *ACTN3* has been suggested as a candidate gene to explain individual variations in volleyball performance (Ruiz et al., 2011), no significant relationship was found between *ACTN3* genotypes and performance in this study. Moreover, the results of this study are supported by findings in literature. Research investigating the potential effect of *ACTN3* rs1815739 gene polymorphism on sprint speed and anaerobic power performance presents results consistent with our findings. Specifically, the *ACTN3* TT genotype has been observed to be associated with anaerobic performance parameters in professional athletes. These results align with previous studies suggesting that *ACTN3* polymorphism is an important genetic marker for athletic abilities such as explosive power and speed (Söyler et al., 2024). In addition, it has been reported that the CT genotype of the *ACTN3* rs1815739 polymorphism is highly prevalent among Turkish bodybuilders, while the TT genotype was not

detected. These findings support the potential impact of the polymorphism on sprint and endurance phenotypes. Further studies with larger cohorts are recommended to validate these results (Polat et al., 2020).

In a study conducted with 66 elite male and female volleyball players, the power and strength values obtained from jump tests (SJ and CMJ) were compared with the athletes' genotypes. It was reported that *ACTN3* did not directly affect the power and strength values of volleyball players (Ruiz et al., 2011). Similarly, Garatechea et al. (2014) reported that *ACTN3* polymorphism, which is associated with explosive muscle strength and is an important phenotype for basketball, was not related to the leg explosive strength of elite basketball players. Additionally, researchers have stated that the *ACTN3* rs1815739 polymorphism is not associated with jump (SJ and CMJ) or sprint ability (30m linear sprint) in non-athletic men and women (Santiago et al., 2009). In volleyball, force transfer during intense activities where the hand makes contact with the ball plays a significant role in scoring. Therefore, hand strength is crucial for transmitting the action generated by the angular movement of the shoulder to the ball. This has raised curiosity about whether there is a relationship between handgrip strength and genetic factors. In our study, no significant relationship was found between handgrip strength and the *ACTN3* gene (p>0.05). α-Actinins, the dominant components of the sarcomeric Z-line in skeletal muscle fibers, are reported to tether actin-containing thin filaments, stabilize the muscle contraction mechanism, and produce fast and strong contractions (MacArthur & North, 2004). However, researchers have reported no relationship between the *ACTN3* rs1815739 polymorphism and handgrip strength (Moran et al., 2007; Chiu et al., 2012). Moreover, Ginevičienė et al. (2011) reported that XX homozygote athletes had greater handgrip strength compared to those with the RR genotype. Contrarily, Shang et al. (2011) found that handgrip strength was significantly lower in the XX group compared to RR individuals. Orysiak et al. (2015) also reported that the *ACTN3* rs1815739 polymorphism was not associated with muscle strength. In volleyball, power generation in both the lower and upper extremities is critical for success. Peak power output serves as a key determinant of performance. Our study investigated the relationship between peak power outputs and the *ACTN3* gene in volleyball players but found no significant association (p>0.05). This study also identified that the *ACTN3* rs1815739 polymorphism was associated with endurance and muscle strength among Turkish football players, with the T allele being more prevalent. These findings align with other studies in the field of sports genetics, emphasizing the impact of the *ACTN3* polymorphism on endurance performance in athletes. Researchers have reported that the genotype frequencies of

volleyball players and non-athletic control groups are similar, indicating that the *ACTN3* rs1815739 polymorphism is not significantly associated with peak power production in elite volleyball players or non-athletes (Ruiz et al., 2011). Similarly, Garatachea et al. (2014) stated that there is no relationship between the *ACTN3* gene and power phenotypes in basketball players. McCauley et al. (2009) found that the *ACTN3* rs1815739 polymorphism had no effect on absolute and relative torque at high angular velocities or the isometric strength of knee extensors in adult males. Likewise, Clarkson et al. (2005) reported no relationship between the *ACTN3* rs1815739 polymorphism and isometric elbow flexor strength in men. The findings suggest that the *ACTN3* rs1815739 polymorphism does not influence performance in volleyball, a sport with high explosive power demands (Ruiz et al., 2011). However, the results of studies highlighting the significant effects of *ACTN3* genotypes on muscle strength and anaerobic performance align with previous research emphasizing the genetic role of *ACTN3* polymorphism in athletic abilities such as speed and explosive power (Zileli et al., 2023).

A study examining the effects of the *ACTN3* rs1815739 polymorphism on athletic performance and position-related roles in football players provides findings consistent with the literature. It was observed that the TT genotype was more prevalent in endurance-requiring positions, while the CC genotype was more common in positions demanding explosive power and speed. Similarly, in volleyball players, positions requiring quick reflexes, explosive jumping power, and endurance may be associated with different *ACTN3* genotypes. Such genetic insights could serve as a valuable guide for optimizing the individual performance of volleyball players and designing position-specific training programs (Muhan et al., 2023).

Based on the data obtained in this study, no significant relationship was found between the *PPARA* gene and the performance outcomes of the selected anaerobic-based activities ($p > 0.05$) (Table 4). When performance values were analyzed according to intragroup genotype differences, it was observed that performance genotypes changed with the varying demands of sprint performance (distance). Athletes with the CG genotype stood out positively in the 10m sprint performance, whereas differences between CG and CC genotypes disappeared as the distance increased to 30m. Regarding leg strength and jumping performance, the best results were observed in athletes with the CC genotype, indicating that similar genotypes explain the lower limb strength and its influence on jumping performance in volleyball players. Athletes with the CG genotype showed the best results in short-distance sprint and agility runs, suggesting that this genotype is prevalent in conditions requiring speed and agility within limited distances. This genotype accounted for 27.3% of the athletes in the study, indicating

that the roles of these athletes in gameplay likely align with short-distance performances. In contrast, for strength, jumping, and 30m sprint performance, athletes with the CC genotype demonstrated better results.

Despite *ACTN3* being identified as a candidate gene to explain volleyball performance outputs (Ruiz et al., 2011), our study found no significant relationship between *ACTN3* and performance outcomes such as strength, speed, and jumping. Instead, the *PPARA* gene CC genotype, the prevalent in 72.7% of the participants, emerged as a potential indicator of individual performance in volleyball. This dominance in such a high percentage of athletes highlights the genotype-training and training-genotype relationship, even when training factors are considered. PPARA (Peroxisome Proliferator-Activated Receptor Alpha), crucial for energy glucose homeostasis and vascular inflammation, supports fatty acid uptake, utilization, and catabolism as a key regulator of lipid metabolism (Végh et al., 2022). It is activated in tissues involved in physical activity, such as the liver, skeletal muscle, and cardiac muscle, under metabolic and physiological stress conditions to meet energy demands by catabolizing fatty acids (Russell et al., 2003). The GG genotype has been associated with type I muscle fibers and high heart rate values commonly found in endurance athletes (Akhmetov et al., 2007), while the C allele is prevalent in speed- and power-oriented athletes with type II muscle fibers, contributing to better anaerobic performance (Ginevičienė et al., 2020). The C allele, particularly in CC genotype athletes, has been linked to anaerobic power (Petr et al., 2014), high grip strength (Ahmetov et al., 2013), muscle mass, and high contraction strength (Ginevičienė et al., 2010). Petr et al. (2014) found statistically significant differences in maximum relative performance in WT30 [Pmax·kg−1] between C allele carriers and GG genotype individuals, with C allele carriers demonstrating higher speed-strength performance.

PPARA plays an important role in endurance training adaptations (Lopez-Leon et al., 2016; Petr et al., 2018), and the C allele is reported to play a significant role in strength development (Alvarez-Romero et al., 2020). Although 72.7% of participants in this study had the C allele, no relationship was established between it and the anaerobic-based performance criteria tested. In a study evaluating the relationship between *PPARA* G/C polymorphism and endurance sports, it was reported that athletes with high skills in endurance sports had a higher frequency of the GG genotype and G allele compared to the control group (Lopez-Leon et al., 2016). Another study among Turkish football players found that the G allele and GG genotype of *PPARA* rs4253778 polymorphism played a significant role as genetic markers for endurance metabolism. These findings are consistent with studies in different populations emphasizing the

positive impact of the G allele and GG genotype on endurance performance (Ulucan et al., 2020). The G allele is associated with the endurance athlete status and is considered part of the group of performance-enhancing polymorphisms that benefit endurance performance (Maciejewska et al., 2011). A study conducted on professional football players and sedentary volunteers reported a higher prevalence of the GG genotype and G allele in rs4253778 *PPARα* polymorphism (Proia et al., 2014). Despite 27.3% of the athletes in our study carrying the G allele, no relationship was observed between this allele and the performance outcomes from the anaerobic-based tests. Tural et al. (2014) reported that the *PPARA* gene significantly influences aerobic performance in elite-level athletes. A study investigating the effects of *ACTN3* rs1815739 and *PPARA* rs4253778 polymorphisms on athletic performance yielded results consistent with previous findings. Specifically, the relationship between *ACTN3* rs1815739 polymorphism and fast-twitch ability, as well as the role of *PPARA* rs4253778 polymorphism in energy metabolism, supports these findings. Further research with a larger sample size could provide a deeper understanding of the effects of these genetic variations on sports performance (Doğan et al., 2024).

Based on the data obtained in this study, no significant relationship was found between the *IL-6* gene and performance outcomes of the selected anaerobic-based activities, except for back strength ($p < 0.05$) (Table 4). There is a significant relationship *IL-6* gene and performance outcomes of back strength ($p< 0.05$). When performance values were analyzed according to intragroup genotype differences, it was observed that the CG genotype, prevalent in 36.4% of the participants, formed the group with the best values in jumping, sprinting, strength, and agility performances. Additionally, a statistically significant relationship was found between back strength and the CG genotype ($p < 0.05$). The back muscles play roles in shoulder, arm, and head/neck movements and assist in respiration through their attachments to the ribs. Deep muscles are essential for maintaining an upright posture, extension, lateral flexion, and rotation of the torso. Even when an athlete is not actively performing motor movements or exercises, they must maintain an upright posture throughout a match, which requires the continuous activation of the back muscles. In volleyball, movements such as trunk extension during spiking, overhead arm retraction, and arm swing in spiking, as well as overhead arm lifting and stabilization during blocking, rely heavily on the back muscles. During the eccentric phase of jumping, the kinetic energy stored is used to generate greater force in the concentric phase (Markovic & Mikulic, 2010). The frequent repetition of spiking and blocking movements during matches or training places additional stress on the back muscles. A volleyball match,

which can last up to five sets with approximately 45 rallies per set (Sánchez-Moreno et al., 2016) and an average of 30 jumps per set (Sheppard et al., 2007), can cause high levels of muscle fatigue in players (Ribeiro et al., 2008). Exercise increases catabolic pro-inflammatory cytokines such as interleukin-6 (IL-6) (Eliakim et al., 2009). It has been reported that exercise alone can induce inflammatory conditions, leading to increased hemolysis and elevated IL-6 levels (Sim et al., 2014). Moderate-intensity volleyball training has been shown to increase IL-6, likely because it is the cytokine most sensitive to exercise-induced inflammation (Eliakim et al., 2009). Other researchers have suggested that the increase in IL-6 during exercise does not originate from immune cells but is primarily driven by circulating skeletal muscle contractions (Febbraio & Pedersen, 2002). Volleyball activities such as jumping, hitting, and diving may lead to subclinical muscle and/or soft tissue damage, triggering significant increases in circulating IL-6 levels (Eliakim et al., 2009). While some studies have found a relationship between training load and IL-6 levels in volleyball players (Eliakim et al., 2009), Suzui et al. (2004) did not observe significant changes in IL-6 levels despite increased training loads over four weeks.

IL-6 plays a significant metabolic role in regulating lipid and glucose metabolism during prolonged and fatiguing exercises (Prestes et al., 2008). Due to the intermittent nature of volleyball, cytokines like IL-6 may vary (Dias et al., 2011). Additionally, inconsistencies in athlete data may be influenced by the timing of blood sampling (Dias et al., 2011). A study conducted by Kazancı et al. (2023) investigating the potential effects of *IL-6* rs1800795 and *PPARA* rs4253778 polymorphisms on endurance sports found results consistent with the literature. The study suggested that the *IL-6* rs1800795 GC genotype and *PPARA* rs4253778 GG genotype might play a supportive role in endurance performance. Verifying these effects in larger sample sizes and across different sports disciplines is essential. Similarly, a study by Ulucan et al. (2020) reported no significant difference in the *IL-6* rs1800795 polymorphism between Turkish skiing athletes and sedentary individuals, leaving its potential role as a genetic marker unclear. These findings align with other studies in the literature examining the polymorphism's effects in strength- and endurance-focused athletes. Interleukin-6 is thought to play a critical mediator role in the inflammatory response needed for muscle repair, whether exercise-induced or not, by increasing during exercise as evidence of muscle damage (Pedersen et al., 2004; Steensberg et al., 2002).

Strengths and Limitations

The study's focus on trained professional female athletes, selected anaerobic performance outputs, and the consolidation of genes frequently discussed in the literature under a single study are considered to be its strengths. One of the important limitations of the study is the sample size. Since the findings obtained belong to a limited number of athletes (n=22), caution should be exercised in the interpretations as this may affect generalizability. Additionally, the uneven distribution of genotypes and/or circulating levels may also be considered other limitations.

Declaration of Conflicting Interests

The authors have no conflicts of interest to declare.

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