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Review

Exploring the nexus between sports performance and genetics: a comprehensive literature review

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Abstract

Sport is a multifactorial phenomenon that is influenced by many factors. Although many factors affect sports performance, genetic factors may be important issues that need to be examined. In addition, the relationship between sports performance and genes is still unclear. Due to the developments in omics technologies, approximately 185 genetic markers have been identified for the relationship between sports performance and genes. These genes are expressed differently in metabolism according to the characteristics of sports performance. The aim of this study was to investigate the relationship between sports and genetics. Pubmed, Pubmed Central and Google Scholar internet search engines were used in current study. Additionally, the PRISMA technique was used in the study design. For this purpose, *COL1A1*, *COL5A1*, *ACTN3* and *ELN* genes may be important regulators on soft tissues. For endurance sports, genes like *ACE*, *ACTN3*, *ADRB2*, *HFE*, *COL5A1*, *BDKRB2*, *NOS3*, *HIF*, *VEGF*, *AMPD* and *PPARGC1A* significantly may influence performance limits. *ACE* and *ACTN3* genes, on the other hand, may determine power/strength and speed skills in athletes. As a result, knowing the athlete's genetic predisposition to sports can be effective in achieving success.

Keywords: Collagen, Endurance, Genetic, Sports, Strength

1. Introduction

Considering the existing infrastructure and scientific achievements in sports, the predisposition of athletes to some sports branches can be discovered in the early stages [1]. Accordingly, when the athletic skill status of the athletes is examined, some of them have similar physical characteristics and even apply the same training program, they have been shown to have different levels of ability [2]. To determine the different ability statuses of athletes, the concepts of elite-level sports performance and elite-level athletes are very important. The level of development of sports ability in relation to the status of elite-level athletes depends on many factors [3, 4]. Genetics, which is one of these factors, is a science that examines gene function, genome structure, gene organization and recombinant rate [5]. When a number of innate characteristics of the athlete in the context of athlete performance were examined, it was found that genetics had a percentage of 66% [6]. This suggests that genetics may be an important biomarker in determining and evaluating elite-level sports performance among athletes [7]. With the completion of the Human Genome Project (HGP) in 2003, the desired physical characteristics in sports began to be elucidated in the human genome [8]. One hundred eighty-five genetic markers related to elite-level sporting performance have been identified in the last two decades. One hundred of them are related to endurance, sixty-nine to strength/power, and sixteen to psychogenetics [9]. Identifying the genetic mechanisms involved in athlete performance can be critical in achieving high-level performance. In addition, knowing the injury sensitivities of athletes and the hereditary mechanisms of their energy systems can significantly increase the percentage of success in sports.

During the literature review, numerous studies were identified that link sports performance to both physiological and psychological factors. These studies broadly cover aspects such as nutrition, physiology, training, ergogenic aids, psychology, and social factors. This review aims to explore the relationship between sports and genetics comprehensively and from multiple perspectives. The findings are expected to serve as a valuable resource for researchers in this field, guiding future scientific endeavors.

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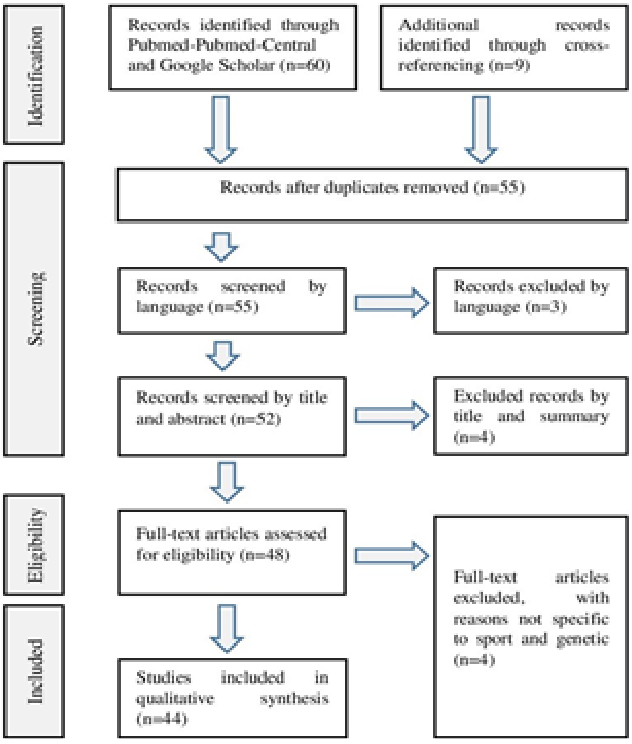

Fig. 1. Study selection based on PRISMA and flow diagram of stages.

2. Materials and Methods

2.1. Search strategy

This review examined studies from PubMed, PubMed Central, and Google Scholar databases, utilizing keywords like genetics, gene and sports, collagen tissue and gene and sports performance, power/strength sports and gene, and endurance sports and gene. The aim was to ensure the data were not only comprehensive but also current. Rigorous evaluation of field-specific studies was conducted to maintain systematic and orderly research.

2.2. Study selection

The publications related to the study were examined comprehensively and those related to the subject were scanned according to the title and included in the review. Studies that were not related to the research were eliminated. The summary sections of the obtained data were examined in detail. Case-control, cross-sectional, systematic review and meta-analysis data were used in the review. The research was include polymorphism, allele and genotype data for the relationship between gene and sports performance. The review did not include any restrictions on the relationship between sports performance and genes, such as gender, ethnicity, language, etc. The relevance of the data was assessed using the PRISMA flow diagram developed by Moher et al. [10] (Figure 1).

3. Results

3.1. Genetic factors affecting collagen structures in sports

Collagen is a substance that is derived from structure of a triple helix protein in extracellular matrix tissues responsible for the elasticity of the skin in which found organs, tissues and cells [11, 12]. The vast majority of the body's collagen tissues are composed of type I collagen fibrils. Type I collagen is a structure that forms the major component of the bone matrix with a strong parallel form of fibril bundles in soft tissues such as organs, skin, muscles, etc [13, 14]. The functioning of type I collagen is controlled by the *COL1A1* gene. Polymorphisms within the *COL1A1* gene are thought to be critical in maintaining the structural integrity of collagen tissues. The *COL1A1* rs1800012 polymorphism is known to be a reduced risk factor for sports-related ligament and tendon injuries [15]. Wang et al. [16] concluded in their study that the *COL1A1* rs1800012 polymorphism may protect athletes against tendon-ligament injuries by affecting the elasticity of soft tissues. In another study by Saito et al. [17] it was concluded that the polymorphism *COL1A1* rs1107946 had a statistically significant difference in the flexibility level of collagen structures.

Another soft tissue formation that can have an effect on collagen tissues is type V collagen. Type V collagen is a soft tissue often found in tissues and cells where type I collagen is excreted to regulate the width of collagen fibrils [18]. The function of type V collagen is controlled by the *COL5A1* gene. The *COL5A1* gene codes for the alpha(α)1 chain of type V collagen. Kahya [19] concluded in his study that *COL5A1* rs12722 *Bst*UI polymorphism may significantly protect athletes against injuries by affecting the structural properties of soft tissues. Guo et al. [20] concluded in their study that the *COL5A1* gene was associated with soft tissue injuries. Heffernan et al. [21] concluded in their study that *COL5A1* rs12722-rs3196378 polymorphisms may significantly protect athletes against soft tissue injuries. In contrast to these results, it was found that there was no relationship between the *COL5A1* gene and soft tissues. Miyamoto-Mikami et al. [22] concluded in their study that the *COL5A1* rs12722 *Bst*UI polymorphism was not related to sports-related muscle injuries. The properties of genes assumed to affect the susceptibility of injury to soft tissues are shown. (Table 1) [23-30].

Recent studies have identified *ACE* rs4646994 and *ACTN3* rs1815739 gene polymorphisms that may be associated with sports injuries. Onori et al. [31] concluded in their study that the *ACE* gene was associated with soft tissue injuries in sports. Almeida et al. [32] concluded in their study that the *ACTN3* R577X polymorphism was associated with non-contact soft tissue injuries in football. In another study by Gutiérrez-Hellín et al. [33] it was found that individuals with the *ACTN3* RR genotype had a higher incidence of injury than the RX and XX genotypes of the *ACTN3* gene. In contrast to these results, Coso et al. [34] concluded in their study that the polymorphism *ACTN3* rs1815739 was not associated with the incidence of injury in sports.

Elastin (ELN), which is responsible for the structural width of collagen tissues, is a protein that has a direct effect on the elasticity level of fibrous connective tissues. The function of the elastin protein is controlled by the *ELN* gene. Artells et al. [35] concluded in their study that *ELN* rs2289360 polymorphism had a key role in regulating soft tissues and reducing medial collateral injuries.

3.2. Genetic structures affecting endurance performance in sports

Endurance is the ability to maintain a physical performance [36]. Although many factors affect endurance performance, there are some ideas that explain this condition with hereditary mechanisms. Accordingly, cardiorespiratory endurance is estimated to be inherited between 31%

Table 1. Characteristics of genes assumed to affect susceptibility to soft tissue injuries.

Gene	Identification	Polymorphism	Dominant Allele
ACE	Angiotensin-Converting Enzyme	rs4646994	I
ACTN3	Alpha Actinin 3	rs1815739	X
AMPD1	Adenosine Monophosphate Deaminase 1	rs17602729	T
CCL2	C-C Motif Chemokine Ligand 2	rs2857656	G
COL1A1	Collagen Type 1 Alpha 1	rs1800012	G
COL5A1	Collagen Type 5 Alpha 1	rs12722	T
COL12A1	Collagen Type 12 Alpha 1 gene	rs240736	A
ELN	Elastin	rs2289360	A
FBN2	Fibrillin-2	rs331079	G
GDF5	Growth/Differentiation Factor 5	rs143383	T
IGF2	Insulin Like Growth Factor 2	rs3213221	C
MLCK	Myosin Light Chain Kinase	rs2700352	C
MMP3	Matrix Metalloproteinases 3	rs679620	G
TGFB1	Transforming Growth Factor Beta 1	rs1800469	T
TTN	Titin	rs10497520	T
TNC	Tenascin C	rs2104772	A

and 85% [6]. Genes may be critical for athletes to be able to use their muscles more effectively during long-term activities. Some genes related to endurance performance in sports and their characteristics are presented. (Table 2) [37-40].

As a result of the examination of the relationship between genes and endurance in sports, some important evidence has been found. *ACE* and *ACTN3* genes are some of them. As a result of *ACE* insertion/deletion, I/D alleles and II, DD and ID genotypes are formed. Regarding the endurance performance of the *ACE* gene, especially athletes with the I allele and II genotypes may have high efficiency in long-term sports activities. In contrast to this result, it is known that athletes with the *ACE* D allele and DD genotype are more successful in sports where speed and strength are dominant. Various variations in the *ACTN3* gene, such as the *ACE* gene, have caused a number of changes in the function of gene. *ACTN3* rs1815739 exon 16 C >T translation decreases alpha-actin level when the 577. amino acid corresponds to the stopping codon instead of arginine. It is known that alpha-actin levels are associated with endurance performance [41-43]. For this reason, Malhotra et al. [44] concluded in their study that *ACTN3* R577X gene polymorphisms may be structures associated with endurance performance. In contrast to this result, another study has also found that *ACTN3* gene variants haven't effect on endurance performance. For this purpose, Papadimitriou et al. [45] concluded in their study that there was no statistically significant relationship between the *ACTN3* R/X and *ACE* I/D alleles and 1.500-3.000-5.000 and 10.000-meter running performances in male and female athletes.

Another structure associated with endurance in sports is *PPARGC1A* gene. *PPARGC1A* gene is known to make positive contributions to endurance performance by increasing the use of fat and glucose in long-term sports activities. For this purpose, Appel et al. [46] found that *PPARGC1A* polymorphism may be associated with endurance performance in sports. Moir et al. [47] concluded in their study that *PPARGC1A* polymorphism was statistically significantly associated with slow-twitch muscle fibers and the ratio of MaxV02. Hall et al. [48] concluded in their study that *PPARGC1A* rs8192678 482Ser allele may make a significant contribution to the improvement of endurance performance. Another study by Tharabenjasin et al. [49] it was found that type I oxidative fibrils in skeletal muscles may be an important regulator in the development of muscle morphology and gene expression.

Another structure that affects the catabolism of fats is the *ADRB2* gene. *ADRB2* gene polymorphisms have important effects on endurance in sports. For this purpose, *ADRB2* 46A/G and 79C/G polymorphisms are critical in the breakdown and metabolism of fat during endurance exercises in sports [50]. Elite-level endurance performance in sports can be an important criterion of sporting success. For this purpose, Semenova et al. [51] concluded in their study that the *HFE* H63D polymorphism was associated with elite-level athletic performance.

The flexibility-related mechanism of the *COL5A1* rs12722 polymorphism is also associated with better running performance in endurance activities [52]. Accordingly, individuals with the *COL5A1* rs12722 *Bst*UI T allele may have better racing performance in the endurance sports branches.

The effect of genetic structures on the vascular surface in sports performance can be significant in endurance performance. For this purpose, *ACE*, *BDKRB2*, *NOS3*, *HIF1-A* and *VEGF* genes may have important effects on the energy demand of aerobic metabolism and maximal oxygen consumption [53].

The ATP which is needed for muscle contraction plays critical a role in endurance performance. ATP production is carried out by AMPD1. AMPD1 catalyzes the deamination of adenosine monophosphate to inosine monophosphate. Owing to chemical reactions, ATP production takes place within muscle cells [54]. As a result, athletes may have more endurance in long-distance sports branches.

3.3. Genetic structures affecting power/strenght and speed performance in sports

Due to the nature of the sport, athletes are constantly improving their performance limits in the desire to be fas-

Table 2. Characteristics of genes that are assumed to affect endurance performance.

Gene	Identification	Polymorphism	Dominant Allele
ACE	Angiotensin-Converting Enzyme	A1u	I
ACTN3	Alpha Actinin 3	rs1815739	X
ADRB2	Adrenerjik Reseptör Beta 2	rs1042713	A
AGT	Angiotensinogen	rs699	C
AGTR2	Angiotensin II Receptor Type 2	rs11091046	C
AMPD1	Adenosine Monophosphate Deaminase 1	rs176602729	T
AQP1	Aquaporin 1	rs1049305	C
BDKRB2	Bradikinin Reseptor Beta 2	+9/-9	-9
CK-MM	Creatine Kinase, M-Type	rs8111989	A
COL5A1	Collagen Type 5 Alpha 1	rs12722	T
CYP2D6	Cytochrome P450 Family 2 Subfamily D Member 6	rs3892097	G
FTO	Alpha-Ketoglutarate Dependent Dioxygenase	rs9939609	T
GABPB1	GA Binding Protein Transcription Factor Subunit Beta 1	rs12594956 rs7181866	A G
GALNTL6	Polypeptide N-Acetylgalactosaminy Transferase Like 6	rs558129	C
GSTP1	Glutathione S-Transferase Pi 1	rs1695	G
HFE	Homeostatic Iron Regulator	rs1799945	G
HIF1A	Hypoxia Inducible Factor 1 Subunit Alpha 1	rs11549465	C
MCT1	Monocarboxylate Transporter 1	rs1049434	T
MtDNA loci	Mitochondrial DNA	MtDNA	H
MYBPC3	Myosin Binding Protein C 3	rs1052373	G
NFATC4	Nuclear Factor of Activated T Cells 4	rs2229309	G
NFIA-AS2	NFIA Antisense RNA 2	rs1572312	C
NOS3	Nitric Oksit Sentaz 3	rs2070744	T
PPARA	Peroxisome Proliferator-Activated Receptor Alpha	rs4253778	G
PPARGC1β	Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1 Beta	rs7732671	C
PPARGC1A	Peroxisome Proliferator-Actived Reseptor Gamma Coactivator 1 Alpha	rs8192678	G
RBFOX1	RNA Binding Fox-1 Homolog 1	rs7191721	G
SPEG	Striated Muscle Enriched Protein Kinase	rs7564856	G
TFAM	Transcription Factor A Mitochondrial	rs1937	C
TSHR	Thyroid Stimulating Hormone Receptor	rs7144481	C
UCP2	Uncoupling Protein 2	rs660339	T
UCP3	Uncoupling Protein 3	rs1800849	T
VEGFA	Vascular Endothelial Growth Factor A	rs2010963	C
VEGFR2	Vascular Endothelial Growht Factor Receptor 2	rs1870377	A

ter, stronger and more endurance. Questions that are about how some difficult or even impossible skills are developed in a short time in sports remain important in sports science. Although many internal and external factors can have an impact on speed and strength/power skills in sports, in recent studies, it has been believed that heredity has a considerable importance on sports. For this reason, it is assumed that heredity is important in maximal sporting skills at rates ranging from 46% to 84% [55]. The genes that have an impact on power/strenght and speed performance are presented. (Table 3) [56-59].

The *ACE* rs4646994 and *ACTN3* rs1815739 genes, which are the most studied in sports performance, are the structures in which the hereditary expression of power/strenght and speed is frequently seen in sports [60]. The ACE enzyme is activated by the *ACE* gene [61, 62]. ACE also forms a regulatory part of the Renin Angiotensin System (RAS) [63]. RAS is an important regulator of blood pressure and fluid balance. The *ACE* gene catalyzes the conversion of angiotensin I to II, enabling the breakdown of the endothelial protein on the inner surface of the vessel. This causes vasoconstriction in the vessels and stimulates the nutrition of cells and tissues. The *ACE* D allele, which is associated with elite sporting performance, is heavily expressed in sports where strenght/power is dominant [64-66]. Regarding the relationship between the *ACE* gene and sprint performance, Albuquerque-Neto et al [67] concluded in their study that *ACE* DD genotype was expressed higher than expected in power/strength athletes. Papadimitriou et al. [68] concluded in their study that sprinters with *ACE* DD genotype had better scores in sprint time than sprinters with II genotype. Costa and Slocombe [69] concluded in their study that the *ACE* DD genotype was related to sprint ability due to high ACE enzyme activity. Pasqualetti et al.

Table 3. Characteristics of genes assumed to have an effect on power/strenght and velocity performance.

Gene	Identification	Polymorphism	Dominant Allele
ACE	Angiotensin Converting Enzyme	rs4646994	D
ACTN3	Alpha Actinin 3	rs1815739	R
ACVR1B	Activin A Receptor Type 1 B	rs2854464	A
ADRB2	Adrenerjik Receptor Beta 2	rs1042713 rs1042714	G G
AGT	Angiotensinogen	rs699	235Thr
AGTR2	Angiotensin II Receptor Type 2	rs11091046	A
CACNG1	Calcium Voltage-Gated Channel Auxiliary Subunit Gamma 1	rs1799938	196Ser
CKM	Creatine Kinase, M-Type	rs8111989	G
CALCR	Calcitonin Receptor	rs17734766	G
CNDP1	Carnosine Dipeptidase 1	rs2887	A
CNDP2	Carnosine Dipeptidase 2	rs3764509	G
CNTFR	Ciliary Neurotrophic Factor Receptor	rs41274853	T
COL12A1	Collagen Type 12 Alpha 1	rs970547	T
COTL1	Coactosin Like F-Actin Binding Protein 1	rs7458	T
CREM	CAMP Responsive Element Modulator	rs1531550	A
DMD	Dystrophin	rs939787	T
GALNT13	Polypeptide Acetylgalactosaminyltransferase 13	rs10196189	G
HIF1A	Hypoxia Inducible Factor 1 Subunit Alpha	rs11549465	582Ser
HIF2A	Hypoxia İnducible Factor 2 Subunit Alpha	rs1867785 rs11689011	G C
HSD17B14	Hydroxysteroid 17-Beta Dehydrogenase 14	rs7247312	G
IGF1	Insulin Like Growth Factor 1	rs35767	T
IGF1R	Insulin Like Growth Factor 1 Receptor	rs1464430	C
IGF2	Insulin Like Growth Factor 2	rs680	G
IP6K3	Inositol Hexakisphosphate Kinase 3	rs6942022	C
MCT1	Solute Carrier Family 16 Member 1	rs1049434	A
MED4	Mediator Complex Subunit 4	rs7337521	T
MPRIP	Myosin Phosphatase Rho Interacting Protein	rs6502557	A
MTHFR	Methylenetetrahydrofolate Reductase	rs1801131	C
NOS3	Nitric Oksit Sentaz 3	rs2070744 rs1799923	T Glu298
NRG1	Neuregulin 1	rs17721043	A
PPARA	Preksizom Proliferator-Activated Receptor Alpha	rs4253778	C
PPARG	Preksizom Proliferator-Activated Receptor Gamma	rs1801282	G
RC3H1	Ring Finger And CCCH-Type Domains 1	rs767053	G
SOD2	Superoxide Dismutase 2	rs4880	Ala16
TPK1	Thiamin Pyrophosphokinase 1	rs10275875	C
UCP2	Uncoupling Protein 2	rs660339	C
ZNF423	Zinc Finger Protein 423	rs11865138	C
WAPL	WAPL Cohesin Release Factor	rs4934207	C

[59] found that *ACE* D allele was often expressed in rugby, where strength/power and speed were important.

ACTN3 is a major component of the Z line to which actinine filaments attach in fast-twitching fibrils [70]. ACTN3 is activated by the *ACTN3* gene. The *ACTN3* gene encodes for alpha-actin 3 [71]. The alpha-actin encoded by the *ACTN3* gene is mostly expressed in fast-twitch muscle fibers [72, 73]. Balberova et al. [74] found that the *ACTN3* R577 allele was frequently detected in sprinters.

Regarding sprinting and power performance in sports, Voisin et al. [75] concluded in their study that the *ACVR1B* rs2854464 A allele was associated with sprint and power performance. In contrast to this result, Bulgay et al. [76] concluded in their study that there was no correlation between the *VDR* rs2228570 polymorphism and sprint and power performance. Chen et al. [77] concluded in their study that the frequency of the *CKM* rs8111989 G allele was expressed higher in strength/power athletes compared to the control group. In contrast to this result, Ginevičienė et al. [78] concluded in their study that the *CKM* rs8111989 polymorphism was not associated with elite-level athletic performance. In a study concluded by Kikuchi et al. [79] it was found that *LRPPRC* rs10186876 A, *MMS22L* rs9320823 T, *MTHFR* rs1801131 C and *PHACTR1* rs6905419 C alleles were important genetic structures in weight lifting sport where strength/power was dominant.

4. Discussion

In the review, it was found that the body's collagen structures may be controlled by some genes. For this purpose, *COL1A1* rs1800012 and *COL5A1* rs12722 *Bst*UI gene polymorphisms may play a key role in soft tissue injuries [80, 81]. Similar results were found in *ACE* I/D and *ACTN3* R577X gene polymorphisms. Recent studies show that *ACE* I/D and *ACTN3* R577X gene polymorphisms are important markers in determining the incidence of sports injuries [31-34]. Some SNPs (single nucleotid polymorphisms) are important in developing endurance capacity in sports. To this end, *ACE* I/D, *ACTN3* R577X, *PPARGC1A* gene polymorphisms may be biomarkers for endurance performance in sports [82, 83]. This is revealed in the present review [44-51]. A number of physiological effects on the vessels in the development of endurance performance may differentiate the characteristics of sports performance. For this purpose, the present review revealed that *ACE*, *BDKRB2*, *NOS3*, *HIF-1A* and *VEGF* genes are important regulators on the vessels [53]. Although many gene polymorphisms have been identified in relation to power/strength and speed ability, *ACE* I/D and *ACTN3* R577X gene polymorphisms have a key role in this [84-86]. In the review, it was found that the physiological effect of *ACE* I/D gene polymorphism on the inner surface of the vessel is important in power/strength and speed sports [63-66]. A similar effect can be seen in the *ACTN3* R577X gene polymorphism, which differentiates muscle morphology. [70, 71].

5. Conclusion

Although a number of sport-specific factors are important in the development of sporting performance limits, some inherited traits from birth may be at least as important as other factors. When the data obtained from the review are evaluated, it can be considered that heredity has a critical importance on athlete performance. The hereditary mechanisms developed by collagen tissues against injuries may be important for the athlete to experience a successful sports life. For this purpose, it was known that the preservation of the structural integrity of the skeletal-muscular system and the response of collagen tissues to healing were explained by genetic factors. In the review, it was found that some genes on endurance ability may bring metabolism to a more efficient state. For this reason, genes and polymorphisms that may contribute to endurance performance were carefully evaluated in the review. In addition, it was taken into consideration in the review that genes may change the performance characteristics of short-term maximal strength/power and speed sports. When the data obtained from the review and the arguments within the scope of the literature are evaluated, it is predicted that sports performance is a phenomenon affected by hereditary factors, but many factors may also be effective in this situation. (Figure 2) [87].

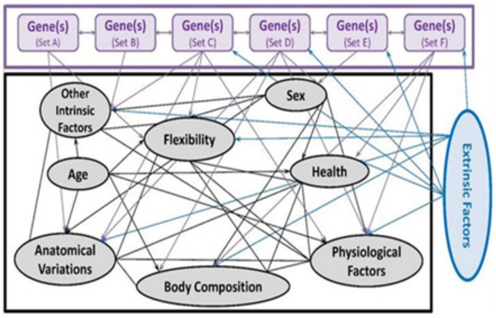

Fig. 2. Complex interaction of factors influencing sporting performance.

As a result, knowing the heredity predisposition of athletes may make great contributions to sports.

Conflict of Interests
The authors' have no conflicts with any step of the article preparation.

Consent for publications
The authors' 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 they did not use any patients in this research.

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

Authors' contributions
Sedat Kahya and Morteza Taheri did all the steps in the research work.

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