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The Impact of Polymorphisms in *AMPD1* and *BMP2* Genes on Performance in Female Athletes

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Abstract
In addition to training, nutrition, psychology, and genetics play a significant role in determining and enhancing athletic performance. Numerous studies have investigated how specific genetic variants affect athletes' physical abilities, such as strength, aerobic or anaerobic endurance, and speed. Among these genes are *Bone Morphogenetic Protein 2 (BMP2)* and *Adenosine Monophosphate Deaminase 1 (AMPD1)*. While the *BMP2* gene is not the direct focus of many studies on sports performance, it is considered a gene with indirect effects in the field of sports genetics. The rs17602729 polymorphism in the *AMPD1* gene is suggested to influence performance in short-term, high-intensity activities. Examining these polymorphisms will significantly contribute to the field. The study included 13 amateur athletes aged 12–16, who were short- or long-distance runners, and 13 sedentary individuals. Blood samples were collected, DNA was isolated, and genotypes were determined using Sanger sequencing. Analyses were conducted using SPSS 24.00, and differences in allele distributions between groups were analyzed using the chi-square test. In the *BMP2* gene A/C polymorphism, 46.15% of the athletes had the AA genotype, 46.15% the AC genotype, and 7.69% the CC genotype. In the control group, the distribution was 53.84% AA, 46.15% AC, and 0% CC. For the *AMPD1* gene C/T polymorphism, 92.30% of the athletes had the CC genotype, 7.69% the CT genotype, and 0% the TT genotype. The control group showed similar distributions: 92.30% CC, 7.69% CT, and 0% TT. The results indicated that the AA and AC genotypes in the *BMP2* gene were more prevalent among athletes. For the *AMPD1* gene, the higher representation of the C allele suggests that it may contribute to better physical performance in the athlete group.

Key Words: *Athlete, Athletic Performance, Gene, Polymorphism, Adenosine Monophosphate Deaminase 1 (AMPD1), Bone Morphogenetic Protein 2 (BMP2)*

Kız Atletlerde *AMPD1* ve *BMP2* Genlerindeki Polimorfizmlerin Performansa Etkisi

Özet
Antrenmanın yanı sıra beslenme, psikoloji ve genetik, atletik performansı belirlemede ve geliştirmede önemli rol oynar. Çok sayıda çalışma, belirli genetik varyantların sporcuların güç, aerobik veya anaerobik dayanıklılık ve hız gibi fiziksel yeteneklerini nasıl etkileyebileceğini araştırmıştır. Bu genler arasında *Kemik Morfogenetik Protein 2 (BMP2)* ve *Adenozin Monofosfat Deaminaz 1 (AMPD1)* bulunmaktadır. *BMP2* geni, spor performansı üzerine yapılan birçok çalışmanın doğrudan odağı olmasa da, spor genetiği alanında dolaylı etkileri olan bir gen olarak kabul edilir. *AMPD1* genindeki rs17602729 polimorfizmi ise, kısa süreli, yüksek yoğunluklu aktivitelerdeki performansı etkilediği öne sürülen bir varyanttır. Bu polimorfizmleri incelemek alana önemli katkı sağlayacaktır. Araştırmaya 12-16 yaş aralığında kısa veya uzun mesafe koşucusu olan 13 amatör sporcu ve 13 sedanter katılmıştır. Katılımcılardan kan örnekleri alınıp DNA izolasyonu yapılmış ve Sanger sekanslama kullanılarak genotipler belirlenmiştir. Analizlerde SPSS 24.00 programı kullanılmıştır. Alel dağılımlarındaki gruplar arasındaki farklılık ki-kare testi ile analiz edilmiştir. *BMP2* geni A/C polimorfizminin genotip dağılımı incelendiğinde, sporcuların %46,15'inin AA genotipine, %46.15'inin AC genotipine ve %7.69'unun CC

genotipine sahip olduğu gözlemlenmiştir. Kontrol grubundaki genotip dağılımı ise %53,84 AA, %46,15 AC ve %0 CC olarak bulunmuştur. *AMPD1* geni C/T polimorfizminin genotip dağılımına bakıldığında, sporcuların %92,30'unun CC genotipine, %7,69'unun CT genotipine ve %0'ının TT genotipine sahip olduğu görülmektedir. Kontrol grubundaki genotip dağılımı da benzer şekilde %92,30 CC, %7,69 CT ve %0 TT olarak bulunmuştur. Yapılan bu araştırmada, *BMP2* geni A/C polimorfizminde, sporcular arasında AA ve AC genotiplerinin daha yüksek oranda temsil edildiği görülmektedir. *AMPD1* C/T polimorfizminde, C allelinin daha fazla temsili, sporcu grubunun fiziksel performans açısından daha başarılı olabileceğini düşündürmektedir.

Anahtar Kelimeler: *Sporcu, Atletik Performans, Gen, Polimorfizm, Adenosine Monophosphate Deaminase 1 (AMPD1), Bone Morphogenetic Protein 2 (BMP2)*

Introduction

Athletic performance refers to the effort an athlete demonstrates to meet specific performance goals within a given timeframe (URL1, 2024). While athletic performance can be improved through training, it is also influenced by several other factors. Along with training, nutrition, psychology, and genetics play crucial roles in determining and enhancing athletic performance.

The influence of genetic factors on athletic performance has garnered increasing attention in recent years. Numerous studies have explored how specific genetic variants can affect athletes' physical abilities, such as strength, aerobic or anaerobic endurance, and speed. Among these genes are *Bone Morphogenetic Protein 2 (BMP2)* and *Adenosine Monophosphate Deaminase 1 (AMPD1)*.

Although the *BMP2* gene is not directly the focus of many studies on sports performance, it is considered a gene with indirect effects in the field of sports genetics. *BMP2* primarily functions in processes such as bone development and tissue regeneration, but some studies have examined its role in the musculoskeletal system following exercise (Ruschke et al., 2012; Jaime et al., 2024). Recent research has explored the effects of *BMP2* on bone and muscle health, suggesting that *BMP2* plays a critical role in the regeneration of bone and muscle tissue, potentially impacting athletes' performance and recovery. However, studies directly linking *BMP2* to sports performance are limited, with most research focusing on bone density, muscle development, and general physical endurance. Nonetheless, *BMP2*'s potential effects on post-exercise recovery and muscle tissue remodeling suggest that it could be a factor influencing sports performance. Further research is needed to better understand its specific effects on athletic performance (Poon et al., 2016; Li et al., 2022; Semenova et al., 2023).

The *BMP2* gene's rs15705 (244A>C) polymorphism is thought to be associated with strength/sprint performance (Miyamoto-Mikami et al., 2017). Individuals with the CC genotype are reported to be more predisposed to strength-oriented sports. Given its broad study with large sample groups and its effects on bone development, *BMP2* is considered an important gene in sports genetics, particularly when detailed studies on its impact on injuries and genotype determination in strength-focused athletes are conducted.

The rs17602729 polymorphism in the *AMPD1* gene is a variant suggested to influence performance in short-duration, high-intensity activities (e.g., sprinting and power sports). Various studies have shown that this genetic variant is more common in sprint and power

athletes and helps optimize their performance by increasing muscle strength (Varillas-Delgado et al., 2023; Bulgay et al., 2024). Another study examined the effect of the *AMPD1* genotype on athletes' physical characteristics, revealing that this genotype could create significant differences in anaerobic performance parameters such as short-term explosive power (STEMP). Specifically, male athletes with the *AMPD1* CC genotype were found to have higher STEMP values compared to those with the CT genotype (Ginevičienė et al., 2014). The *AMPD1* gene is thought to be particularly related to energy metabolism and muscle fatigue. Research has shown that the C allele is more common among sprint and power athletes, while the T allele is less prevalent, suggesting that the C allele may provide an advantage in anaerobic performance. This genetic variant has been linked to increased muscle strength and explosiveness, making it more common among elite athletes involved in short-duration, high-power sports (Ginevičienė et al., 2014).

While genetic factors such as *AMPD1* and *BMP2* have been scientifically shown to shape athletic performance, more research is needed to fully understand their impact on performance. These findings emphasize the importance of genetic analysis in sports science, enabling the development of training and nutritional strategies tailored to athletes' individual genetic profiles. Additionally, the effect of genetic variants on athletic performance is complex and should be evaluated in conjunction with other factors, such as gene-gene and gene-environment interactions. While genes may yield practical results, polymorphisms in genes—defined as gene variants—arise due to gene-environment interaction. Studying these polymorphisms also contributes significantly to the field. By considering these variables, athletes' genetic profiles can be identified, and training programs can be individualized. This approach enables the achievement of optimal performance (Del Coso & Lucia, 2021).

In conclusion, these findings emphasize the growing importance of genetic analysis in sports science, enabling the development of personalized training and nutritional strategies based on athletes' genetic profiles. By identifying the genetic characteristics of athletes, their sports performance can be maximized, and training programs can be tailored to their genetic structure. A review of the literature reveals that specific studies investigating the role of the *AMPD1* and *BMP2* genes in athletes are quite limited. Most existing research focuses on other genes related to athletic performance. The reason for examining both *BMP2* and *AMPD1* genes in this study is that both are associated with anaerobic endurance and strength, and studies on these genes are rare. Therefore, addressing both genes in the same study is expected to make valuable contributions to the literature.

Materials and Methods

Research Group

The study involved 13 amateur females athletes, aged 12-16, who were either short- or long-distance runners, and 13 sedentary females within the same age range. During the current research, the Higher Education Institutions Scientific Research and Publication Ethics Directive was followed. The research protocol was prepared in accordance with the second directive of the Helsinki Declaration and was approved by the Ethics Committee of Gümüşhane University (approval number E-95674917-108.99-245411, dated March 27, 2024). Prior to the study,

detailed information was provided to the athletes regarding the analyses to be conducted and the interpretation of the results. Each participant signed an informed consent form. Additionally, assistance was provided by their coaches and healthcare teams during all measurements.

Data Collection Tools

Age

The ages of the athletes participating in the study were recorded on the data form based on the day, month, and year from their license documents.

Height Measurement

The heights of the athletes in the study were measured with a tape measure with a sensitivity of 0.01 cm while they were in an anatomical position and barefoot. The determined values were recorded in centimetres on the data form.

Body Weight, Body Fat Percentage and Body Mass İndex Measurement

The Inbody device was used to measure body fat percentage and body mass index. The measurements were taken for each participant at the same time of day, on an empty stomach, and in sportswear.

Sample Collection and Genetic Testing

Since blood samples were to be taken from the participants, this was clearly stated in the Parental Consent Form and Child Assent Form. At the outset, individuals were checked by the medical team and informed about potential complications. The materials used for collecting the blood samples were sterile, designated for single use per individual, and did not have any adverse health effects. Throughout the testing process, support was provided by healthcare personnel and the athletes' coaches.

Examined Single Nucleotide Polymorphisms

In the study, the polymorphisms *BMP2* gene rs15705 (244A>C) and *AMPD1* gene rs17602729 (c133C>T) were examined, and the SNPs analyzed are indicated in Table 1.

Table 1. SNPs examined in the study

Gene	Polymorphism	SNP Code
BMP2	A/C	rs15705
AMPD1	C/T	rs17602729

DNA Extraction and DNA Isolation from the Research Group

To obtain DNA from the study group, 2 mL of blood was collected into purple-capped EDTA tubes (whole blood). DNA isolation was carried out using the RTA Genomic DNA Isolation Kit. A total of 26 samples were processed using 96-well plates. The RTA Genomic DNA Isolation Kit protocol was followed for the procedure. The quality of the extracted DNA samples was measured using the Nanodrop D1000 device.

Primer Design

Two pairs of polymerase chain reaction (PCR) primers were designed for the two studied polymorphisms. Primers were designed using Primer 3 Plus and NCBI Primer Blast programs.

Sanger Sequencing

The names of the samples to be sequenced were entered using the Foundation Data Collection program. After purification, the samples were loaded sequentially into a 96-well plate and sealed with a septa. Then, they were placed into the ABI 3130 XL 16 capillary device, and the sequencing process was initiated. The sequencing was performed using the Illumina company's MiSeq device. Since index PCR was performed, an additional sample preparation kit was not used. The measured purified product was properly diluted and loaded directly. The sequencing was conducted using the v2 300-cycle kit. The analysis of the samples was performed using the Illumina MiSeq Reporter software and the IGV 2.3 software developed by the Broad Institute.

Results

The study included 13 amateur females athletes aged between 12 and 16, and 13 sedentary females in the same age range. The *BMP2* and *AMPD1* gene polymorphisms of the participants were examined, and no significant difference in gene distribution between the control group and the athlete group was detected for either gene.

Table 2. Descriptive Statistical Data of Athletes and Control Group (n:26)

	Number (n)	Age (years)	Height (cm)	Weights (kg)	BMI (kg/m2)	Fat Percentage (%)
Athletes	13	13.85 ± 1.57	157± 0.68	46.11± 9.94	18.46± 3.03	20.57± 2.33
Control Group	13	13.77 ± 1.53	158± 0.31	52.12 ± 5.45	20.63 ± 2.07	16.32 ± 4.99

Descriptive information for the athletes and sedentary participants (age, height, weight, BMI, and body fat percentage) are shown in Table 2. According to the data in Table 2, the athletes had an average age of 13.85 (± 1.57), an average height of 157 cm (± 0.68), an average weight of 46.11 kg (± 9.94), an average body mass index (BMI) of 18.46 (± 3.03), and an average body fat percentage of 20.57% (± 2.33). In the control group, the average age was 13.77 (± 1.53), the average height was 158 cm (± 0.31), the average weight was 52.12 kg (± 5.45), the average BMI was 20.63 (± 2.07), and the average body fat percentage was 16.32% (± 4.99).

Table 3. *BMP2* rs15705 genotype and allele distributions in athletes and control groups

	***BMP2* Genotype**			**Allele Frequency**	
	AA	**AC**	**CC**	**A**	**C**
Athlete (n=13)	6	6	1	18	8
%	%46.15	%46.15	%7.69	%69.23	%30.76
Control (n=13)	7	6	0	20	6
%	%53.84	%46.15	%0	%76.92	%23.07

$p<0.05$, $p=0.58$

The genotypes of *BMP2* rs15705 and allele distributions in athletes and control groups are shown in Table 3. No significant difference was found in the allele distribution between the athlete and control groups ($p<0.05$). When examining the genotype distribution of the *BMP2* gene A/C polymorphism, it was observed that 46.15% of athletes have the AA genotype, 46.15% have the AC genotype, and 7.69% have the CC genotype. In the allele distribution among athletes, it was determined that 69.23% carry the A allele, and 30.76% carry the C allele. The genotype distribution in the control group was 53.84% AA, 46.15% AC, and 0% CC. The allele distributions were 76.92% for the A allele and 23.07% for the C allele.

Table 4. *AMPD1* rs17602729 genotype and allele distributions in athletes and control groups

	***AMPD1* Genotype**			**Allele Frequency**	
	CC	**CT**	**TT**	**C**	**T**
Athlete (n=13)	12	1	0	25	1
%	%92.30	%7.69	%0	%96.15	%3.84
Control (n=13)	12	1	0	25	1
%	%92.30	%7.69	%0	%96.15	%3.84

$p<0.05$, $p=1.00$

The genotypes of *AMPD1* rs17602729 and allele distributions in athletes and control groups are shown in Table 4. No significant difference was found in the allele distribution between the athlete and control groups ($p<0.05$). When looking at the genotype distribution of the *AMPD1* gene C/T polymorphism, it is observed that 92.30% of the athletes have the CC genotype, 7.69% have the CT genotype, and 0% have the TT genotype. In terms of allele distributions among athletes, 96.15% carry the C allele, while 3.84% carry the T allele. The genotype distribution in the control group was similarly found to be 92.30% CC, 7.69% CT, and 0% TT. The allele distributions were 96.15% for the C allele and 3.84% for the T allele.

Discussion and Conclusion, Recommendations

Although research on the impact of the *BMP2* rs15705 polymorphism on endurance performance is limited, studies in this area continue to emerge. Previous research has indirectly linked this polymorphism to muscle mass regulation and myogenic differentiation, which could influence athletic traits. While some studies suggest that this polymorphism affects muscle characteristics, the literature does not consistently establish a direct relationship between *BMP2* rs15705 and endurance performance. Most research examining the genetic factors influencing endurance and strength sports tends to focus on more widely studied genes like *ACTN3* and *ACE* (Appel et al., 2021; Psatha et al., 2024). To date, the effects of *BMP2* on endurance remain speculative, and further studies are needed to confirm any specific correlation with endurance sports. In this study, looking at the genotype distribution of the *BMP2* gene A/C polymorphism, it was found that 46.15% of athletes had the AA genotype, 46.15% had the AC genotype, and 7.69% had the CC genotype. The allelic distribution among athletes showed that 69.23% were carriers of the A allele, while 30.76% carried the C allele. A comparison of the gene and allele distributions between the control group and the athletes did not reveal any significant differences ($p<0.05$). Despite the limited research on the relationship between *BMP2* gene polymorphism and endurance performance, existing studies suggest that the *BMP2* gene

rs15705 (244A>C) polymorphism might be associated with strength/sprint performance (Miyamoto-Mikami et al., 2017). According to Miyamoto-Mikami et al. (2017), individuals with the CC genotype are more likely to be predisposed to strength-focused sports. In our study, the genotype distribution among athletes shows a higher representation of the AA and AC genotypes. Given that the athletes are middle and long-distance runners, it can be speculated that these genotypes may contribute positively to aerobic performance. Among this group of amateur athletes, carriers of the C allele might be better suited for strength-oriented sports, suggesting that athletes could potentially be directed towards such disciplines.

Furthermore, research on the relationship between *BMP2* rs15705 polymorphism and growth indicates that this genetic variant plays a role in bone development and related growth characteristics. The *BMP2* gene is crucial for bone formation and differentiation, and its polymorphisms, including rs15705, have been studied for their effects on bone mass, structure, and growth in both humans and animals (Fang et al., 2010; Fritz et al., 2006). It has been suggested that the A allele for the *BMP2* rs15705 polymorphism is generally more favorable for bone growth and development. Research indicates that individuals with the AA genotype or carrying the A allele tend to have better bone density and enhanced osteoblast activity, contributing to healthier bone formation (Fritz et al., 2006).

Regarding the *AMPD1* rs17602729 polymorphism, no significant difference in allele distributions was found between athletes and control groups ($p<0.05$). When analyzing the genotype distribution of the *AMPD1* gene C/T polymorphism, it was found that 92.30% of athletes had the CC genotype, 7.69% had the CT genotype, and none had the TT genotype. The allele distribution among athletes showed that 96.15% were carriers of the C allele, while 3.84% carried the T allele. In the control group, the genotype distribution was 92.30% CC, 7.69% CT, and 0% TT. The allele distributions were 96.15% C and 3.84% T. The effect of the *AMPD1* rs17602729 polymorphism on athletic performance is linked to a reduction in enzyme activity, which leads to the accumulation of adenosine monophosphate (AMP) in muscles. In particular, individuals carrying the T allele may experience slower energy metabolism due to reduced enzyme activity. This could result in decreased physical performance and increased fatigue during exercise (Zöllig et al., 2006). Studies suggest that individuals with the *AMPD1* rs17602729 polymorphism might experience impaired performance in endurance sports and activities requiring high exertion. A study by Rubio et al. (2005) observed that athletes carrying the T allele, especially in activities requiring muscle endurance, showed reduced performance. Similarly, Zöllig et al. (2006) reported that individuals with this polymorphism felt more fatigue after exercise and had longer recovery times. In our study, the frequency of the T allele is quite low (3.84%). The higher representation of the C allele suggests that the athlete group might be more successful in terms of physical performance. However, the effects of the polymorphism on athletic performance also interact with environmental factors such as individual differences, training levels, and nutrition, meaning that the impact may not be the same for every individual. A study by Norman et al. (2010) demonstrated that this polymorphism interacts not only with the genetic makeup but also significantly with an individual's lifestyle and training programs. Therefore, while the athlete group with identified genotypes may seem advantaged in terms of

physical performance potential, this alone is not sufficient. Appropriate nutrition and training programs should be implemented to improve and develop the athletes' performance.

Ethics Committee Permission Information

Ethics review board: Gümüşhane University Scientific Research and Publication Ethics Board
Date of the Ethics Review Document: 27/03/2024
Number of the Ethics Assessment Document: E-95674917-108.99-245411

Declaration of Contribution Rates of Researchers

The entire research was carried out by the sole author of the study.

Conflict Statement

There is no conflict of interest.

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