ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/337313333

The Effects of the Angiotensin-Converting Enzyme (ACE) Genotype on 3000 m Running (VO2max) Performance & Body Composition in Turkish Army Soldiers: Longitudinal Study

Article · July 2019

CITATIONS
0

READS
21

1 author:



Mesut Cerit
Lokman Hekim University
15 PUBLICATIONS **39** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

The Effects of the Angiotensin-Converting Enzyme (ACE) Genotype on 3000 m Running (VO2max) Performance & Body Composition in Turkish Army Soldiers: Longitudinal Study View project

Relationship between ACE genotype and short duration aerobic performance development View project

All content following this page was uploaded by Mesut Cerit on 19 November 2019.

The user has requested enhancement of the downloaded file.

The Effects of the Angiotensin-Converting Enzyme (ACE) Genotype on 3000 m Running (VO2max) Performance & Body Composition in Turkish Army Soldiers: Longitudinal Study

Cerit M[1] ABCDE

1 Head of Recreation Department in School of Physical Education and Sport, Cyprus International University; Nicosia, Cyprus

Authors' Contribution: A – Study design; B – Data collection; C – Statistical analysis; D–Manuscript Preparation; E – Funds Collection.

Abstract

Purpose: The main objectives of this study is to determine the effect of ACE gene polymorphism on the parameters tested in the follow-up study, which has been carried out for many years and to find out whether the differences in ACE gene's metabolism due to the influence of parameters such as environmental factors, lifestyle and training, have a role in the development of sportive performance or not.

Methods: The study group consisted of 59 male army officers. The male subjects participating in the research study did not regularly deal with any sports activities as professionally. All subjects were measured for certain body mass and body composition variables before the accomplishment of the 3000m running test.

Results: ACE gene polymorphisms were examined by PCR method. The dispersion of genotypes in the entire group (16.90 % II, n = 10; 44.10 % ID, n = 26; 39.00 % DD, n = 23) did not diverge from substantially from those estimated by the Hardy–Weinberg equilibrium. All ACE genotype groups have shown significant increase on body fat mass & fat percentage, on the other hand; free fat mass (FFM) & body mass index (BMI) and 3000m running performance (VO2max) have shown significant decrease in the test as compared to the 2004 initial levels.

Conclusion: The results obtained from this study will be able to reveal whether the metabolic effects in organism created by ACE gene polymorphism are triggered or not as a result of exercise and life-style.

Keywords: genetics, polymorphism, physical fitness, training.

Introduction

Relationship between genetic and sportive performance, fitness or healthy life is revealed by cross-sectional studies which have been carried out over the last quarter century and which include a new finding coming out each passing day. A great majority of the conducted researches are restricted in terms of their status due to insufficiencies related to both economy and sample group and cannot reflect the society-wide. The minority of the conducted researches related to the development of genetic and sportive performance is longitudinal. Repeating the genetic studies conducted on individuals for a long period of time and revealing the differences or similarities between the obtained results and the other genotypes can create a new point of view and perception effect. Within this framework, the changes in behaviors or physical abilities caused by individual differences in time under the umbrella of environmental factors and life-style and the effects that they create in metabolism can be understood much better.

The codes of cells stored in the structure of the DNA vary according to each individual. These differences between individuals may result in different levels of effects to the warnings or reactions (training loads, training adaptation, environment adaptation, the way of diet, type of muscle fibers, blood pressure etc.) they have encountered. Genetic structure affects individuals fitness level and exercise adaptation. Thus, individuals with the same genotype structure can respond to exercises performed in a similar manner on a regular basis [1]. In this study, we specifically focus on angiotensin I-converting enzyme (ACE) gene, which has been one of the most extensively studied polymorphisms in the field of performance genetics.

The ACE gene is known to have effects on the muscular force & the degree of fatigue (aerobic endurance) and adaptation to workout sessions [2]. ACE has an essential role in the regulation of cardiovascular function and metabolic processes in muscles. The renin-angiotensin-aldosterone-system exerts an important role in systemic regulation of blood circulation and blood pressure [3]. ACE catalyzes

the conversion of angiotensin I to angiotensin II, which causes vasoconstriction and through the release of aldosterone influences the regulation of electrolytes and water. In addition, ACE reduces the vasodilatory effect of bradykinin causing an increase in blood pressure [4,5].

ACE gene includes a polymorphism enclosing of the availability (insertion, I) or nonentity (deletion, D) of a 287 base pair sequence in intron 16 [5,6].comprising 26 exons and encode for ACE, which perform operative role on various substrates. ACE gene polymorphism appears to have significant mission on ACE at a tissue level [2,7] and may effect angiotensin II production [8] Higher ACE levels increase angiotensin II productivity and thus the increased level of plasma angiotensin II restricts the blood flow to the tissues[1].

ACE genotype variants have different characteristics (polymorphism) respectively; DD homozygous, II homozygous and ID heterozygous [9,10]. D allele is associated with high ACE activity, leading to increased levels of angiotensin II and improving performance in strength training, I allele assists the performance of endurance athletes through factors such as the mechanical efficiency of skeletal muscles and the muscle fiber ratio [11], and the I/D (compound heterozygous) allele is associated with normal ACE activities, partial advantage is observed for both properties [9,10,11].

Researches in which a lot of genes have been used and which reflect the great majority of the society can reveal clearer and more explanatory information. Even though the characteristics related to physical performance pass down, it is known that factors such as life-style and environmental factors affecting individual differences, exercise, healthy diet and stress determine the physical status or fitness level of the individuals. Analyses of the genetic contribution to the physical performance phenotypes provide not only insight into the importance of genetic factors but also in the contribution to the environmental factors [12]. Having the ideal genes does not guarantee Olympiad success or protection from cardiovascular diseases (high blood pressure, diabetes, heart diseases, Alzheimer, paralysis etc.).

Genes which are the determiners of lifetime are triggered as positive or negative with the effect of life-style and environmental factors. Individuals who have genetic susceptibilities to endurance characteristics can succeed in the activities where aerobic capacity or aerobic power is effective. It is a minimal chance that these individuals can be a successful sprinter or a bodybuilding athlete. The important thing is realizing the effects that genotypes can create and being able to adapt the manners (life-style) into the features in question.

The main objectives of this study is to determine the effect of ACE gene polymorphism on the parameters tested in the follow-up study, which has been carried out for many years and to find out whether the differences in ACE gene's metabolism due to the influence of parameters such as environmental factors, lifestyle and training, have a role in the development of sportive performance or not. This study may also reveal whether individual differences caused by genes will have any positive or negative role in performance unless there is a change in behavior or lifestyle.

Methods

Participants

The study group consisted of 59 male Turkish army officers (total number of the subjects participated in the study were 186 in 2004). The subjects who were not involved in the follow-up study (127 subjects) leaved from the army for special or health related reasons. No contact was made with the subjects during the 15-years period. The subjects took care to maintain their physical performance capabilities only under the task intensity & scope, and regularly participated in physical ability evaluation tests (two minutes push-ups, sit-ups, pull-ups, & 3000m run) and comprehensive health checks every year. The male subjects participating in the research study did not regularly deal with any sports activities as professionally. The subjects took care to maintain their physical performance capabilities only under the task intensity and scope, and participated in physical ability evaluation tests (two minutes push-ups, sit-ups, pull-ups, & 3000m run) and comprehensive health checks every year. Mean age of the subjects was 26 ± 1.4, body weight was 73 ± 2.2 kg, and height was 175 ± 2.4 cm. All subjects have provided written consent to participate in the study and appropriate ethics committee approval has also been granted.

3000m running test (VO_2max)

The subjects were given detailed information about the importance of the study before the tests began. All subjects participated in tests with sportswear. Subjects performed warm-up exercises for 20 minutes before starting the test. All subjects had attended 3000m running test. The tests were performed on the athletics track and the measurements were recorded with the hand stopwatch.

Body composition measurements

All subjects participated in body composition measurements with empty stomach early in the morning (subjects were informed about the purpose of the test before body composition measurement). Body weight and body composition were measured with the bio impedance technique using a INBODY 2000 electronic scale. The device was plugged in and calibrated to account for the weight of clothing (0.2 kg). Afterwards, data regarding a participant's age, body height, and sex were entered. Then, the subjects stood on the scale with their bare feet on the marked places. The device analyzes body composition based on the differences of the ability to conduct electrical current by body tissues (different resistance) due to different water content. All subjects were measured for certain body weight and body composition variables. The following measurements were made; body weight (kg), fat mass (kg), fat mass percentage (PBF), fat free mass (FFM, kg) & body mass index (BMI, kg/m2).

Genetic analysis

The ACE genotype was assessed essentially as described in [13].Each subject provided a written consent to participate in the study and appropriate ethics committee approval. Peripheral venous blood of subjects receiving the approvals were collected on K2EDTA scrapers and stored at -20 ° C until used for DNA isolation. All molecular analyses were carried out in the Molecular Medicine Research Laboratory of the Department of Pediatrics, Ege University Medical Faculty Hospital. "Genomic DNA was extracted from 200 l of EDTA-anti coagulated peripheral blood leucocytes using the QI Amp Blood Kit (QIAGEN, Ontario, Canada, Cat. no: 51,106). Amplification of DNA for genotyping the ACE I/D polymorphism was carried out by polymerase chain reaction (PCR) in a final volume of 15 l containing 200 M dNTP mix, 1.5 mM MgCl2, 1£ Buffer, 1 unit of AmpliTaq® polymerase (PE Applied Bio systems) and 10 pmol of each primer. The primers used to encompass the polymorphic region of the ACE were 5-CTGGAGACCACTCCCATCCTTTCT-3 and 5 -ATGTGG CCATCACATTCGTCAGAT-3" [14]. DNA is amplified for 35 cycles, each cycle comprising denaturation at 94°C for 30 s, annealing at 50°C for 30 s, extension at 72°C for 1 min with final extension time of 7 min. The initial denaturizing stage was carried out at 95°C for 5 min. The PCR products were separated on 2.5% agarose gel and identified by ethidium-bromide staining. Each DD genotype was confirmed through a second PCR with primers specific for the insertion sequence" [15]."The samples with II and DD homozygote genotypes and ID heterozygote genotype were selected at random. These samples were then purified by PCR products purified system (Genomics, Montage PCR, Millipore) and directly sequenced by the ABI 310 Genetic Analyzer (ABI Prisma PE Applied Biosystems)" [16].

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 10 (SPSS Inc., Chicago, IL, USA). Methods applied were frequencies, descriptive statistics and means. Statistical significance was set at the P< 0.05 level. The mean differences between groups that have been split on two within-subject factors that are ACE genotype group and time were compared with two-way repeated measures ANOVA. The post hoc analysis was conducted with Least Significant Difference method (LSD). Lastly, the differences between 2004 and 2019 values with in each ACE genotype group were observed and analyzed by box-plot and paired t-test respectively.

Results

ACE genotype was determined in 59 subjects who form the basis of this report[13]. The dispersion of genotypes in the entire group (16.90 % II, n = 10; 44.10 % ID, n = 26; 39.00 % DD, n = 23) did not diverge from substantially from those estimated by the Hardy–Weinberg equilibrium. There was no significant deviation in the distribution of genotypes in the complete group in comparison to those stipulated by the Hardy-Weinberg equilibrium. All ACE genotype groups have shown significant increase on body fat mass & fat percentage, on the other hand; free fat mass (FFM) & body mass index (BMI) and 3000m running performance (VO_2max) have shown significant decrease in the test as compared to the 2004 initial levels [1,13](P < 0.05 for all).

Genotype	n	2004	2019	Time Effect (Within subject) *P Value*	Genotype Effect (Between subject) *P value*
II	10	44.63±2.63	29.18±4.59	0.000	0.019
ID	26	47.29±2.89	31.21±3.16		
DD	23	47.81±3.81	31.57±3.67		

Table1: Effect of ACE genotype on 3000m running (VO_2max) performance over time. (Significance level *P < 0.05)

The mean 3000m running (**VO_2max)** performance scores achieved, both in 2004 and 2019, were highest for subjects with genotype DD, intermediate for subjects with genotype ID, and lowest for subjects with genotype II. It is proven that there is a significant decrease in the 3000m running (**VO_2max)** performance on

the average for all genotypes (p=0.000). After applying LSD test, it is showed that ID and DD genotypes have significantly greater 3000m running (**VO_2max)** scores compared to genotype II. In other words, the genotype does have a significant effect on this decrease. However, p value for interaction between decrease in 3000m running (**VO_2max)** score and genotype is 0.448, which is insignificant.

Genotype	n	2004	2019	Time Effect (Within subject) *P Value*	Genotype Effect (Between subject) *P value*
II	10	9.04±3.63	20.68±7.94	0.000	0.683
ID	26	8.96±2.03	18.9±5.92		
DD	23	9.1±2.33	18.5±4.82		

Table 2: Effect of ACE genotype on fat mass (FM) over time. (Significance level *P < 0.05)

The mean fat mass (FM) achieved, both in 2004 and 2019, were highest for subjects with genotype DD, intermediate for subjects with genotype II, and lowest for subjects with genotype ID in 2004 [1]. However, it was highest for with genotype II, intermediate for subjects with genotype ID and lowest for subjects with genotype DD in 2018. It is revealed that there is a significant increase in the fat mass on the average for all genotypes (p=0.000). However, the differences between fat mass of three genotypes were not significant by one-way ANOVA (p=0.683). In other words, the genotype does not have a significant effect on this increase. Also, p value for interaction between increase in fat mass and genotype is 0.33, which is insignificant.

Genotype	n	2004	2019	Time Effect (Within subject) *P Value*	Genotype Effect (Between subject) *P value*
II	10	61.95±5.18	36.49±5.06	0.000	0.786
ID	26	62.64±4.52	36.55±3.75		
DD	23	62.5±3.68	36.47±3.21		

Table 3: Effect of ACE genotype on fat free mass (FFM) over time. (Significance level *P < 0.05)

The mean fat free mass (FFM) achieved, both in 2004 and 2019, were highest for subjects with genotype ID, intermediate for subjects with genotype DD, and lowest for subjects with genotype II in 2004 [1]. However, it was highest for with genotype ID, intermediate for subjects with genotype II, and lowest for subjects with genotype DD in 2019. It is revealed that there is a significant decrease in FFM on the average for all genotypes (p=0.000). However, the differences between FFM of three genotypes were not significant by one-way ANOVA (p=0.786). In other words, the genotype does not have a significant effect on this decrease. Also, p value for interaction between increase in FFM and genotype is 0.759, which is insignificant.

Genotype	n	2004	2019	Time Effect (Within subject) *P Value*	Genotype Effect (Between subject) *P value*
II	10	12.41±3.96	23.68±5.83	0.000	0.805
ID	26	12.25±2.36	23.13±5.13		
DD	23	12.54±2.43	22.23±4.72		

Table 4: Effect of ACE genotype on fat percentage (%, FM) over time. (Significance level *P < 0.05)

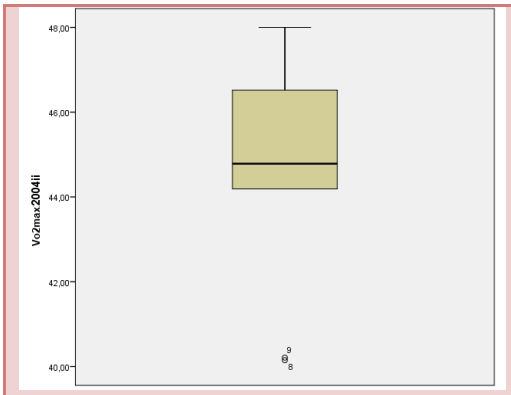
The mean amount off fat percentage (%, FM) achieved, both in 2004 and 2019, were highest for subjects with genotype DD, intermediate for subjects with genotype II, and lowest for subjects with genotype ID in 2004 [1]. However, it was highest for with genotype II, intermediate for subjects with genotype ID, and lowest for subjects with genotype DD in 2019. It is revealed that there is a significant increase in the fat percentage on the average for all genotypes (p=0.000). However, the differences between fat percentage of three genotypes were not significant by one-way ANOVA (p=0.805). In other words, the genotype does not

have a significant effect on this increase. Also, p value for interaction between increase in fat percentage and genotype is 0.358, which is insignificant.

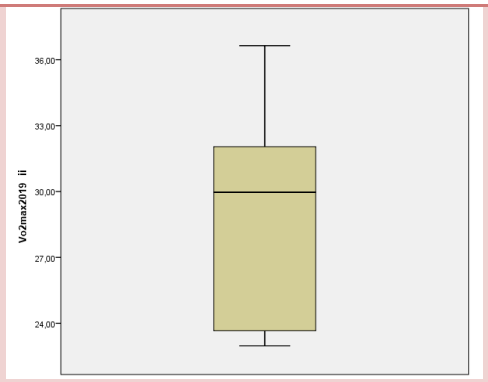
Genotype	n	2004	2019	Time Effect (within subject) *P Value*	Genotype Effect (between subject) *P value*
II	10	22.4±2.4	26.25±3.99	0.000	0.860
ID	26	22.53±1.71	26.05±2.89		
DD	23	22.5±1.71	25.71±2.27		

Table 5: Effect of ACE genotype on body mass index (BMI) over time. (Significance level *P < 0.05)

The mean BMI achieved, both in 2004 and 2019, were highest for subjects with genotype ID, inter mediate for subjects with genotype DD, and lowest for subjects with genotype II in 2004 [1]. However, it was highest for with genotype II, intermediate for subjects with genotype ID, and lowest for subjects with genotype DD in 2019. It is revealed that there is a significant increase in the BMI on the average for all genotypes (p=0.000). However, the differences between BMI of three genotypes were not significant by one-way ANOVA (p=0.860). In other words, the genotype does not have a significant effect on this increase. Also, p value for interaction between increase in BMI and genotype is 0.501, which is insignificant.

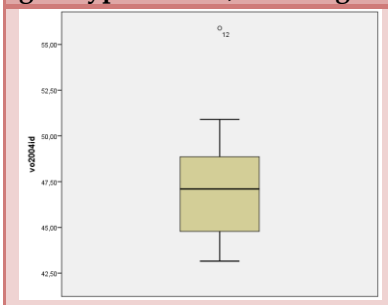


2004

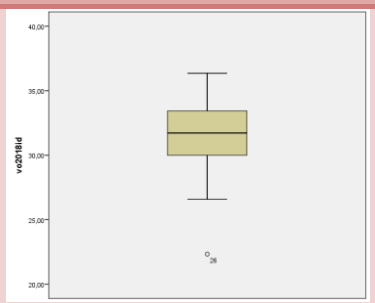


2019

Figure 1: It is seen that the median of 3000m running (VO_2max) score decreased over time for genotype II. Also, It has right skewed distribution in both 2004 and 2019.

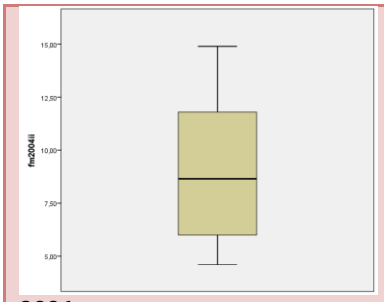


2004

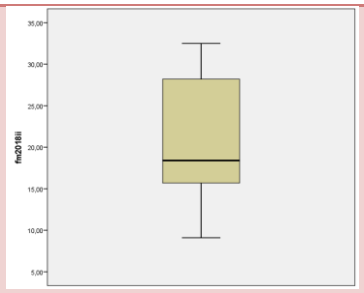


2019

Figure 3: It is seen that the median of 3000m running (VO_2max) decreased over time for genotype ID. Also, It has almost symmetric distribution in both 2004 and 2019.

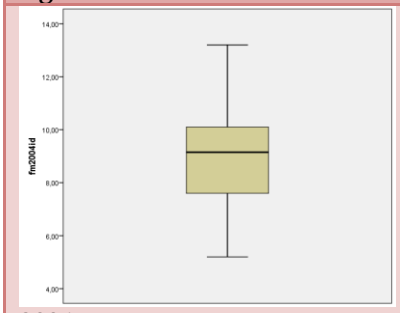


2004

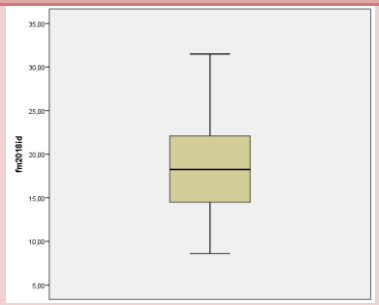


2019

Figure 4: It is seen that the median of fat mass increased over time for genotype II. It has right skewed distribution both in 2004 and 2019.

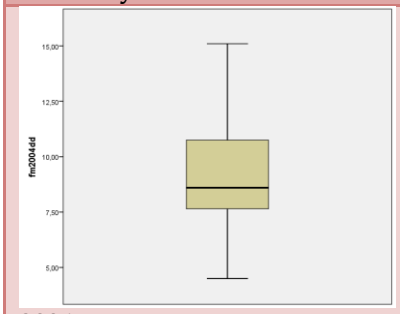


2004

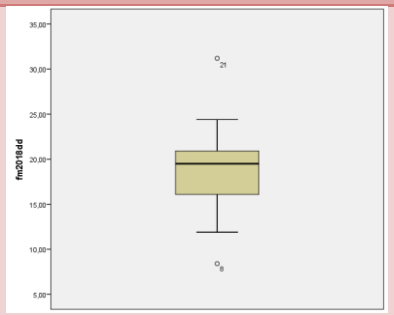


2019

Figure 5: It is seen that the median of fat mass increased over time for genotype ID. It has almost symmetric distribution both in 2004 and 2019.

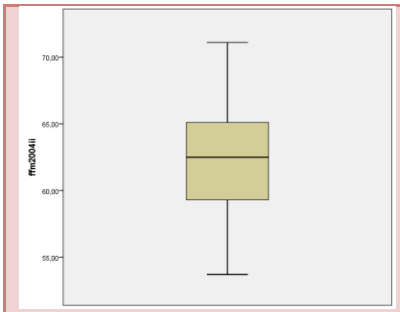


2004

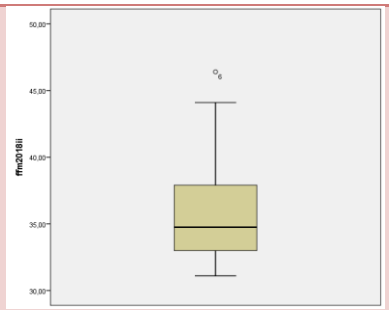


2019

Figure 6: It is seen that the median of fat mass increased over time for genotype DD. It has right skewed distribution in 2004, but it has left skewed distribution in 2019. Also, there are two outliers in 2019.



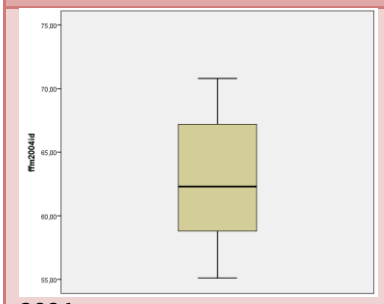
2004



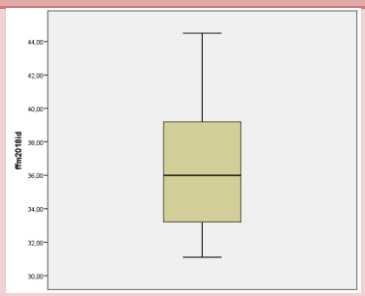
2019

Figure 7: It is seen that the median of FFM decreased over time for genotype II. It has symmetric distribution in 2004, but it has right skewed distribution in 2019. Also, there is an

outlier observation in 2019.

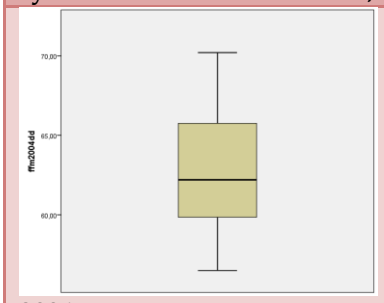


2004

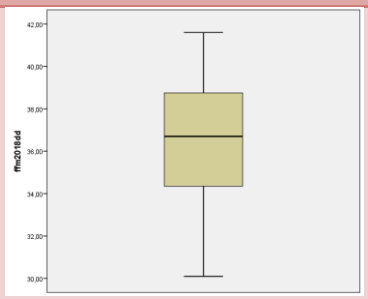


2019

Figure 8: It is seen that the median of FFM decreased over time for genotype ID. It has symetric distribution in 2004, but it has right skewed distribution in 2019.

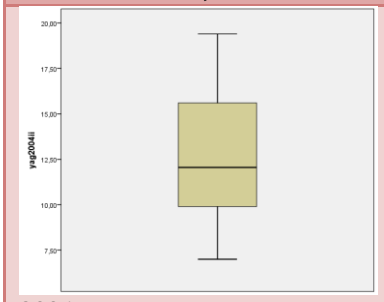


2004

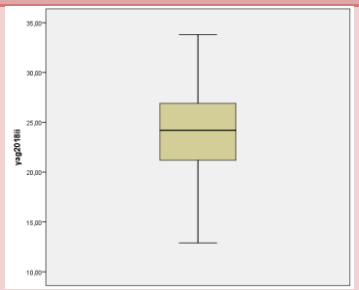


2019

Figure 9: It is seen that the median of FFM decreased over time for genotype DD. It has right skewed in 2004, but it has left skewed distribution in 2019.

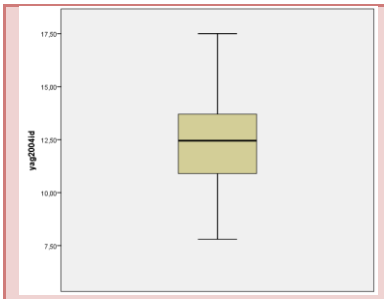


2004

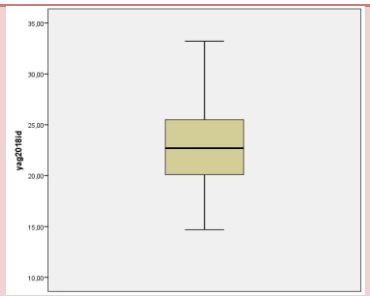


2019

Figure 10: It is seen that the median of fat percentage (%) increased over time for genotype II. It has right skewed distribution in 2004, but it has symmetric distribution in 2019.

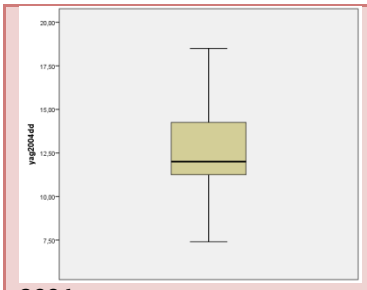


2004

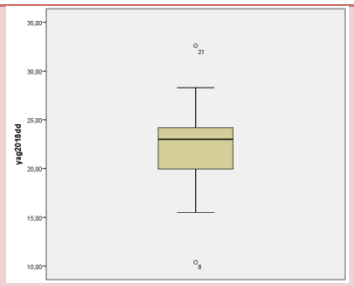


2019

Figure 11: It is seen that the median of fat percentage (%) increased over time for genotype ID. However, it has symmetric distribution both in 2004 and 2019.

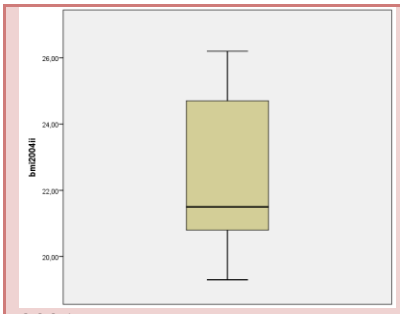


2004

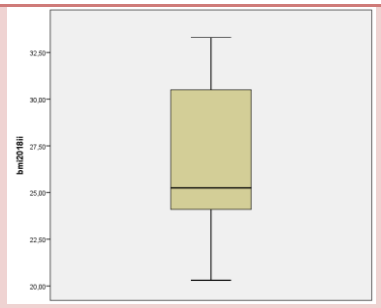


2019

Figure 12: It is seen that the median of fat percentage (%) increased over time for genotype DD. It has right skewed distribution in 2004, but it has left skewed distribution in 2019. Also, there are two outlier observations in 2019.

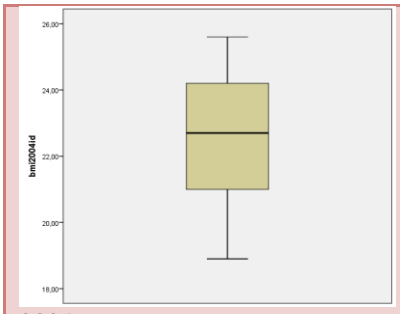


2004

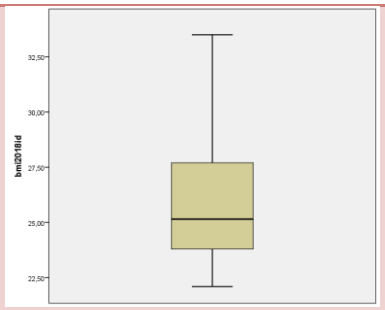


2019

Figure 13: It is seen that the median of BMI increased over time for genotype II. However, it has right skewed distribution both in 2004 and 2019.

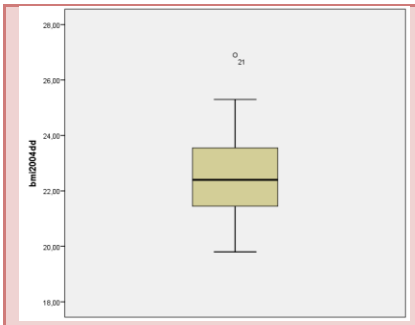


2004

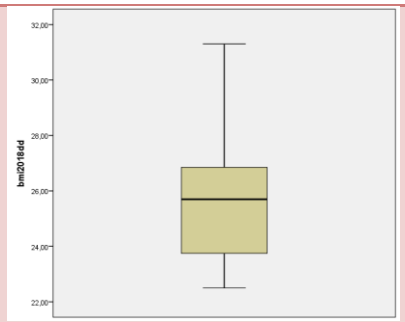


2019

Figure 14: It is seen that the median of BMI increased over time for genotype ID. It has left skewed in 2004, but it has right skewed distribution in 2019.



2004



2019

Figure 15: It is seen that the median of BMI increased over time for genotype DD. It has almost symmetric distribution and an outlier observation in 2004, but it has right skewed distribution both in 2019.

Discussion

In this study, we have focused on the effects of the ACE genotypes on VO_2max and body composition among the army officers. The study project maintained both cross-sectional and follow-up study.

Throughout this study; during the first two weeks of the 12-week boot camp in 2004, 2400m run, 3000m run, 3000m run with military equipment, push-ups, sit-ups and pull-ups and body composition measurement (pre-test) & analysis of the ACE genotypes (II, ID, DD) was performed on 186 subjects. Subjects were participated combined training exercise program (aerobic endurance, anaerobic endurance, muscular endurance and military obstacle training) for two sessions, 6 days per week for 12 weeks. All subjects were re-enrolled in the above-mentioned performance tests (post-test) after completing the 12-week exercise program [13]. At the end of the cross sectional study, the first search on the data obtained from the subjects [13] which was stated in Zudin et al. (2011) review article about the first published report of the ACE genotype being associated with physical performance in the last 12 years [17].

Adaptations to physical exercise differ significantly while some individuals are more responsive than others to physical exercise intervention. Therefore, there is no strong correlation between the responses of individuals, they may gain improvements in one area; on the other hand changes are not seen in others. [18]. In this respect, individual variation in the response to exercise can be observed in many parameters such as blood pressure, body composition, muscular strength, aerobic & [19,20]. anaerobic capacity, anatomical structure and somatotypes (mesomorph, ectomorph & endomorph).

Genetic factors are determinants in 20-80% of the variation of important characteristics of athletic performance [21]. The study of Bouchard (2008) in sedentary individuals notifyed that the average increase in VO2max was 25%, uniformed training ranging from baseline to doubling VO2max in different exercises show interaction between the environment and genes [22]. In this regard, analyses of the genetic contribution to physical performance phenotypes provide not only insight into the importance of genetic factors but also in the contribution of environmental factors [12]. In this respect, overall gains in VO2max in response to endurance training depend on numerous factors, including the baseline fitness status of an individual, the duration and intensity of the training program, single workout ([23]. knowledge of the trainer and the talent of the athletes.

Likewise, genetic variants that determine the body composition and muscle fiber type ratio may have a positive or negative effect on athletic performance. Additionally, aerobic or anaerobic training ability varies between individuals. It appears to be genetically determined among individuals, partly due to the composition of the muscle fiber type (type I & type II [24]. Type I fibers (slow twitch oxidative fibers) have high resistance to fatigue (and are thus suited for endurance performance), type IIa fibers (fast twitch oxidative glycolytic fibers) are better suited for medium-term anaerobic exercise, and type IIb fibers (fast twitch glycolytic fibers) are adapted for short bursts of high speed and power [24,25,26]. Normally, the fast twitch muscle fibers are important for short-duration and high-intensity work bouts, where as the slow twitch muscle fibers are better suited for sub-maximal and prolonged activities[24] Similarly, Cerit et al. (2006) reported that "ACE DD genotype seems to have an advantage in development in short duration aerobic performance development that requires high level VO2max. There was also a linear trend in performance enhancement as ACE DD > ID > II ACE DD" [13].

After realizing the relationship between ACE genotypes on muscle fiber type & the development of VO2max, it is important to figüre out the cardiovascular effects of the ACE gene in metabolism and muscle. ACE gene has an essential role in the regulation of cardiovascular function and metabolic processes in muscles. High ACE activities converts the angiotensin I into angiotensin II and which causes, vasoconstriction, and the short and long term effects on the organism are observed as weight loss, protein fragmentation in skeletal muscle mass and an increase in oxygen level or consumption[27]. These mentioned effects of ACE gene polymorphism can determine the behavior or performance differences between individuals partially or completely. For instance; ACE DD genotype is related with higher ACE activity[6],

angiotensin II secretion rate & the high rate of the fast twitch muscle fiber [8,3]. This genotype plays a key role in the development of speed & power parameter, which is the determinant of anaerobic activities [28,29]. Additionally, it has more advantage in low volume high intensity type of anaerobic workout period [3].

There are many cross-sectional studies in the literature about the effects of ACE gene polymorphism on metabolism. In the framework of this studies, after the long term breaks given to exercise brings about loss of improvement, in order to obtain the results of VO2max & body composition measurements of the same subject group (59 officers) whether the factors affecting individual performance can result from gene polymorphism or not.

In our study, we obtained in advance the results of the body composition measurement of the subjects in order to compare the effects of ACE gene polymorphism on VO2max performance during cross-sectional & follow-up studies. To be able to reveal the differences occurring in the body composition and aerobic performances by re-testing (3000 m run & body composition variable) the individuals' changing metabolism almost 59 individuals from the same sample group (186 subjects) as in the research in 2004, due to the life-style and environmental factors 15 years later again after the data obtained from research carried out in 2004 [1,13].

In this framework, due to the fact that ACE DD and ID genotypes have high level of anabolic structure (using high rate of fast twitch muscle fibers) in comparison to II genotype, it is assessed that they may have lost more energy and that's why they incur losses of body weight and percentage of fat [1]. Moreover, ACE DD genotype improves the aerobic capacity and increases the VO2max levels and shows better performance in short duration aerobic endurance training [13,2,3]. and performance improvement in maximal efforts, in which VO2max is dominant and lasting between 8-10 minutes[13,2] (Cerit et al.2006; Rieder et al. 1999). The study of Agnes et al. (2016) showed a more remarkable trend of increase in the VO2peak during the 5-year period among skiers (male & female) with the ACE ID genotype. However, no significant genotype-related associations were found in the dynamics of the VO2peak during the 5-year period [30]. Similarly, Holdys et al. (2011) reported that no association was found between I/D polymorphism in the ACE gene with VO_2max values. All of the subjects (154 men and 85 women) in their study were professional athletes representing various sport disciplines and levels of fitness. They also stated that I allele was found to have an advantageous effect on higher VO_2max values[31].

Unlike these studies, we found the performance level of VO_2max were highest for subjects with genotype DD (47.81±3.81; 31.57±3.67), intermediate for subjects with genotype ID (47.29±2.89; 31.21±3.16) and lowest for subjects with genotype II (44.63±2.63; 29.18±4.59), both in 2004 [1], and 2018. It is proven that there is a significant decrease in the VO2max performance on the average for all genotypes. Our study showed that ID and DD genotypes have significantly greater VO2max performance compared to genotype II. In other words, the genotype does have a significant effect on this decrease. However, p value for interaction between decrease in VO2 max performance and genotype is 0.448, which is insignificant (Table 1).

Studies of Sander et al. (2015) supporting our study, they stated that subjects carrying D allele demonstrated larger improvements in VO2max and capillary length after the training stimulus of recreational skiing [32]. Furthermore, Nicole et al. (2014) reported that D-allele carriers showed positive improvement in VO2max following high intensity interval training, as a result of the ergometry exercise performed in 20 active healthy adults 3 days a week for 6 weeks. However, ACE I-allele carriers would be expected to gain greater VO2max improvements following continuous moderate exercise than high intensity interval training [6]

In contrast to our study, Frederiksen et al. (2003) reported that they found no substantial effects of ACE genotype on physical performance in neither the cross-sectional nor the follow-up study [33]. However, in our studies all ACE genotype groups showed significant differences about VO2max & body composition variables in the follow-up study (2019) compared to (2004) cross-sectional research [1]. (Table 1, 2, 3, 4). Similar to our result, Zhao et al.(2003) reported that individuals with ACE DD genotype have a greater VO2max than those with the ACE II genotype[34]. In a number of previously conducted studies has been

stated that ACE DD genotype is affect VO2max in healthy adults [35] and some studies have shown that there is no relationship between ACE genotypes and VO2max development [20].

In the literatüre, some studies has been expresed that a maximal a-VO2 diff decrease with ageing partially contributes to age-reductions in VO2max [36,37,38,39] and muscle mass usually peaks at 25–30 years and there-after begins to decline[40]. Also in our study, VO2max and muscle mass level decreased in all subjects with increasing age.

The effects of ACE gene polymorphism on the development of VO2max may also be create a substantial changes on body composition. Montgomery et al. (1999) reported that "The effect of genetic factors as well as other variables, such as the training that creates changes in body composition, is an undeniable reality" [41]. Thus, body fat and body weight could be raised and lowered accordingly by stimulating and inhibiting the production of Ang I [42]. In studies involving genetic and sportive performance relationships, the ACE II genotype is indicated to have a close relationship with the low body fat percentage (%, FM) and uses fatty acids efficiently as an energy source [43,44,45]. The body fat percentage increase of the ACE I variant has been clarifyed to be unable to effectively provide the fuel source of fatty acids during the long-term aerobic activities, whereas losing more fat mass during high-intensity workout periods [41,46].

Bassame et al. (2007) reported that the ACE II genotype was observed as not only increasing the muscle strength compared to other genotypes following the training period of 10 weeks, but also increasing the fat mass & lean mass [47]. Likewise, Passaro et al. (2011) & Kijin et al (2012) stated that ACE ID polymorphisms are associated with fat distribution. The effects of exercise on body composition was more effective in I allele. However, D allele of ACE gene is postulated to manifest lower body fat mass (%, FM) compared to I allele. [48].

Another studies comparing body composition of ballet dancers with normal adults stated that ballet dancers had significantly lower score not only for fat mass rate but also free fat mass compared to the control group of women of the same age. They also found that ACE DD genotype of ballet dancers had higher percentage of body fat and fat mass compared to ACE II genotype when comparing body composition of ballet dancers per genotype. From the result of this study, ACE DD genotype from ACE ID polymorphism was related to higher percentage of body fat for ballet dancers [44].

In this regard, our study showed that amount of fat mass were highest for subjects with genotype DD (9.1±2.33), intermediate for subjects with genotype II (9.04±3.63), and lowest for subjects with genotype ID (8.96±2.03) in 2004 [1]. However, it was highest for with genotype II (20.68±7.94), intermediate for subjects with genotype ID (18.9±5.92), and lowest for subjects with genotype DD (18.5±4.82) in 2018 (Table 2). It is revealed that there is a significant increase in the fat mass on the average for all genotypes (p=0.000). However, p value for interaction between increase in fat mass and genotype is 0.33, which is insignificant.

Studies of [49] investigate the effect of 12 weeks of combined training on changes in body composition (weight, body fat percantage, percantage of muscle mass, body mass index) according to the ACE gene polymorphism in 21 senior Korea Air Force Academy cadets. They reported that body composition factors among ACE gene polymorphism groups between pre & post-training in all groups were not statistically significant [49].

Exercise-mediated change on body composition may differ according to ACE gene polymorphism [48].Data from a study of Lemes et al. (2013) stated that angiotensin converting enzyme insertion/deletion polymorphism is associated with increased adiposity and blood pressure in obese children and adolescents showed that DD and ID have lower body fat when compared to II genotype[50,51]. On the other hand, studies related with the European population did not demonstrate differences for body fat in any group related to ACE gene[52]. Similar to these expression, it is indicated in another study that there is no significant correlation between body composition and ACE genotype [53].

In our study, we reported that the amount of free fat mass were highest for subjects with genotype ID, intermediate for subjects with genotype DD, and lowest for subjects with genotype II in 2004 [1]. However, it was highest for with genotype ID, intermediate for subjects with genotype II, and lowest for subjects with genotype DD in 2018 (Table 3). It is revealed that there is a significant decrease in free fat mass on the

average for all genotypes. However, the genotype does not have a significant effect on this decrease. Also, p value for interaction between increase in free fat mass and genotype is 0.759, which is insignificant. In addition, we found the amount off fat percentage were highest for subjects with genotype DD, intermediate for subjects with genotype II and lowest for subjects with genotype ID in 2004 [1]. However, it was highest for with genotype II, intermediate for subjects with genotype ID, and lowest for subjects with genotype DD in 2018. It is revealed that there is a significant increase in the fat percentage on the average for all genotypes. However, the genotype does not have a significant effect on this increase (Table 4).

In another study on the respective gene, the ACE II genotype has been determined to increase the body mass index in normal subjects [27]. Katsuya et al. (1995) reported that patients with the DD genotype had lower BMI than individuals with the ID genotype [54]. The studies of Oishi et al. (2016), analyzed the ACE I/D gene polymorphism among the Brazilian rafting team. They found that no differences between the percentage of fat among athletes of the DD and ID genotypes, but athletes carrying the I allele had significantly higher BMI and muscle mass[11].

We may also found that, the mean BMI were highest for subjects with genotype ID (22.53±1.71), intermediate for subjects with genotype DD (22.5±1.71), and lowest for subjects with genotype II (22.4±2.4) in 2004[1]. However, it was highest for with genotype II (26.25±3.99), intermediate for subjects with genotype ID (26.05±2.89), and lowest for subjects with genotype DD (25.71±2.27) in 2018. It is revealed that there is a significant increase in the BMI on the average for all genotypes (Table 5). However, the genotype does not have a significant effect on this increase. Also, p value for interaction between increase in BMI and genotype is 0.501, which is insignificant ($P < 0.05$ for all).

In conclusion, we found significant effects of ACE genotype on physical performance & body composition measurement for the cross-sectional study. We observed considerable change of physical performance and body composition measurement on the subjects for the follow-up study, ACE polymorphism does not have a significant effect on this alteration.

We hypothesis that individual performance differences caused by genes will not provide a meaningful development in the way that there are no changes in the behaviors or lifestyles of individuals. The results obtained from this study will be able to reveal whether the metabolic effects in organism created by ACE gene polymorphism are triggered or not as a result of exercise and life-style.

Acknowledgements

This study was carried out with the approval of Turkish Military Academy. Financial support for this research was received from Ege University, Izmir, Turkey. Special thanks to Prof. Dr. Muzaffer Çolakoğlu, Prof. Dr. Afig Berdeli, Prof. Dr. Fethi Sırrı Cam, Ass. Prof. Murat Erdogan & Suat Gürcan for their valuable help and contributions to this study.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this paper.

References

1. Cerit M., Hypothetical approach to the location of genotypes (ACE & ACTN3) associated with energy system for the athletic performance. Journal of Sport Science Researches, 2018 1:15–25.
2. Mizuiri S., Hemmi H., Kumanomidou H. Decreased renal ACE mRNA levels in healthy subjects with II ACE genotype and diabetic nephropathy. J Am Soc Nephrol 1997 8 115A
3. Paola Valdivieso P.,Toigo M., Hans Hoppeler H. and Flück M. T/T homozygosity of the *tenascin-C* gene polymorphism rs2104772 negatively influences exercise-induced angiogenesis PLoS One. 2017 12(4): e0174864.
4. Thompson & Binder-Macleod, Association of genetic factors with selected measures of physical performance. Phys Ther. 2006 86(4): 585–591.
5. Mägi A. The association analysis between ace and actn3 genes polymorphisms and endurance capacity in young cross-country skiers: longitudinal study. Journal of Sports Science and Medicine, 2016 15: 287-294.

6. Goddard N., Baker M., Higgins T., Cobbold C. The effect of angiotensin converting enzyme genotype on aerobic capacity following high intensity interval training. International Journal of Exercise Science ,2014 7(3): 250-259.
7. Guth L. M. and Roth S. M. Genetic influence on athletic performance. Curr Opin Pediatr. 2013 Dec; 25(6): 653–658.
8. Papadimitriou. ACTN3 R577X and ACEI/D gene variants influence performance in elite sprinters: a multi-cohort study. BMC Genomics, 2016; 17:285.
9. Alvarez R., Terrados N., Ortalano R., Iglesias CG., Requero JR., Batalla A., Cortina A. Genetic variation in the renin-angiotensin system and athletic performance. Eur J Appl Physiol. 2000;82 (1–2) 117–120.
10. Gayagay G., Yu B., Hambly B., Boston T., Hahn A., Celermajer DS., Trent RJ. Elite endurance athletes and the ACE I allele the role of genes in athletic performance. Human Genetics, 1998;103:48–50.
11. Oishi J., Castro C.A., Silvestre J.G.O., Garcia A.C., Duarte O. An analysis of the ACE I/D gene polymorphism in the athletes of the twice world champion Brazilian rafting team. EFDeportes.com Revista Digital Año 2016; 21 N° 218.
12. Gaston P., Beunen, Martine AI Thomis & Maarten W. Peeters. Genetic Variation in Physical Performance. The Open Sports Sciences Journal, 2010; 3, 77-80).
13. Cerit M., Çolakoğlu M., Erdoğan M., Berdeli A., Cam FS. Relationship between ACE genotype and short duration aerobic performance development. European Journal of Applied Physiology, DOI,2006; 10.1007/s00421-006-0286-6.
14. Rigat B., Hubert C., Corvol P., Soubrier F., PCR detection of the insertion/deletion polymorphism of the human angiotensin converting enzyme gene (DCP1) (dipeptidylcarboxy- peptidase 1). Nucleic Acids Res, 1992;20:1433.
15. Shanmugam V., Sell KW., Saha BK., Mistyping ACE heterozygotes. Pubmed, PCR Methods Appl,Oct, 1993;3(2):120–1.
16. Berdeli A., Sekuri C., Cam FS., Ercan E., Sağcan A., Tengiz I., Eser E., Akın M. Association between the eNOS (Glu298Asp) and the RAS genes polymorphism and premature coronory artery disease in a Turkish population. Clinica Chimica Acta, 2005; Volume 351, Issues 1-2.
17. Zudin Puthucheary, James R.A. Skipworth, Jai Rawal, Mike Loosemore, Ken Van Someren and Hugh E. Montgomery. The ACE gene and human performance: 12 Years on. Sports Med 2011; 41 (6): 433-448 DOI: 10.2165/11588720-000000000-00000) 3 (1), 97-105, ISSN:2548-0723.
18. Lakka TA., Bouchard C. Genetics, physical activity, fitness and health: what does the future hold J R Soc Promot Health, 2004;124(1):14-15).
19. Bouchard C., Rankinen T. Individual differences in response to regular physical activity. Med Sci Sports Exerc.Jun 2001; 33(6 Suppl):S 446-51 S452-3.
20. Rankinen T., Wolfarth B., Simoneau JA. No association between the angiotensin-converting enzyme ID polymorphism and elite endurance athlete status. Journal of Applied Physiology,2000; 88:1571– 1575. PMID: 10797114.
21. MacArthur D. & North KN. ACTN3: A genetic influence on muscle function and athletic performance. Exercise and Sport Sciences Reviews, 2007;35, 30–34.
22. Bouchard C. Gene-environment interactions in the etiology of obesity: defining the fundamentals. Obesity (Silver Spring) 2008;16 Suppl 3:S5-S10.
23. Tabata I., Irisawa K., Kouzaki M., Nishimura K., Ogita F., Miyachi M. Metabolic profile of high intensity intermittent exercises. Med Sci Sports Exerc1997;29(3):390-395).
24. Bouchard CR. An P. Rice T., Skinner JS., Wilmore JH., Gagnon J. Familial aggregation of VO2max response to exercise training: results from the Heritage Family Study. Journal of Applied Physiology, 1999;87, 1003-1008.).
25. Ahmetov I., Vinogradova O. L. & Williams A. G. Gene polymorphisms and fiber-type composition of human skeletal muscle. International Journal of Sport Nutrition and Exercise Metabolism, 2012;22(4), 292-303].
26. Farrell P.A., Joyner M.J., & Caiozzo V.J., ACSM's Advanced exercise physiology (2nd ed). Hong Kong: Wolters Kluwer. pp. 2012;39-40.

27. Vigano A., Relationship between angiotensin-converting enzyme gene polymorphism and body composition, functional performance, and blood biomarkers in advanced cancer patients. Clin Cancer Res, 2009;15(7].
28. Myerson SG., Hemingway H.,Budget R., Martin J., Humphries S., Montgomery H. E. Human angiotensin I-converting enzyme gene and endurance performance. Journal of Applied Physiology, 1999; 87, 1313-1316.
29. Nazarov IB., Woods DR., Montgomery HE., Shneirder OV., Kazakov I., Tomilin NV., Rogozkin VA. The angiotensin converting enzyme I/D polymorphism in Russian athletes. Eur J Hum Genet 2001;9(10):797–801.
30. Agnes M.,The Association Analysis between ACE and ACTN3 Genes Polymorphisms and Endurance Capacity in Young Cross-Country Skiers: Longitudinal Study. Journal of Sports Science and Medicine, 2016;15, 287-294.
31. Holdys J., Jakub KrysCiak, Daniel Stanisławski, Piotr Gronek. ACE I/D Gene Polymorphism in Athletes of Various Sports Disciplines. Human Movement, vol. 12 (3), 2011;223–231, doi: 10.2478/v10038-011-0022-x.
32. Ginkel V.G., Haan A.H., Woendeman J., Vanhees L., Serne E., Koning D.J., Flück M., Exercise intensity modulates capillary perfusion in correspondence with ACE I/D modulated serum angiotensin II levels. Applied and Translational Genomics 2015;4: 33-37.
33. Frederıksen H., Angiotensin I-converting enzyme (ace) gene polymorphism in relation to physical performance, cognition and survival—a follow-up study of elderly danish twins, ann epidemiol,2003;13:57–65.
34. Zhao B., Moochhala SM., Tham S. Relationship between angiotensin-converting enzyme ID polymorphism and (VO2max) of Chinese males. Life Sc.2003; 73(20):2625–30, PMID: 12967686.
35. Vaughan D., Huber-Abel FA., Graber F., The angiotensin converting enzyme insertion/deletion polymorphism alters the response of muscle energy supply lines to exercise. European Journal of Applied Physiology, 2013;v.113, n.7, p.1719–1729.
36. Hossack K.F., Bruce R.A., Maximal cardiac function in sedentary normal men and women: comparison of age-related changes. J. Appl. Physiol.1982;53, 799–804.
37. Ogawa T., Spina R.J., Martin W.H., Kohrt W.M., Schechtman K.B., Holloszy J.O., Ehsani A.A., Effects of aging, sex, and physical training on cardiovascular responses to exercise. Circulation,1992; 86, 494–503.
38. Rivera A.M., Pels A.E., Sady S.P., Sady M.A., Cullinane E.M., Thompson P.D., Physiological factors associated with the lower maximal oxygen consumption of master runners. J. Appl. Physiol.1989; 66, 949–954.
39. Wiebe C.G., Gledhill N., Jamnik V.K., Ferguson S., Exercise cardiac function in young through elderly endurance trained women. Med. Sci. Sports Exerc.1999;31, 684–691.
40. Janssen I., Heymsfield S.B., Wang Z.M., Ross R., Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr,2000; J. Appl. Physiol. 89, 81–88.
41. Montgomery HE., Clarkson P., Bernard M., Bell J., Brynes A., Dollery C., Hemingway H., Mercer D., Jarman P., Marshall P., Rayson M., Saeed N., Talmud P., Thomas L., Jubb M., World M., Humphries S. Angiotensin-converting-enzyme gene insertion/deletion polymorphism and response to physical training. Lancet, 1999; 13;353(9152):541-5.
42. B.H.Jones,M.K.Standridge, N.Moustaid., Angiotensin II increases lipogenesis in 3T3-L1 and human adipose cells. Endo- crinology, vol. 1997;138, no. 4, pp. 1512–1519.
43. Montgomery HE., Marshall R., Hemingway H., Myerson S., Clarkson P., Human gene for physical performance. Nature,1998; 393:221–222.
44. Jun H., Kim E., Sun J., Chul H., Kim H., Youn H., Rye K., Genetic associations of body composition, flexibility and injury risk with ACE, ACTN3 and COL5A1 polymorphisms in Korean ballerinas. J Exerc Nutr Biochem,2014;18(2):205-214.
45. Vitor M., Association of genetic polymorphisms with physical capacities and body composition in older women. 33'rd International Conference on Biomechanics in Sports, Poitiers, France, 2015; June 29 - July 3].

46. Shweta S., Suparna T., Jaspal S., Amarjeet SB. Association of angiotensin converting enzyme gene polymorphism and Indian Army triathletes performance. Asian Journal of Sports Medicine, Vol 1, 2010; p. 143-150.
47. Bassami M., Doran D., Ahmadizad S., Maclaren D. Effects of exercise intensity and duration on fat metabolism in trained and untrained older males. European Journal of Applied Physiology,2007;DOI: 10.1007/s00421-007-0523-7.
48. Kijin K., Comporision of Body Composition and 12 week combined exercise intervention-mediated effects according to ACE and IDGF-1 polymorphism in children. Department of Physical Education, Keinyung University.2012.
49. Keun-Soo K., Myung-Soo K.., Woo J.H. . The Effects of aerospace fitness training on ace gene polymorphism of kafa cadets in body composition and cardiorespiratory fitness,2009; DOI: 10.5352/JLS.2009.19.9.1277.
50. Lemes V.A., Neves A.L., Guazzelli I.C., Angiotensin converting enzyme insertion/deletion polymorphism is associated with increased adiposity and blood pressure in obese children and adolescents. Gene,2013;532, 197-202.
51. Passaro A., Nora E.D., Marcello C., PPARɣ Pro12Ala and ACE ID polymorphisms are associated with fat distribution, but not metabolic syndrome. Cardiovascular Diabetology,2011;10, 112.
52. Bonnet F., Patel S., Laville M., Influence of the ACE gene insertion/deletion polymorphism on insulin sensitivity and impaired glucose tolerance in healthy subjects. Diabetes Care,2008;31,789-94.
53. Orysiak J., Zmijewski P., Klusiewicz A., Kaliszewski P., Malczewska LJ., Gajewski J., Pokrywka A. The association between ace gene variation and aerobic capacity in winter endurance disciplines. Biol Sport,2013;30, 249-53.
54. Katsuya T., Horiuchi M., Chen YD., Koike G., Pratt RE., Dzau VJ., Reaven GM. , Relations between deletion polymorphism of the angiotensin-converting enzyme gene and insulin resistance, glucose intolerance, hyper insulinemia, and dyslipidemia. Arteriosclerosis Thrombosis Vascular Biology.1995;Jun;15(6):779-82.

View publication stats