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RESEARCH ARTICLE

GENETIC DIFFERENCES IN PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR ALPHA GENE IN ENDURANCE ATHLETES (LONG DISTANCE RUNNERS) AND POWER/ENDURANCE ATHLETES (WRESTLERS, FOOTBALL PLAYERS)

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ABSTRACT

Purpose: Peroxisome proliferator-activated receptor alpha gene plays an important role in the expression of genes involved in fatty acid, glucose, and energy metabolism. *PPARα* intron 7 G/C polymorphism (rs4253778) is one of the genes associated with athletic performance. This study aimed to investigate the genotype distribution and allele frequencies of *PPARα* G/C of endurance-oriented athletes (long-distance runners) and power/endurance-oriented athletes (wrestlers and football players) and non-athletic individuals.
Material and Methods: The elite Turkish wrestlers (n=53), football players (n=71), long-distance runners (n=34), and non-athletic individuals (n=56) were involved in the study. The PPARα G/C polymorphism in intron 7 was analyzed using polymerase chain reaction (PCR) primers and restriction fragment length polymorphism method (RFLP). Genomic DNA was extracted by the phenol/chloroform method. Genotyping for the intron 7 G/C variant was performed by PCR and restriction enzyme digestion. The amplified fragment of 266 bp digested by *TaqI* restriction enzyme generated 216 bp and 50 bp in the presence of the CC genotype, and only 266 bp in the presence of the GG genotype.
Results: Genotypes and allele frequencies of *PPARα* intron 7 G/C were compared between endurance-oriented athletes (long-distance runners) and power/endurance-oriented athletes (wrestlers, and football players) categorized according to their sport disciplines. In addition, athletes were compared to non-athletic individuals. The genotype and allele frequencies of *PPARα* intron 7 G/C were similar in the groups of athletes and non-athletic individuals ($p>0.05$). There was no statistically significant association in genotype distribution and allele frequencies of the *PPARα* gene among endurance-oriented athletes, power/endurance-oriented athletes, and non-athletic individuals ($p>0.05$).
Conclusion: The *PPARα* gene polymorphism may not be considered as a distinctive genetic marker in endurance and mixed sport disciplines.

Keywords: Genetics, *PPARα*, rs4253778 polymorphism, sports

INTRODUCTION

It is now well established that genetic variations are associated with health and physical performance (1). The completion of the human genome project in 2003, in addition to revealing the number, structure, and physical maps of human genes also lead to an increasing interest in the genetic influence on athletic performance (2). Human athletic performance is a multifactorial phenomenon and influenced by environmental (physical training, diet, advances in equipment, technological help, etc.) and genetic factors (3). Such components of athletic performance as strength, power, endurance, muscle fiber size and composition, susceptibility of musculoskeletal injuries, and other phenotypes are significantly influenced by genetics (4). It has previously been observed that athlete status is a heritable trait: genetic factors account for nearly 66% of the variance in athlete status. The rest of the variance is owing to environmental factors (5). Therefore, identification of performance-associated polymorphisms is highly essential for talent identification, choice of favorable sport, and to maximize the talent of athletes (6). Numerous studies have been conducted on genetic polymorphisms that have an impact on athletic performance and inter-individual variation (4,7). In this context, genes such as angiotensin I-converting enzyme (*ACE),* and α-actinin-3 (*ACTN3*) have been largely studied (47). However, the importance of the *PPARα* gene has only recently been paid attention to (8-10).

PPARα, a transcriptional factor that belongs to the nuclear receptor family located on chromosome 22 has been one of the genes studied on health and athletic performance in recent years (11,12). *PPARα* controls the expression of genes implicated in left ventricular growth, control of body weight, glucose, and fatty acid metabolism, including fatty acid transport, uptake by the cells, intracellular binding, activation, catabolism (especially mitochondrial fatty acid oxidation), or storage (13,14). The expression level of *PPARα* is moderate, primarily within the kidney, brown fat, and large intestine (11), but higher in tissues implicated in fatty acids utilization such as liver, skeletal and cardiac muscle (15,16).

In the early 2000s, *PPARα* intron 7 G/C polymorphism (rs4253778) was associated with left ventricular growth and the risk of coronary artery disease (17,18). The highly comprehensive study also found out that athletes with combined power/endurance activity (wrestling, boxing, ice hockey, court tennis) had a higher frequency of the *PPARα* intron 7 CC genotype compared to controls (19). On the contrary, Cieszczyk et al found more prevalent frequency of G allele and GG genotype in elite combat athletes (wrestling, boxing) than controls (20). It was demonstrated that *PPARα* CC homozygous carriers of males and females had a higher jumping performance (reactive strength index) than GG and GC genotypes (21). Also, Gineviciene et al indicated that male athletes with *PPARα* CC and *PPARα* GC genotypes had significantly increased muscle mass and single muscular contraction power than GG homozygotes (8). Similarly, middle-school students with *PPARα* C allele outperformed of handgrip strength testing than GG homozygotes (22). However, Broos et al observed that the *PPARα* intron 7 G/C polymorphism does not affect strength traits in the sedentary population (23). Studies showed that GG homozygotes and G allele were more dominant with the types of endurance athletes (18,24,25). The meta-analysis has revealed that being the C allele carrier may provide an advantage to be an elite level soccer player, whereas the G allele may be beneficial to be an elite level endurance athlete (26). Furthermore, the C allele of *PPARα* was significantly more frequent in football players compared to controls (27). On the contrary, the G allele frequency was found to be higher in soccer players than in combat sports athletes and motorcycle riders (28).

Though it is hypothesized that the intron 7 C allele affects power and mixed power/endurance and G allele affects endurance performance, previously published studies on the effect of *PPARα* intron 7 G/C polymorphism on power and endurance performance are not consistent. There is no general agreement about the effect of *PPARα* intron 7 G/C polymorphism on power, mixed power/endurance, and endurance performance. Therefore, the present study aimed to examine allele frequencies and genotype distribution of *PPARα* intron 7 G/C in elite Turkish football players, wrestlers, long-distance runners, and compare endurance-oriented athletes with power/endurance-oriented athletes.

MATERIAL AND METHODS

Subjects

The elite Turkish wrestlers (n=53), football players (n=71), long-distance runners (n=34), and non-athletic individuals (n=56) were selected from individuals residing and born in Turkey (n=214). Detailed information about the study protocol before

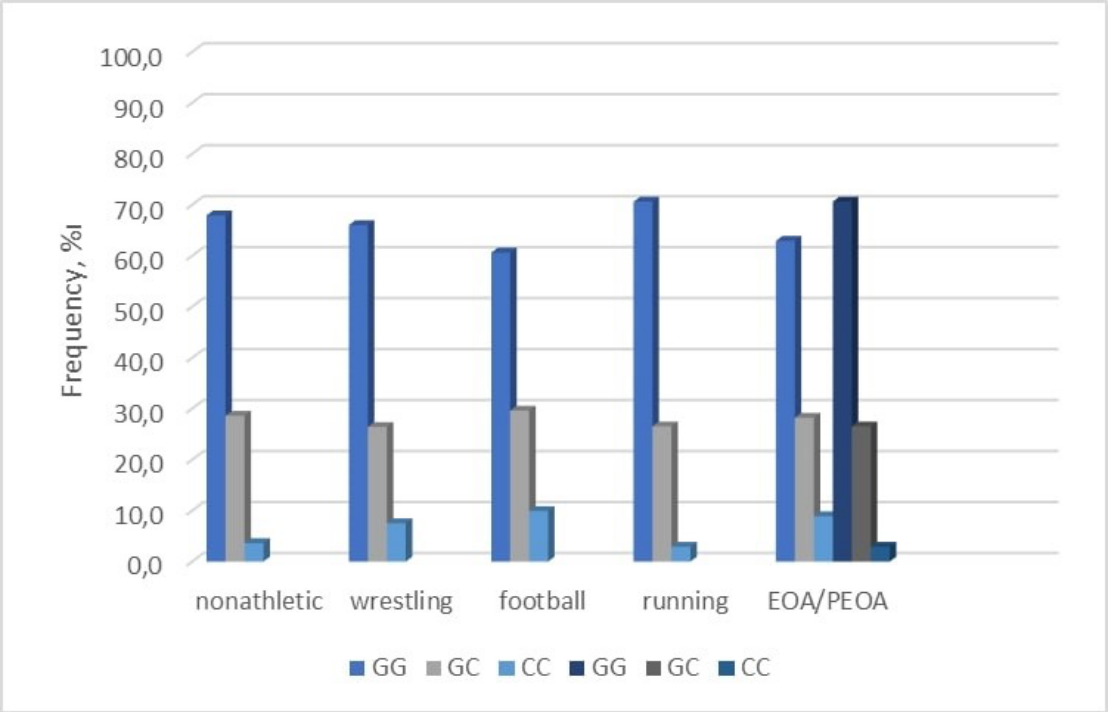

Figure 1. Distribution of PPARα 7 intron genotypes among Turkish athletes and non-athletic individuals EOA: endurance-oriented athletes, PEOA: power/endurance-oriented athletes (p> 0.05)

the study were given to the players, runners and wrestlers and signed informed agreement forms were obtained from them. This study was conducted in accordance with the principles of the Declaration of Helsinki II. Turkish athletes were chosen from men who participated in both national- and international-level competitions. The characteristics of 214 men were aged 22-26; height 170.1 ± 178.8 cm, weight 62.4 ±77.5 kg. The footballers were from 3 professional teams: Kayserispor, Kayseri Erciyespor, Tavşanlı Linyitspor. The wrestlers training at the camp for free style juniors and seniors national wrestling team were included. The track and field athletes were elite long distance runners. The athletes were classified into two groups according to their sport disciplines included endurance-oriented athletes (5000, 10,000 meters or marathon runners) and power/endurance-oriented athletes (wrestlers and football players). The study was approved by Gazi University, (Non-Invasive) Clinical Research Ethical Committee with the number of 217 and the date 23/05/2012.

Genotyping

Blood samples were obtained from 158 elite Turkish athletes, and 56 non-athletic individuals randomly selected (control group). Genomic DNA was extracted by the phenol/chloroform method (29). *PPARα* intron 7 G/C polymorphism was carried out by polymerase chain reaction-restriction fragment length polymorphism method with *Taq1* enzyme (PCR-RFLP). Forward-ACAATCACTCCTTAAATATGGTGG and reverse-AAGTAGGGACAGACAGGACCAGTA primers were used for *PPARα* intron 7 G/C polymorphism, generating a fragment of 266 bp. PCR amplification was performed for 35 cycles, each of which consisted of 94°C for 30 s, 56°C for 30 s, and 72°C for 1 min. *Taq1* digestion of the PCR products was carried out by adding 6 U of *TaqI*, and 1x restriction enzyme buffer in a volume of 20 µl, and incubation for 4 hours at 65°C (30). The fragment of 266 bp digested by *TaqI* generated 216 bp and 50 bp in the presence of the CC genotype, and 266 bp in the presence of the GG genotype. PCR and restriction products were separated by 2% and 3% agarose gel electrophoresis, respectively, and visualized in UV light.

Statistical Analysis

The genotype distribution of *PPARα* intron polymorphism was assessed and compared within each athlete group and between each of the five groups of athletes (wrestling, football, running,

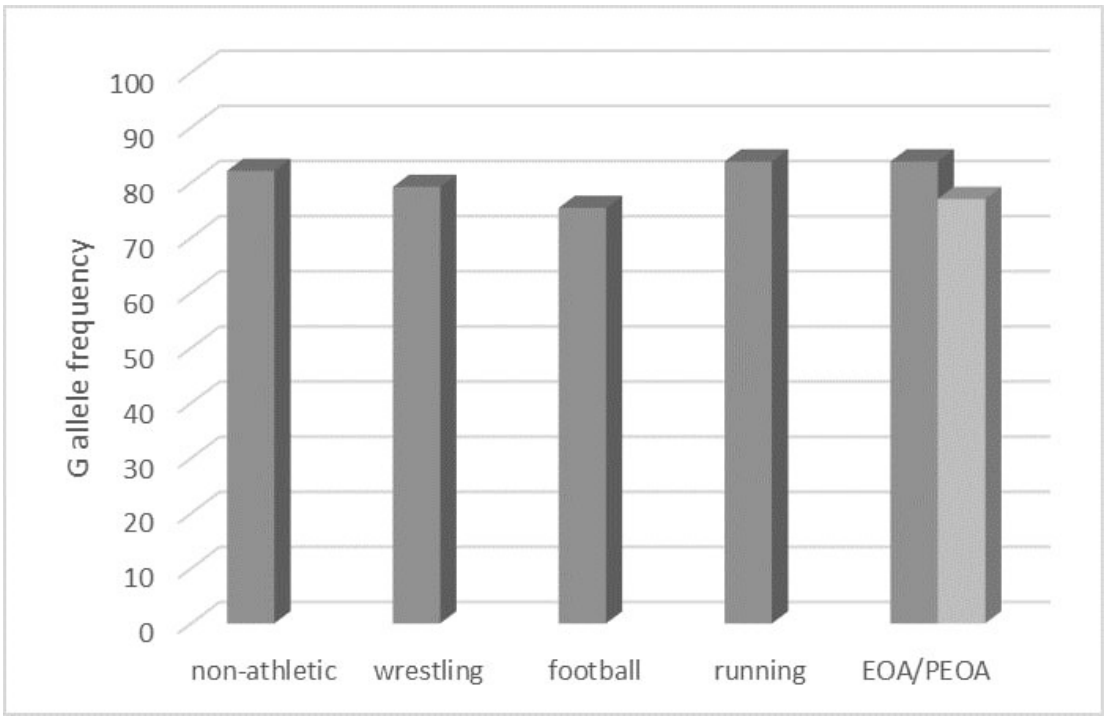

Figure 2. Distribution of PPARα intron 7 G allele among Turkish athletes and non-athletic individuals EOA: endurance-oriented athletes, PEOA: power/endurance-oriented athletes (p> 0.05)

endurance-oriented athletes, power/endurance-oriented athletes) and non-athletic individuals by chi-square test or Fisher exact test. Allele frequencies were determined by the gene-counting method. The allele frequencies were compared within each athlete group and between each of the five groups of athletes and non-athletic individuals by Z-test (31). P values <0.05 were considered statistically significant.

RESULTS

The study was performed on 158 elite Turkish athletes and 56 non-athletic individuals. Athletes were classified into two groups by their sport disciplines, as endurance-oriented (long-distance runners) and power/endurance-oriented (wrestlers, and football players). The genotype distribution and allele frequencies of the *PPARα* intron 7 G/C were determined in the three-sport disciplines (wrestling, football, and running) and non-athletic individuals

PPARα genotype distributions in all athletic groups were in agreement with Hardy–Weinberg equilibrium. *PPARα* genotype distributions were determined and compared within each athlete group and between each of the five groups of athletes (wrestling, football, runners, endurance-oriented athletes, power/endurance-oriented athletes) and non-athletic individuals by chi-square test or Fisher exact test (p> 0.05) (Figure. 1).

Furthermore, the frequencies of the *PPARα* G allele in all athlete groups and non-athletic individuals were calculated and compared between each of the five groups of athletes and non-athletic individuals using the Z-test (Figure. 2).

G allele frequencies in endurance-oriented and power/endurance-oriented athletes were 84% and 77%, respectively. There were no significant differences in genotype distribution and allele frequencies of *PPARα* among different groups of athletes (p>0.05).

The frequencies of *PPARα* 7 GG genotype in athletes and non-athletic individuals were higher than those of *PPARα* CC genotypes. The *PPARα* GG genotype was more common among endurance-oriented athletes (70.6%) than those of power/endurance-oriented athletes (62.9%). However, the frequency of *PPARα* CC genotype was low level in endurance-oriented athletes (2.9%) in comparison with power/endurance athletes (8.9%).

DISCUSSION

Athletic performance is a complex trait and it is affected by genetic and environmental factors. Numerous polymorphisms are more common in elite

athletes than in the general population. A variety of genetic factors associated with metabolic pathways are known to affect athletic performance. *PPARα* regulates the expression of multiple genes implicated in the metabolism of energy, fats, and glucose in the skeletal muscle as well as other tissues (32).

In this study, the allele and genotype frequencies of *PPARα* intron 7 G/C polymorphism were investigated in elite Turkish football players, wrestlers and long-distance runners by PCR and RFLP methods and compared allele and genotype frequencies of this polymorphic region within each athlete group and between athlete groups and non-athletics. The three-sport disciplines (wrestling, football, and running) were categorized according to sports disciplines, as endurance-oriented (long-distance runners) and power/endurance-oriented (wrestlers, and football players). There was no considered statistically significant difference among groups for allele and genotype comparisons. ($P<0.05$). GG genotype frequency 66%, 60.6%, 70.6 and 67.9; GC genotype frequency was 26.4%, 29.6%, 26.5% and 28.6 and CC genotype was 7.5%, 9.9%, 2.9% and 3.6% for wrestlers, footballers, runners and controls respectively. G allele frequency 79.2%, 75.4%, 83.8 and 82.1 and C allele frequency was 20.8%, 24.6%, 16.2% and 17.9 for wrestlers, footballers, runners and controls respectively.

Studies on *PPARα* and other polymorphisms in elite Turkish wrestlers are limited (33). This is the first study on the association of *PPARα* intron 7 G/C polymorphisms with elite Turkish wrestlers. *PPARα* gene G/C polymorphism was not found significantly different between elite Turkish wrestlers, long-distance runners, footballers, and non-athletic individuals. The frequency of the GG genotype is less likely in mixed power/endurance sports such as wrestling, football, and boxing (8). Ahmetov et al found no significant difference in C allele frequencies between Russian wrestlers and controls (9). However, in the whole cohort, these authors found that the C allele is associated with anaerobic components of physical performance. They suggested that the C allele may be advantageous for power-related sports disciplines (19,34). Contrarily, Cieszczyk et al found significantly higher frequencies of the GG genotype and the G allele in elite Polish combat athletes such as judo, wrestling, and boxing (20). The acyclic nature of combat sports, uncertainty in effort performed during combat sports and the dissimilarity of participants may affect the results.

While aerobic metabolism is dominant for the energy supply during a football match, power and strength play a more critical role in the determination of success in football. A 90-minute match is played at an intensity near to anaerobic threshold and it requires various explosive activities involving jumping, kicking, tackling, turning, sprinting, changing speed, and powerful contractions to maintain balance and control of the ball against the defensive press (35).

There are controversial studies investigating *PPARα* intron 7 G/C polymorphism on footballers, pointing out a significant or no significant relationship between football players and controls. The association of the G allele and GG genotype with endurance athletes was repeated in several studies (18,24,25), whereas the association of the C allele on mixed power-endurance and power/strength is not clear. The G allele and GG genotype were found to be higher in professional and young Turkish football players (36,37. In this study, GG genotype distribution and G allele frequency of elite football players were similar to those of non-athletic individuals. Similar to the current study, Gineviciene et al obtained no significant difference in *PPARα* (G/C) polymorphisms of professional Lithuanian football players compared to controls (38).

One study investigating *PPARα* gene G/C polymorphism on Russian team sports athletes found that footballers had a significantly higher frequency of C allele among 14 team sports athletes. The finding suggested that anaerobic metabolism may be vital for game performance in footballers. The C allele may facilitate glucose utilization rather than fatty acid oxidation in response to anaerobic exercise (27). Similarly, Egorova et al showed that elite Russian football players had a higher frequency of the *PPARα* C allele (39). In contrast, Cocci et al found that the G allele frequency was meaningfully higher in soccer players than in combat sports athletes and motorcycle riders (28). Proia et al found a higher frequency of G allele and GG genotype in professional Italian soccer players (40). The present study detected higher the frequencies of GG genotype and G allele than those of the frequency of the *PPARα* C allele among groups.

It is hypothesized that *PPARα* is activated during endurance exercise**.** Several studies have supported that the G allele and GG genotype is associated with endurance athletes (26). Ahmetov et al found a higher frequency of GG genotypes in a group of Russian endurance-oriented athletes (swimmers, cross-

country skiers, skaters, and triathletes) compared to controls (19). Mavlyanov et al reported a higher frequency of G allele and G/G genotype of cyclists and runners than in rowers (45). One possible explanation of this result is the similarity of physical fitness components between runners and cyclists. Eynon et al observed a higher frequency of GG genotypes in elite Israeli endurance athletes compared to sprinters (25). Endurance athletes (rowing, marathon, biathlon, triathlon, cross-country skiing, swimming, skating (3,000-5,000), and road cycling) demonstrated a higher frequency of GG genotype and G allele compared to controls (17,18). Ginevičienė et al found that the frequency of *PPARα* GG genotype was higher in Lithuanian elite endurance athletes compared to in speed/power and mix sports (8). Maciejewska et al revealed that elite Polish endurance athletes had a higher prevalence of *PPARα* intron 7 G allele, and GG genotype compared to controls (24). It was found a higher frequency of GG genotype and G allele between power/endurance-oriented (wrestlers, and football players) (63%) and endurance-oriented (long-distance runners) (70.6%) sports disciplines in this study.

There are also studies reported no association between the *PPARα* intron 7 G/C polymorphism and athletes. *PPARα* intron 7 G/C polymorphism was not significantly different in endurance-oriented athletes (long-distance runners) compared to the control group. Similarly, it was shown that there was no significant difference among Ukrainian athletes such as endurance-oriented: cross-country skiers, and rowers; and power-oriented: short-distance runners, short-distance swimmers, jumpers, and throwers (41). The PPARα gene rs4253778 G/C polymorphism has no major effect on physical performance in endurance athletes (42,43). Tsianos et al found no association between *PPARα* rs4253778 G/C polymorphism and marathon performance of runners (44). Tural et al found a significant association between the *PPARα* GG genotype, G allele and aerobic performance in elite Turkish endurance athletes (46). The findings in the present study indicate no strong association between *PPARα* intron 7 G/C polymorphism and mixed power/endurance and endurance athletes. In the study, while the *PPARα* gene GG genotype and G allele were not statistically different in athlete groups, a tendency to have increased GG genotype (70.6%) and G allele (84%) was observed in endurance-oriented athletes. There may be possible explanations for these results. Each gene polymorphism may have a limited contribution to endurance performance (18). This study included 34 elite endurance athletes. Firstly, it is thought that it would be appropriate to increase the number of athletes to interpret a definite association with endurance performance. A proper number of participants are needed for a genetic study. There is a good deal of studies on endurance athletes from different sport disciplines (swimmers, cross-country skiers, skaters, and triathletes, rowing, etc.) but, studies specifically on long-distance runners are rare. The athletic status and ethnicity of athletes may affect the results of the study.

CONCLUSION

The findings in the present study indicate no strong association between *PPARα* intron 7 G/C polymorphism and mixed power/endurance and endurance athletes. Elite Turkish endurance athletes tend to have a higher frequency of GG genotype and G allele. While *PPARα* intron 7 G/C polymorphism is a novice candidate for athletic performance, it may be a favorable gene for endurance performance. Further study with larger sample size and homogeneous groups is needed to clarify the association between PPARα polymorphism and endurance athletes. Also, *PPARα* polymorphism needs to be investigated on sport disciplines (as sprints, jumps, throws) requiring high force output for a short period of time.

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Conflict of interests: The authors declare no conflict of interest.

Ethical approval: The study was approved by Gazi University, (Non-Invasive) Clinical Research Ethical Committee with the number of 217 and the date 23/05/2012.

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