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Comparison of athletic performance of Turkish ice hockey players with ACE I/D (rs1799752), ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms

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Abstract

Our study is aimed at examining the Ice Hockey National Team players with regard to ACE I/D (rs1799752), ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms and physical tests. This study was participated by 21 players from ice hockey national team. While ACE I/D (rs1799752) polymorphism was obtained using conventional polymerase chain reaction method (PCR), ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms were produced by real time polymerase chain reaction method (qPCR). Athletic performance analysis, on the other hand, was based on the assessment of maximal oxygen consumption capacity (VO2max), anaerobic performance, flexibility and strength tests. In our cohort, ACE I/D (rs1799752) polymorphism was determined as 24% genotype II, 33% genotype ID, and 43% genotype DD. ACTN3 (rs1815739) polymorphism was determined as 24% genotype RR, 43% genotype RX, and 33% genotype XX. PPARA (rs4253778) polymorphism was observed as 71% genotype GG, 14.5% genotype GC, 14.5% genotype CC. HIF1A (rs11549465) polymorphism was found to be 67% genotype CC, 33% genotype CT. Concerning physical tests, the evaluation of flexibility test results among genotype groups did not yield significant differences (p=0.365). No significant difference was found among genotype groups with respect to leg strength test results (p=0.691). The evaluation of handgrip strength test results among genotype groups did not reveal significant differences (p=0.679). No significant differences were found among genotype groups when VO2 max test results were examined (p=0.686). A significant relationship was found in the speed test and HIF1A rs11549465 polymorphism evaluation (p = 0.008). No significant results were detected when comparing the speed test with other polymorphisms (p = 0.65). The results of our study support the previous studies which had focused on the potential relation between the relevant gene polymorphisms and athletic performance of ice hockey players. However, doing further studies with larger cohorts is recommended in order to understand the relationship between the relevant polymorphisms and athletic performance of ice hockey players.

Keywords: ACE I/D (rs1799752), ACTN3 (rs1815739), HIF1A (rs11549465), Ice hockey, PPARA (rs4253778), Physical test.

1. Introduction

Athletic performance is defined as the energy-use capacity of the athlete during aerobic and anaerobic conditions, the performance of neural and muscular functions, the level of muscular power and strength as well as the motivation and psychological condition of the athlete, all combined together during the efficient performance of a success-oriented physical activity (1). Talent selection is one of the first steps in the performance assessment of athletes. Athletic performance tests involve the measurement of such parameters as strength, flexibility, agility, speed, time, and balance coordination (2). Genetic factors were also added to these parameters in recent times. Athletic performance is defined as quantitative and multifactor genotypes because it is influenced by both polygenic inheritance and environmental factors. In recent studies, some polymorphism researches have found that allele/genotype frequency does not lead to significant differences among populations (3). On the other hand, these studies also indicate that there is a series of genetic changes that affect

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athletic performance. Nevertheless, acquiring genetic knowledge and using it in individualized training can be a good formula for the success of athletes and teams (1).

The angiotensin-converting enzyme (ACE) InDel polymorphism has been reported to be associated with the physical performance characteristics of elite-level athletes. This gene is located in the chromosome 17q23. It comprises a polymorphism caused by a deletion (D) or an insertion (I) of a 287 bp Alu sequence in intron 16 (4). Studies so far have shown that individuals with DD genotype have higher concentrations of tissue and plasma ACE compared to individuals with ID and II genotypes (5). In light of this information, allele I is associated with lower serum and tissue ACE activity and better performance in endurance sports, whereas allele D indicates that increased circulation and tissue activity improve performance in strength or sprint sports (6).

ACTN3 protein plays a role in muscle fibers of glycolytic type and type IIX that are in charge of fast-twitch muscle groups. ACTN3 is known as the "speed gene" (7). The protein-coding gene ACTN3 is localized at 11q13.1. ACTN3 is formed by the cytosine-thymine (C1729T) and can be transformed in the 16th exon of rs1815739 polymorphism. This transformed results in the formation of stop codon (X) instead of the arginine (R)-coding codon in the codon (R577X) that codes the 577th amino acid of the protein. Thus, ACTN3 R allele is expressed only in type II muscle fibers (fast twitch) (8). Athletes who carry the RR genotype and R allele in the ACTN3 gene are reported to be advantageous for athletic disciplines that require explosive power such as short runs with a tendency to strength-oriented athletic performance (9-10-11). On the other hand, athletes with XX genotype and X allele have a muscular structure which is beneficial for athletic disciplines that require endurance (5).

Due to its lipid metabolism, glucose energy homeostasis and role in vascular inflammation, PPARA gene is indicated as a good candidate gene for analyzing athletic ability (12). PPARA is localized at 22q13.31. It is known to have a functional polymorphism (rs4253778) at intron 7. The G allele of this polymorphism is associated with high gene expression, therefore having an effect on the oxidation of fatty acids in various tissues. Commenting on the relation between polymorphism and muscle fibers, Ahmetov et al. (2006) have reported that GG homozygote is prone to endurance metabolism whereas CC homozygote is significantly correlated to strength-related metabolism (14).

Glycolysis is the main source of anaerobic energy in humans and this metabolic path can be induced by transcription factor hypoxia under low oxygen conditions. This process is regulated by Factor-1α (HIF-1 α) which can be induced by hypoxia. HIF1A (rs11549465) is localized at 14q23.2. At the 12th exon is a polymorphism that can be transformed into C / T (Pro / Ser) (15). It has been demonstrated that the HIF1A 582Ser variant is significantly correlated with the increasingly fast twitching muscle fibers in the vastus lateralis muscles of Russian all-round speed skaters (13).

All sports have their specific physical requirements which can be significantly varied among the sports disciplines. Therefore, any study involving the effects of genes on performance must be planned in consideration of the performance components that best fit the sports being examined (16). In the last twenty years, there has been a growing body of evidence on the relationship between certain genes and such physical qualities as strength, endurance, flexibility and speed that define athletic performance (17-6). In the literature, ACE I/D (rs1799752), ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) polymorphism have been associated with athletic performance.

This study aimed to examine the effects of ACE I/D (rs1799752), ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms on flexibility, leg strength, handgrip strength, maximal oxygen consumption (VO2max) and speed test.

2. Materials and methods

2.1. Participants

21 male (aged 19.47 ±3.93) Turkish National Ice Hockey players volunteered for the study. The study was approved by Uskudar University Ethical Committee (61351342-/ 2019-35) and performed in accordance with the seventh revision of the principles of the Declaration of Helsinki. All players were informed of the experimental procedure and any potential ethical implications, and all participants provided written informed consent. The athletes' age, weight, success (medal status), parental consanguinity, presence of any genetically transmitted diseases, doping bans, and ancestry were obtained before being invited to the study.

2.2. Phenotyping

30 m sprint values of the subjects were measured using the New test 300 device (Newtest 300, Finland). (A distance of 30 m was marked prior to testing and photocells were placed at the start and end points. The device began recording the time when the start point was passed and the recording automatically stopped on arrival at the end point. The recorded time was automatically sent to and saved by the computer. The Sprint test was done twice with resting intervals of 5 minutes and the best score was noted (18).

The maximal oxygen consumption capacity test was performed with 20 m Shuttle Run tests. The team wore sportswear and they performed warm-up exercises for 30 minutes before starting the Shuttle Run tests. The shuttle run tests were performed as previously described (19). The number of repetition runs was recorded and the estimated oxygen consumption was determined using the following formula:

$Y = –24.4 + 6.0 X$ (Y = VO2max ml/kg /min, X = running speed), as previously described.

The measurements of mid-thigh pull strength test were taken by using the TKK 5402 Takei brand dynamometer (Takei Scientific Instruments CO, Tokyo, Japan). In the measurements, after 5 minutes of warm-up students were asked to step on the top platform of the dynamometer. The length of the chain held by the students was adjusted for tight (straight) torso and knees bent at 125 degrees. For this measurement, students were asked to pull the bar, which is connected to the dynamometer with chains, upwards with all their power. After two trials, the best value was recorded (20).

The measurements of handgrip (grasp) strength test were done with the TKK 5401 Takei brand hand dynamometer (Takei Scientific Instruments CO, Tokyo, Japan). With the subjects standing and elbows kept tight, arms

kept loosely down without contact with the body. When the subjects were ready, they grasped the handgrip of the clench dynamometer, keeping the position of their bodies, and squeezed the handgrip with maximum effort. The score in kg displayed on the dynamometer was read. These measurements were repeated twice for both hands and the best value was recorded (20).

Flexibility of the subjects was measured using sit and reach test. Soles are placed on a tea table with shoes taken off and legs stretched out. Subjects lean forward with their hands ahead and reach as far as they can without bending their knees. At that furthest position, they wait for 1 or 2 seconds without stretching forward or backward. Then the score on the sit and reach table is noted in cm.

2.3. Genotyping

Genomic DNA isolation from the buccal epithelial of the athletes was performed with a commercial kit (The Invitrogen extraction kit, USA) by following the manufacturer's guidelines. Purity of the samples was calculated by the OD260/OD280 ratio. The process of genotyping of ACE I/D (rs1799752) was carried out using conventional PCR amplifications. Forward 5'-CTGGAGACCACTCCC ATCCTTTCT-3' and reverse 5'-GATGTGGCC ATCACATTCGTCAGAT- 3' primers were used for the amplification. Amplification products were visualized under a UV light following electrophoresis on a 2% agarose gel stained with ethidium bromide. The 490 bp amplicons were considered as the I allele, and the 190 bp amplicon was considered as the D allele.

The processes of genotyping of ACTN3 (rs1815739), PPARA (rs4253778) and HIF1A (rs11549465) were carried out by Real-Time Polymerase Chain Reaction (qPCR) on QuantStudio 3 (Thermo Fisher Scientific, Inc.) by using commercially provided Taqman Genotyping Assay (Applied Biosystems Foster City, CA, ABD). The sequences of the primers used for genotyping are listed (Table 1). T (X allele) and C (R allele) alleles were determined using VIC and FAM primers, respectively for ACTN3 (rs1815739). Likewise, PPARA (rs4253778) and HIF1A (rs11549465) are represented by the alleles VIC and FAM (Table 1).

2.4. Statistical analysis

G Power analysis was carried out to determine the number of subjects. A priori power analysis was conducted to determine the sample size, which was calculated to be 15 participants with a desired level of power of 0.80, a significance level of 0.05 and an effect size of 0.60 to detect strong correlation. The adjusted sample size after taking into consideration a 30% dropout rate was 21 participants. The statistical analysis was performed by using the SPSS 21 (Statistical Package for Social Sciences) software program. The descriptive statistics of age, height, weight, body mass index (BMI) and VO2max, Sprint measurements, mid-thigh pull strength, handgrip (grasp) strength test and flexibility measurements were presented as minimum, maximum, and mean. Normality was tested using the Kolmogorov-Smirnov test. Visual methods such as histograms and probability plots were also used to determine the normality. To compare the VO2max results and genotypes, we used one-way analysis of variance (ANOVA). $p<0.05$ was accepted as statistically significant.

3. Results

Our study involved 21 male athletes (aged 19.47±3.93). Their height, weight, and body mass index (BMI) means were determined as 1.78 ± 0.05 meters, 72.42 ± 11.31 kilograms, and 22.81 ± 3.33 kg/m2 respectively.

The genotype distribution in the athletes' cohort resulted as follows: ACE rs1799752 (43% DD, 33% ID, 24% II); ACTN3 rs1815739 (24% RR, 43% RX, 33% XX); PPARA rs4253778 (71% GG, 14.5% GC, 14.5% CC); HIF1A rs11549465 (67% CC, 33% CT).

The allele distribution in the athletes' cohort resulted as follows: ACE rs1799752 (60% D, 40% I); ACTN3 rs1815739 (45% R, 55% X); PPARA rs4253778 (79% G, 21% C); HIF1A rs11549465 (83% C, 17% T) (Table 2).

Although ACE gene represents a higher frequency of DD and ID polymorphisms compared to II polymorphism, this difference was not found to be statistically significant (p=0.056). ACTN 3 gene has a higher distribution of RX and XX frequencies than RR frequency but with no statistical significance (p=0.56). PPARA gene exhibits a higher frequency of GG polymorphism compared to GC and CC frequencies (p=0.001). In HIF1A gene, CC frequency is higher than that of CT. However, HIF1A results are not statistically significant (p=0.127).

In the comparison of ACE I/D rs1799752 polymorphism with flexibility, leg strength, handgrip strength, VO2 max and speed test results, II, ID, DD genotypes were identified as 14.4±8.31. 9.28±6.55. 9.22±6.31 cm. 150.4±37.82. 141.21±12.22. 139.44±19.69 kg. 97.82±21.78. 89.01±14. 90.65±17.81 kg. 49.74±4.31. 47.34±4.83. 46.43±8.77 kg/ml. 3.28±0.16. 3.20±0.19. 3.28±0.15 sec respectively. Although athletes with II genotype scored higher mean values in the physical tests of flexibility and strength and athletes with genotype ID scored better mean values in the speed test. no statistical significance was observed in the overall physical test results (p>0.05) (Table 3).

The comparison of ACTN3 rs1815739 polymorphism with flexibility. leg strength. handgrip strength. VO2 max and speed test results yielded the respective values of 5.2

Table1. Sequences of the primers used for genotyping ACTN3 rs1815739, PPAR rs4253778 and HIF1A rs11549465

***ACTN3* rs1815739 Sequences 5'-3'**
VİC/FAM
CAAGGCAACACTGCCCGAGGCTGAC[T/C]GAGAGCGAGGTGCCATCATGGGCAT
***PPAR* rs4253778 Sequences 5'-3'**
VİC/FAM
ACACTTGAAGCTTGATATCTAGTTT[G/C]GATTCAAAAGCTTCATTTCCCATAT
***HIF1A* rs11549465 Sequences 5'-3'**
VİC/FAM
GTTACGTTCCTTCGATCAGTTGTCA[C/T]CATTAGAAAGCAGTTCCGCAAGCCC

Table 2. Distribution of polymorphism and alleles over genes.

		Genotype frequency			Allele frequency		Chi-square	df	p
		II	**ID**	**DD**	**I**	**D**			
ACE I/D rs1799752 (21)	**Number**	5	7	9	17	25	1.143a	2	.565
	Percent	24%	33%	43%	40%	60%			
		RR	**RX**	**XX**	**R**	**X**			
ACTN3 rs1815739 (21)	**Number**	5	9	7	19	23	1,143a	2	.565
	Percent	24%	43%	33%	45%	55%			
		GG	**GC**	**CC**	**G**	**C**			
PPARA rs4253778 (21)	**Number**	15	3	3	33	9	13.714a	2	.001
	Percent	71%	14.5%	14.5%	79%	21%			
		CC	**CT**	**TT**	**C**	**T**			
HIF1A rs11549465(21)	**Number**	14	7	-	35	7	2.333b	1	.127
	Percent	67%	33%	-	83%	17%			

Table 3. Comparison of the athletic features of ACE I/D rs1799752 genotypes.

		N	Mean ±std. Deviation	Minimum	Maximum	F	p
Flexibility (cm)	II	5	14.4±8.31	8	23.5	1.066	0.365
	ID	7	9.28±6.55	-3.5	17		
	DD	9	9.22±6.31	-2.5	16.5		
	Total	21	10.47±6.9	-3.5	23.5		
Leg strength (kg)	II	5	150.4±37.82	88.5	191	0.377	0.691
	ID	7	141.21±12.22	126	164.5		
	DD	9	139.44±19.69	114.5	170.5		
	Total	21	142.64±22.50	88.5	191		
Handgrip (kg)	II	5	97.82±21.78	64.7	119.6	0.396	0.679
	ID	7	89.01±14	69	115.8		
	DD	9	90.65±17.81	67.3	116.4		
	Total	21	91.81±17.12	64.7	119.6		
Speed (sec)	II	5	3.28±0.16	3.13	3.56	0.441	0.65
	ID	7	3.20±0.19	3.01	3.54		
	DD	9	3.28±0.15	3.11	3.53		
	Total	21	3.25±0.16	3.01	3.56		

±7.66. 11.77 ±5.91. 12.57 ±6.5 cm. 139.2 ±31.82. 144.33 ±23.78. 142.92 ±15.63 kg. 90.84 ±17.05. 89.91 ±14.59. 94.95 ±21.94 kg. 46.3 ±2.68. 48.43 ±3.53. 47.22 ±10.96 kg/ml. 3.32 ±0.22. 3.22 ±0.09. 3.25 ±0.2 sec for RR. RX. XX genotypes. Although athletes with RX and XX genotypes exhibited better flexibility performance than athletes with RR genotypes in the physical tests of flexibility. the difference was not statistically significant (p=0.143). Athletes with RX genotype scored higher performance in leg strength (p=0.926) and athletes with XX genotype scored higher performance in handgrip strength. but the difference was not statistically significant (p=0.848). In oxygen consumption capacity tests. athletes with RX genotype scored higher than those with RR and XX genotypes bu the difference was not statistically significant (p=0.567 (Table 4).

The comparison of PPARA rs4253778 polymorphism with flexibility. leg strength. handgrip strength. VO2 max and speed test results gave the respective values of 11.8± 7.13. 5.5±7.08. 8.83±4.04 cm. 138.76±21.2. 170.5±17.7 134.16±13.75 kg. 91.56±17.9. 106.03±4.82. 78.86±9.8 kg. 46.72±7.49. 47.6±3.41. 51.43±0.80 kg/ml. 3.25±0.17 3.30±0.19. 3.19±0.15 sec for GG. GC. CC genotypes. In the physical tests of flexibility. GG. CC and GC genotypes respectively have the highest flexibility but this result is not statistically significant (p=0.337). With regard to leg strength. athletes with GC genotype have produced more power than athletes with GG and CC genotypes but the results were not significant (p=0.05). In handgrip strength athletes with GC genotype scored higher than athletes with GG and CC genotypes but the results were statistically indifferent (p=0.151). Athletes with CC genotype scored higher with regard to oxygen consumption capacity but the result was not statistically significant (p=0.551). With respect to speed. athletes with CC genotype had better speed properties but this characteristic was not statistically significant either (p=0.757) (Table 5).

In the comparison of *HIF1A* rs11549465 polymorphism with flexibility. leg strength. handgrip strength. $VO_{2\,max}$ and speed test results. CC. CT genotypes were found to be 12±6.01. 7.42±8.01 cm. 142.17±16.8. 143.57±32.67 kg. 92.5±16.13. 90.42±20.24 kg. 49.01±5.12. 44.54±8.47 kg/ml. 3.19±0.1. 3.38±0.2 sec respectively. In the physical test for flexibility. athletes with CC genotype scored higher than those with CT genotype (p=0.158). in oxygen consumption capacity athletes with CC genotype again scored higher than those with CT genotype (p=0.146) but this difference was not statistically significant. No differ-

Table 4. Comparison of the athletic features of ACTN3 rs1815739 genotypes

		N	Mean ±std. Deviation	Min.	Max.	F	p
Flexibility (cm)	RR	5	5.2 ±7.66	-3.5	12		
	RX	9	11.77 ±5.91	6.5	23.5	2.167	0.143
	XX	7	12.57 ±6.5	2.5	23.5		
	Total	21	10.47 ±6.9	-3.5	23.5		
Leg strength (kg)	RR	5	139.2 ±31.82	88.5	170.5		
	RX	9	144.33 ±23.78	114.5	191	0.077	0.926
	XX	7	142.92 ±15.63	128	165		
	Total	21	142.64 ±22.5	88.5	191		
Handgrip strength (kg)	RR	5	90.84 ±17.05	64.7	108.6		
	RX	9	89.91 ±14.59	67.3	111.6	0.166	0.848
	XX	7	94.95 ±21.94	69	119.6		
	Total	21	91.81 ±17.12	64.7	119.6		
$Vo_{2\ max}$ (kg/ml)	RR	5	46.3 ±2.68	43	49.3		
	RX	9	48.43 ±3.53	43.7	52.5	0.165	0.85
	XX	7	47.22 ±10.96	26.4	57.5		
	Total	21	47.52 ±6.57	26.4	57.5		
Speed (sec)	RR	5	3.32 ±0.22	3.04	3.56		
	RX	9	3.22 ±0.09	3.02	3.34	0.586	0.567
	XX	7	3.25 ±0.2	3.01	3.54		
	Total	21	3.25 ±0.16	3.01	3.56		

Table 5. Comparison of the athletic features of PPARA rs4253778 genotypes.

		N	MEAN ±STD. DEVIATION	Minimum	Maximum	F	p
FLEXIBILITY (cm)	GG	15	11.8± 7.13	-3.5	23.5	1.157	0.337
	GC	3	5.5±7.08	-2.5	11		
	CC	3	8.83±4.04	6.5	13.5		
	Total	21	10.47±6.9	-3.5	23.5		
LEG STRENGTH (kg)	GG	15	138.76±21.2	88.5	170.5	3.386	0.056
	GC	3	170.5±17.7	159	191		
	CC	3	134.16±13.75	120.5	148		
	Total	21	142.64±22.5	88.5	191		
HANDGRIP STRENGTH (kg)	GG	15	91.56±17.9	64.7	119.6	2.103	0.151
	GC	3	106.03±4.82	103.2	111.6		
	CC	3	78.86±9.8	69	88.7		
	Total	21	91.81±17.12	64.7	119.6		
$VO_{2\ MAX}$(kg/ml)	GG	15	46.72±7.49	26.4	57.5	0.615	0.551
	GC	3	47.6±3.41	44	50.8		
	CC	3	51.43±0.80	50.5	51.9		
	Total	21	47.52±6.57	26.4	57.5		
SPEED (sec)	GG	15	3.25±0.17	3.01	3.56	0.283	0.757
	CG	3	3.30±0.19	3.19	3.52		
	CC	3	3.19±0.15	3.02	3.3		
	Total	21	3.25±0.16	3.01	3.56		

ences were found as to the strength scores p>0.05. In the comparison comparing HIF1A rs11549465 polymorphism with speed test results. the average speed of CC and CT genotypes is 3.19±0.1sec and 3.38±0.2sec respectively. When the speed average of the genotypes was examined. it was determined that the CC genotype average was high. The speed test results were evaluated statistically between genotype groups and a significant relationship was found (p = 0.008). It was determined that the HIF1A rs11549465 CC genotype had a better speed value than the CT genotype (Table 6).

4. Discussion

In recent studies. the relationship between sports genetics and athletic performance is among the primary areas of research by sports scientists and biologists. For an athlete to attain the maximum level of success. it is vitally important to discover the talents at an early age. channel them wisely within the discipline of sports and apply training programs accordingly.

Table 6. Comparison of the athletic features of HIF1A rs11549465 genotypes.

		N	Mean ±std. Deviation	Min.	Max.	F	p
	CC	14	12±6.01	2.5	23.5		
Flexibility (cm)	CT	7	7.42±8.01	-3.5	16.5	2.16	0.158
	Total	21	10.47±6.9	-3.5	23.5		
	CC	14	142.17±16.8	114.5	170.5		
Leg force (kg)	CT	7	143.57±32.6	88.5	191	0.01	0.898
	Total	21	142.64±22.5	88.5	191		
	CC	14	92.5±16.13	67.3	119.6		
Handgrip force (kg)	CT	7	90.42±20.24	64.7	115.8	0.06	0.801
	Total	21	91.81±17.12	64.7	119.6		
	CC	14	49.01±5.12	38.5	57.5		
$Vo_{2\ max}$(kg/ml)	CT	7	44.54±8.47	26.4	50.8	2.29	0.146
	Total	21	47.52±6.57	26.4	57.5		
	CC	14	3.19±0.1	3.01	3.34		
Speed (sec)	CT	7	3.38±0.2	3.04	3.56	8.70	0.008
	Total	21	3.25±0.16	3.01	3.56		

Ice hockey as a game relies mainly on explosive power. speed. agility. flexibility. endurance and strength. This game is characterized by a turn of speed. fixed speed. accelerated changes of direction. intermittent and intense use of skates. potential of bodily contact with high impact and performance of several maneuvers with talent (21-22). Of the studies done so far. none has focused on comprehensive physical tests as well as an assessment of genotypes.

In this study. ice hockey players were analyzed with respect to polymorphism and physical tests were done along with athletic performance measurements. ACE I/D (rs1799752). ACTN3 (rs1815739). PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms were taken as genetic markers. Physical tests. on the other hand. included the Maximal Oxygen Consumption Capacity test. Anaerobic Performance test. Flexibility test. and Force test. An evaluation of Genotype-Allele frequency was done which was then compared to physical test evaluations and the effects on athletic performance were reported.

The mean values of ACE (rs1799752) endurance-related I allele. ACTN3 (rs1815739) X allele. PPARA (rs4253778) G allele and HIF1A (rs11549465) C allele (1-23-24). flexibility. leg force. hand force and Vo2max are in support of our hypothesis (Tables 2-5) but the results were not statistically significant. These data emphasize the importance of studies focused on individuals.

Angiotensin Converting Enzyme (ACE) has been analyzed in many studies conducted in the field of sports genetics. ACE is an important enzyme that performs an effective role in the regulation of homeostasis. a key actor in circulation. In our cohort. the ACE gene holds a higher frequency of DD and ID polymorphisms than II polymorphism but this difference is not statistically significant (p=0.056).

It was reported in a meta-analysis study performed between 2008 and 2016 by Weyerstra et al. (2017) that athletes of the Caucasian race have statistically significant levels of ID genotype than DD genotype. Our findings are correlated with this meta-analysis (25).

In the article we had previously published. considering the relation between ACE InDel polymorphism and VO2max. II genotype is believed to be something desirable for ice hockey players (26). In the physical tests of flexibility and force. II polymorphisms have better mean values compared to ID and DD. and with respect to speed. ID polymorphism has a better mean value. In spite of this. the results of none of the physical tests among the groups of genotypes were found to be statistically significant (p>0.05).

Flexibility is an important factor for athletic performance and for preventing and curing sports injuries not related to impact. Literature gives us only a small amount of data regarding the genetics of flexibility in ice hockey players. In a study conducted with 97 ballet dancers where the ACE I/D gene was compared with the value of flexibility. ID genotype was observed to be more highly correlated with flexibility than DD genotype. a similarly significant correlation was not found in our cohort (27). In the same study. X allele of the said ACTN3 gene was reported to exhibit a lower level of flexibility than R allele.

Force is the sum of the reaction muscles give against resistance and the endurance muscles show against resistance. In general. being successful in sports is connected to the ability of a player to produce high amounts of force in a short period of time and is an indicator of endurance (28). Force is one of the qualities that substantially affect athletic performance in ice hockey. In a physical contact game like ice hockey. players are expected to have both lower-body and upper-body strength (29). In a study conducted with professional ice hockey players. muscle performance values have been examined and individual differences have been identified. Folland et al. (2000). Kritchevsky et al. (2005) and Pescatello et al. (2006) have concluded that ACE genotype is not correlated with the muscle strength in the upper arm or upper leg (30-31-32). Williams et al. (2005). to the contrary. have reported that in knee extensors ACE genotype is significantly correlated with pre-training isometric and isokinetic strength and DD homozygotes have the highest levels of strength (63). In a study by Pescatello et al. (2006). it was stated that by training more increase can be achieved in maximal voluntary contractions in I allele carriers than DD homozygotes (32). 266 athletes participated in a study conducted by Orysiak et al. (2013) in Poland (41). ACE I/D rs1799752 and ACTN3 rs1815739 gene regions were compared against handgrip strength and no correlation was found (32). In

this study. although it was found that in the physical tests of strength II polymorphisms had a higher mean score than ID and DD no significant results were obtained. Our findings support the studies in the literature.

Speed is a quality that can be affected by genetic and environmental factors. In the last 20 years. much research has been done on the consistent basic influence of genetic on speed adaptation (33).

In a study conducted with 555 athletes. sprint periods for 100m. 200m and 400m were determined and compared with ACE I/D polymorphism. It was found that the sprints with ACE DD genotype have the best 200-meter sprint period which is faster than ACE II (21.33 ± 0.56). Also. the sprints with ACE DD genotype have been reported to have shorter 400 meters sprint period compared to ACE II genotype. Although sprint performance depends on a large number of gene variants and epigenetic conditions. the sprint period variance as reported by ACE is significant at elite level and may even influence world records (34). In a study by Jeremic et al.. (2019). 5mt speed test was performed with football players (35). The results obtained in the 5 mt sprint test of ACE DD and ACE ID groups have been reported as 1.15±0.05 s and 1.10±0.05 s respectively and the two genotypes have been reported to exhibit significant differences (p=0.42). In our study. ID polymorphism had a better mean value (3.20±0.19 s) with respect to speed (Table 3). The studies are correlated with our research.

In muscle histology. ACTN3 gene codes the ACTN3 protein in the skeletal muscle which is a structural component of Z disc. ACTN3 rs1815739 (R/X) polymorphism has been reported to affect sportive performance and muscle performance and it has been stated that ACTN3 deficiency changes the physiology of fast-twitching fibers and activates the aerobic paths in muscle metabolism. providing endurance. It also says in the literature that individuals with R allele have a dominant sprinter characteristic and individuals with X allele benefit from endurance (10).

In our study. although RX and XX frequency distribution of ACTN3 rs1815739 polymorphism is higher than RR frequency distribution. it was not statistically significant (p=0.56). In an ACTN3 meta-analysis study performed in 2011 by Alfred et al.. it has been reported that European athletes have higher RR genotype than sedentary individuals. In another study conducted with 37 athletes and 37 sedentary individuals. Günel et al. (2014) found that RX genotype and X endurance allele were at high levels in the study cohort (36). This study goes in parallel with ours.

This polymorphism has been compared to flexibility. leg strength. handgrip strength. VO2 max and speed test results. As for the mean flexibility of genotypes. the mean of XX genotype is high (12.57 ±6.5 cm). Regarding the quality of flexibility. although RX and XX genotypes exhibit better flexibility performance than RR genotype. this difference is not significant (p=0.143). In a comparison of ACTN3 gene and flexibility in 97 ballet dancers. ACTN3 XX genotype of the ballet dancers was found to be lower than RR and RX genotypes and it was significant ($p < 0.05$) (37).

In another study by Kikuchi et al.. (2017) a comparison of ACTN3 and flexibility was made for two different groups of athletes. In the first cohort (n=776). the 35.3 ± 0.7 cm of RR genotype was significantly lower than the 37.2 ± 0.3 cm of RX and XX genotypes ($P < 0.01$). In the second cohort (n=1257) on the other hand. RR genotype was identified as 38.1 ± 0.6 cm and RX and XX genotypes as 39.1 ± 0.3 cm. the flexibility value of RR genotype tended to be lower but the result was not statistically significant. (P = 0.114). In the total analysis of both cohorts. RR was correlated with a significantly lower degree of flexibility than RX and XX (P = 0.009). In our results also RR genotype yielded a lower level of flexibility (5.2 ±7.66 cm) but the result was not significant (37).

The players have to have strong muscles for performing speed-ups. sudden stops. passes and changes of direction in ice hockey training and competitions. In addition. players have to exert the highest levels of strength to hit the puck in order to score points (29). Although RX genotype exhibited fine performance in leg strength (p=0.926) and XX genotype showed high performance in handgrip strength in the study. there was no statistical discrepancy (p=0.848).

It was found that the isometric strength of knee extensors was not affected by the ACTN3 genotype in our cohort. Similarly. when examining isometric elbow flexor strength. Clarkson et al. (2005) have reported that ACTN3 R577X genotype is not correlated with muscle phenotype in males. but these researchers have stated that for ACTN3 577X allele (XX) homozygote females have lower isometric strength than heterozygotes (RX) (38). McCauley et al. (2009) have reported that ACTN3 R577X polymorphism has no effect on the isometric strength of knee extensors in adult males at high speed. Ruiz et al. (2011) compared ACTN3 R577X polymorphism of 66 elite male and female volleyball players with power and strength test results. The researchers have argued that ACTN3 gene expression was not directly influential on power and strength values in volleyball players. These results are in support of our study (39).

In a study performed by Ahmetov et al.. (2013) on a study group consisting of children (n =457). handgrip strength has not been found to be significantly correlated with ACTN3 R577X polymorphism. However. it has been reported that children with RR genotype had a high mean value (15.5) (40). In our study. the mean value of athletes with RR genotype was found to be 90.84 ±17.0 kg. 266 athletes were involved in a study conducted by Orysiak et al. (2018) in Poland. ACTN3 rs1815739 gene regions and handgrip strength were compared and no correlation was found (41). These results are in support of our findings.

Maximum Oxygen Consumption Capacity (VO2max) is the highest volume of oxygen taken in. carried and consumed by the metabolism during sports (42). Oxygen consumption capacity is defined as reliable cardiovascular system and aerobic mechanism capacity (43-44). It has been reported that it speeds up resting in between intense and rapid actions involved in ice hockey and that repeated sprint quality is correlated with maximal O2 consumption (45). In this study. we aimed to examine the effects of genetic differences on VO2max.

As for the mean VO2max value of genotypes. the mean value of RX genotype is found to be higher than RR and XX genotypes (Table 4). No significant differences were found when VO2max test results were compared among the genotype groups (p=0.567). In a study conducted by Lucia et al.. (2006) 50 elite long-distance cyclists (VO2max: 71-75 ml/min/kg) were compared to 52 long-distance runners (VO2max: 70-75 ml/min/kg) with regard to

oxygen consumption capacities based on the distribution of ACTN3 R577X polymorphism and no significant difference was found in both of the groups (p> 0.05) (46). In a study by Moran et al.. (2007). voluntary athletes were grouped into two as females (n=525) and males (n=467) in order to perform an ACTN3 R577X polymorphism study and a physical test for VO2max. No statistically significant results were obtained in this group (p= 0.316) (47). In a research by Pimenta et al.. (2013). the VO2max values were measured for 200 elite Brazilian football players. The football players with XX genotypes were found to score a higher mean value of VO2max than those with RR genotype (48). A study by Koku et al.. (2019) compared the VO2max values of football players (n=100) and sedentary individuals (n=101). No significant difference was found in this study involving VO2max evaluation (49). These data indicate correlation with our study. In a study conducted in China. a group of athletes (n=60) and a control group (n=200) were compared with regard to ACTN3 and VO2 max. ACTN3 RR genotype combination has been reported to be correlated with higher values of VO2max in defensive players compared to the others. It has been stated that R allele is premium with regard to VO2max value (50). This study is not in support of the results of our study.

The term speed has various definitions made by different researchers. It can generally be defined by many features such as making quick decisions. quickly changing directions. making quick motions. stopping quickly. and starting quickly. This is a sportive ability that is known to be of benefit to all athletes. Speed and agility are important components of ice hockey. It has been stated in many studies that skate acceleration and highest skate speed is the most important physical determinants of performance in this sport. (51).

With regard to the mean speed of genotypes. RX genotype has been found to have a lower mean value (Table 4). No significant difference was found when speed test results were compared among genotype groups (p>0.05).

In a study performed by Moran et al.. (2007) voluntary athletes were grouped into two as females (n=525) and males (n=467) in order to conduct an ACTN3 R577X polymorphism study and a physical test for 40 mt sprint run. The researchers have reported that ACTN3 R577X polymorphism is correlated with sprint ability as a phenotypic feature. This finding is in support of previous studies where ACTN3 577R allele has been found to be correlated with the case of elite sprint athletes. In a study involving a total of 555 athletes. of which 346 are sprinters. sprint times were recorded for 100m. 200m and 400m and compared to ACTN3 R577X polymorphism. It has been reported that sprinters with RR genotype scored a shorter 200-meter sprint time compared to individuals with XX genotype (21.19 ± 0.53 sec versus 21.86 ± 0.54 sec. p = 0.016). (31). These results indicate a correlation between R allele and speed and these results are also in support of our study (Table 4). In a study by Papadimitriou et al.. (2018) involving 1064 athletes (441 males and 257 females) individual run times were analyzed for 1500. 3000. 5000. 10.000 m and marathon races. Based on ACTN3 RR. RX. XX genotype distribution (Mean (SD) marathon times (in s) were: ACTN3 RR 9149 (593). RX 9221 (582). XX 9129 (582) p = 0.94) and no difference was identified in the evaluation (52).

A further gene that is correlated with endurance and explosive power in sportive performance is the gene that codes Peroxisome Proliferator-Activated Receptor Alpha (PPARA). In periods of long-term fasting. the free fatty acids that are in motion in the adipose tissue again get connected to PPARA. This increases the hepatic fatty acid oxidation and the secretion of acetone bodies in order to suppress hypoglycemia (53).

PPARA gene has a higher frequency of GG polymorphism (71%) than the frequencies of GC and CC. but this is not statistically significant (p=0.001). In one of the initial studies on PPARA gene and athletic performance. muscle fiber composition has been identified in 40 young males. slow-twitching fibers have been found to comprise more of CC genotype but the result was not statistically significant (14). Ginevičienė et al. (2010) have examined the related polymorphism in 193 Lithuanian elite athletes. The researchers have reported that GG genotype has been correlated with endurance and CC genotype with explosive power. In the evaluation of athletes in this study. the high level of C allele was statistically significant in contrast to our study (p = 0.046) (54).

Similar to our study. Akçamlı et al. (2018) have analyzed 64 Turkish football players. In the related study. GG genotype and G allele have been found to be at significantly high levels. This study is also in support of our research (23). In a study conducted with 113 Italian elite athletes including martial arts. motorcycling and football. the frequency of GG genotype and G allele has been found to be high in football players. This research is in support of our study. In addition. the researchers have reported that PPARA polymorphism can be used as a genetic marker among mixed sports disciplines (55).

In the comparison of PPARA rs4253778 polymorphism with flexibility. leg strength. handgrip strength. VO2 max and speed test results. athletes with GG genotype had the highest flexibility compared to athletes with CC and GC genotypes but the result was not statistically significant (p=0.337). No studies have been found in the literature on the physical testing of flexibility for PPARA rs4253778.

In the comparison of PPARA rs4253778 polymorphism with leg strength. it has been found that athletes with GC genotype produce more strength than athletes with GG and CC genotypes (p=0.05). No studies have been found in the literature on the physical testing of leg strength for PPARA rs4253778. polymorphism.

In the comparison of handgrip strength. although GC genotype produces more strength than GG and CC genotypes. the results were not statistically significant (p=0.151).

In a study performed by Ahmetov et al.. (2013) with a study group comprising children (n =457). PPARA rs4253778 has been evaluated with regard to physical testing of handgrip strength and C allele of PPARA gene has been reported to be correlated with better handgrip strength test results (P = 0.037) (40).

In the comparison of PPARA rs4253778 polymorphism with VO2 max. oxygen consumption capacity has been found to be better in athletes with CC genotype. The result is statistically insignificant though (p=0.551). In a study by Tural et al.. (2014). PPAR-a and PPARGC1A gene zones were compared for oxygen carriage capacity. According to aerobic performance test parameters. an analysis of PPAR-a and PPARGC1A genotype distribution indicates a statistically significant relationship between speed. time and

maximum oxygen consumption and PPAR-a and PPAR-GC1A genotypes (p =0.001). It has been reported in the literature that particularly long-chain fatty acids carriage and fatty acid oxidation genes and sequence variants can improve VO2max. Our study and similar future studies can be pioneering for the testing and verification processes (56).

With regard to the speed characteristic of PPARA rs4253778 polymorphism. although individuals with CC genotype scored better speed values. no significant difference was found in relation to this characteristic (p=0.757). In a study conducted with 586 athletes. sprint testing was done with PPARa gene. The researchers have reported that PPARa gene variant genotypes were correlated with significant differences in multistage 20-meter shuttle runs and that GG allele group exhibited substantially better performance than GC / CC allele groups (3). In our study. on the other hand. athletes with CC genotype have been found to run faster.

Hypoxia-inducible Factor Alpha gene (HIF1-A). which is a transcription factor related to athletic performance and regulates the expression of genes that ensure cell adaptation to hypoxia. is one of the genes with which researches on genetic and athletic performance are conducted (57). Factors that can be stimulated under hypoxia conditions (Hypoxia-inducible Factors. HIF's) help cells adapt to hypoxia conditions and also support athletes get better adapted especially to aerobic exercises (58).

In our study group. HIF1A gene exhibited a higher frequency of CC (Pro/Pro) (67%) than that of CT(Pro/ser). However. this result was not statistically significant (p=0.127). TT genotype was not encountered in this study group. The HIF1A rs11549465 in Russian weightlifters and wrestlers has been found to provide a tendency to sportive success. HIF1A Ser allele has been reported to be correlated with the dominance of fast-twitching muscle fibers (Pro/Ser 46.2%. Pro/Pro 31.4%; p=0.007) (13). Eynon et al. (2010) analyzed HIF1A rs11549465 Pro582Ser (C/T) polymorphism in a study conducted with 155 Israeli athletes with strength orientation and endurance and 240 sedentary individuals (59). In the study. no statistically significant difference was found among the control group. the sprinter group and the endurance group and Pro (C) allele has been reported to be at high levels in the cohort. Döring at al.. (2010) conducted research with 316 male professional endurance athletes and 304 sedentary individuals (60). It has been identified that Pro582Ser polymorphism has a strong tendency to create a difference in the distribution of genotypes among athletes and control groups (P = 0.017). These studies are correlated with our work with respect to the high levels of C allele. A similar study was done in 2012 with Polish athletes (n=127) with strength-orientation (sprinters). In the analysis between the control group and the athletes. CT genotype was found to be significantly higher in the athletes. The researchers have stated that HIF1A rs11549465 polymorphism can be an important genetic marker in athletes with strength orientation (sprinters) (61). A HIF1A Pro582Ser (rs11549465) polymorphism study was conducted with a total of 33 Turkish professional ski runners. 22 males and 11 females. The said study is remarkable for the high frequency of Pro/Pro (CC) genotype and Pro (C) allele. This study is also in support of our findings (62).

In the comparison of HIF1Ars11549465 polymorphism in the physical testing for flexibility. CC genotype has been found to be higher than CT genotype but the difference was not significant (p=0.158). No studies have been encountered in the literature where physical testing for flexibility was performed with HIF1A rs11549465 polymorphisms.

In our study group. the comparison of HIF1A rs11549465 polymorphism with the test results of leg strength. the mean value of CT genotype has been found to be high (p>0.05). The comparison of HIF1A rs11549465 polymorphism with the test results of handgrip strength among our athletes yielded a high mean value for CC genotype. No significant difference was found among the handgrip test results of genotype groups (p>0.05). This meant no difference with regard to strength scores. No studies have been identified in the literature where physical testing for handgrip strength and physical testing for leg strength were performed with HIF1A rs11549465 polymorphisms.

In our study. the comparison of HIF1A rs1154946 polymorphism with VO2max test results has revealed higher results for athletes with CC genotype than those with CT genotype (p=0.146). but this high level was statistically insignificant.

With the help of these studies. we are trying to have a good grasp of the genetics of human endurance. Some researchers adopt a skeptical approach to the importance of genetics especially in relation to VO2max. Reviewing the literature in light of this information. we have seen that the HIF1A gene is associated with the development of VO2max value (63).

In a study conducted in (2003) by Prior et al.. (n=233) the researchers created the groups on the basis of age differences (58). The first group that represented age 55 did not exhibit a statistically significant difference. In the groups of age 60 and age 65. VO2max values of the individuals with CC genotype have been found to be significantly high. Also. the researchers made VO2max measures on the volunteers after they had completed an aerobic exercise training of 24 weeks and it has been reported that post-training oxygen consumption capacity was higher.

Comparing HIF1A rs11549465 polymorphism with the speed test results of our volunteers. we have found speed to have a better value in CC genotype (p=0.008). No studies have been found on the physical testing of speed for HIF1A rs11549465 polymorphisms.

5. Conclusion

For the last 20 years. detailed studies have been conducted on the consistent basic effect of genetics on adaptation to exercise (33). Genetics is known to have an effect on both exercise performance (16) and adaptation (64). Studies of genetics are generally focused on the effects of single nucleotide polymorphisms (SNP's) and a combination of these polymorphisms (65).

Somatic qualities of athletes. such as body height – body weight – and body mass index (BMI). influence the competition in a certain working discipline and the techniques and tactics that constitute the adaptation of the athlete. Therefore. these somatic variables have important repercussions on the training strategy (66). In every competition where seconds count. success is governed by physical qualities. Nevertheless. acquiring genetic knowledge and using it in individualized training can be a good for-

mula for the success of athletes and teams.

The literature comprises researches on the effect of ACE I/D (rs1799752) and ACTN3 (rs1815739) polymorphisms on physical tests. Our study is comparable in that regard to those in the literature. On the other hand. as far as we have seen in searches. this is the first time PPARA (rs4253778) and HIF1A (rs11549465) polymorphisms are compared with physical tests.

Our limitation is having a small number of cohorts. Although our data have exhibited a correlation in support of our theory. we were unable to obtain a significant difference due to the limited number of participants.

It is recommended to work with larger cohorts in future studies. We believe that our findings will contribute to literature and lead the way for further researches.

Conflict of Interests

The author has no conflicts with any step of the article preparation.

Consent for publications

The author read and approved the final manuscript for publication.

Ethics approval and consent to participate

No human or animals were used in the present research.

Informed Consent

The authors declare that no patients were used in this study.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request

Author contributions

Canan Sercan Doğan conducted the experiment. analyzed the data and wrote the manuscript. Muhammet İrfan Kurudirek and Korkut Ulucan analyzed the methodology and data. Orkun Akkoc and Meltem Özağır contributed to the concept and design of the research. Canan Sercan Dogan. Orkun Akkoç. Sinan Avcı and Selin Biçer Baikoğlu investigated the original draft and checked the last version. The authors confirm the sole responsibility for study conception. design. data collection. analysis of results and manuscript preparation.

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