Angiotensin-converting enzyme polymorphism in Turkish male athletes: relationship to left ventricular mass and function

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Abstract

Angiotensin-converting enzyme (ACE) is a key enzyme in the production of angiotensin II. The cloning of the ACE gene has made it possible to identify a deletion (D)-insertion (I) polymorphism that appears to affect the level of serum ACE activity. The aim of our study was to analyse the ACE gene I/D polymorphism in Turkish male athletes and to evaluate its relationship to left ventricular mass and function.

Forty male athletes (mean age 23.4±1.8 years) were included in this study, and they underwent both complete echocardiographic assessment and analysis of ACE I and D allele frequencies in peripheral blood by polymerase chain reaction. They were separated into three subgroups according to their ACE DD (n=13), DI (n=16) and II (n=11) genotypes. Thickness of the interventricular septum (IVS), the left ventricular posterior wall (LVPW) and left ventricular mass (LVM) and LVM index (LVMI) were measured by the M-mode. Left ventricular ejection fraction was calculated using Simpson's method, and so was the myocardial performance index.

There was no statistically significant differences between the ACE DD, DI and II genotypes at the p>0.05 level by age, body mass index, heart rate, systolic and diastolic blood pressures. The thickness of the IVS (12 mm) and LVPW (10.7 mm), and LVM (302.8 g) and LVMI (157.3 g/m²) in ACE DD genotypes were higher than for both ACE DI (10.8 mm; 9.7 mm; 231.9 g; 125.3 g/m²) and II genotypes (9.0 mm; 8.6 mm; 185.0 g; 107.5 g/m²) in athletes. Left ventricular systolic and global functions among the three ACE genotypes were not different statistically.

Our findings suggest that left ventricular hypertrophy is partially determined by genetic disposition and DD genotype of ACE is a potential genetic marker associated with an elevated risk of left ventricular hypertrophy.

Key words: ACE polymorphism, athletes, left ventricular mass, left ventricular function.

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Introduction

Angiotensin-converting enzyme (ACE) is a key enzyme in the production of angiotensin II. The cloning of the ACE gene has made it possible to identify a deletion (D)-insertion (I) polymorphism that appears to affect the level of serum ACE activity.[1] Although the training and performance of an elite athlete have complex characteristics, including a wide range of environmental and behavioural factors, genetic predisposition to athleticism might also be an important parameter.[2]

The aim of our study was to analyse the ACE gene I/D polymorphism in Turkish male athletes, and to evaluate its relationship to left ventricular mass and function.

Material and methods

Subjects

Forty Turkish male athletes (mean age 23.4±1.8 years) were included in this study, and they underwent both complete echocardiographic assessment, and analysis of ACE insertion (I) and deletion (D) allele frequencies in peripheral blood. The athletic individuals were selected from volunteer endurance athletes (25 middle-distance runners, 15 football players). All the athletes had been competing at national or international level for several years. None of the athletes had a history of cigarette smoking, hypertension, coronary artery disease, diabetes mellitus, renal or hepatic dysfunction, or a positive family history of hypertrophic cardiomyopathy. No medication, including anabolic steroids, was being taken by any of the athletes. The

Table 1. Basic characteristics of Turkish male athletes in angiotensin-converting enzyme (ACE) DD, DI and II genotypes

	ACE genotypes DD (n= 13)	DI (n=16)	II (n=11)	p value
Age (years)	22.6±1.1	23.7±2.4	23.5±1.2	NS
BMI (kg/m²)	21.5±1.8	21.3±1.8	21.8±2.0	NS
Heart rate (beats/min)	62.5±8.5	66.7±10.5	69.0±6.0	NS
Systolic BP (mmHg)	116.5±7.4	116.9±6.0	117.3±8.5	NS
Diastolic BP (mmHg)	75.0±7.1	74.4±6.0	73.6±4.5	NS

Key: NS = not significant; BMI = body mass index; BP = blood pressure

study was approved by the Pamukkale University Ethics Committee, and written informed consent was obtained from each participant.

Genotyping

DNA samples from these male athletes were analysed to determine the ACE I and D allele frequencies, and they were separated into three subgroups according to their ACE DD (n=13), DI (n=16) and II (n=11) genotypes.

The human ACE gene is located at chromosome 17q23. Genomic DNA from the subjects was prepared from peripheral blood by a standard phenol/chloroform extraction method, as published elsewhere.[3] Polymerase chain reaction (PCR) was used to detect the presence of the I and D alleles in intron 16 of the ACE gene according to the method described by Rigat *et al*.[4] The size of amplified fragments was determined by 2% agarose gel electrophoresis, UVI gel documentation system.

Echocardiographic measurements

All measurements were performed with the subjects in the left lateral decubitus position by M mode, two-dimensional (2D) and Doppler ultrasound echocardiography. The ultrasound equipment used was made by Control, Sigma Iris with a 2.5–MHz probe. Basic measurements of left ventricular dimensions in diastole, thickness of interventricular septum (IVS) and left ventricular posterior wall (LVPW) and left ventricular mass (LVM) were measured by the M-mode technique. LVM was divided by body surface area to obtain left ventricular mass index (LVMI). Left ventricular ejection fraction (LVEF) was assessed using Simpson's method. The left ventricular myocardial performance index (MPI) was calculated as (isovolumetric relaxation time + isovolumetric contraction time)/aortic ejection time.

Statistics

All analyses were performed by the computerised SPSS 10.0 program. Results are given as mean±standard deviation. The Kruskal-Wallis test was used for the three ACE genotypes, and Mann-Whitney U test was used to compare the two groups. P value <0.05 was considered statistically significant.

Table 2. Assessment of left ventricular diameters and functions of Turkish male athletes in angiotensin-converting enzyme (ACE) DD, DI and II genotypes

	ACE genotypes DD (n= 13)	DI (n=16)	II (n=11)	p value
Diameters (mm)				
IVS-diastolic	12.0±2.1	10.8±1.8	9.0±1.7	0.004
LVPW-diastolic	10.7±2.1	9.7±1.7	8.6±0.9	0.021
Left ventricular mass				
LVM (g)	302.8±101.7	231.9±53.9	185.0±44.4	0.001
LVMI (g/m²)	157.3±50.0	125.3±27.1	107.5±18.2	0.004
Left ventricular functions				
Ejection fraction (%)	66.5±2.8	67.0±2.1	69.2±2.6	NS
MPI	0.62±0.1	0.59±0.1	0.56±0.1	NS

Key: IVS = interventricular septum; LVPW = left ventricular posterior wall; LVM = left ventricular mass; LVMI = left ventricular mass index; MPI = myocardial performance index

Results

There was no statistically significant differences between the three ACE genotypes by age, body mass index, heart rate, systolic and diastolic blood pressures (table 1).

Assessment of left ventricular diameters and function is shown in table 2. There were significant differences in LVM, LVMI, diastolic thickness of IVS and LVPW in the three ACE genotypes. All these parameters were found to be higher in the ACE DD genotype subgroup compared to the DI and II genotype subgroups. The greatest difference was found between ACE DD and ACE II genotypes for each parameter. Each one of these parameters were also significantly different between ACE DI and II genotypes. Although LVM differed significantly (p=0.037) between the ACE DD and ACE DI genotypes, LVMI, IVS and LVPW diameters did not (at the p<0.05 level). Left ventricular systolic and global functions among the three ACE genotypes were not different statistically.

In athletes, both LVM and LVMI were positively correlated with IVS diameter (r=0.726, p<0.001 and r=0.807, p<0.001) and with LVPW diameter (r=0.609, p<0.001 and r=0.807, p<0.001).

Discussion

We performed this study to investigate the association between left ventricular hypertrophy (LVH), as assessed by echocardiography, and genetic factors determined by a deletion (D)-insertion (I) polymorphism of the ACE gene in Turkish male athletes. It has been suggested that the cardiac renin-angiotensin system has an important role in cardiac hypertrophy and heart failure. ID polymorphism in intron 16 of the gene coding for the ACE has been used to study the role of this gene in physical performance. Performance in endurance sports is a multifactorial phenotype influenced by several factors, such as physical, biomechanical, physiological, metabolic, behavioural, psychological and social

Key messages

- Genetic background may influence the development of left ventricular hypertrophy
- The DD genotype of angiotensin-converting enzyme may serve as a critical marker for left ventricular hypertrophy in male athletes

characteristics.[5] There is increasing evidence that the propensity for hypertrophy is determined genetically, in response to physical training. Also, there is some indication that ACE gene polymorphism may affect the hypertrophic response to training. For instance, the DD genotype seems to predispose to greater hypertrophy in response to training, and the D allele has been associated with a higher ACE activity, when compared to the ACE I allele.[6] In our study we established that the thickness of IVS (12 mm), LVPW (10.7 mm), and LVM (302.8 g) and LVMI (157.3 g/m^2) in ACE DD genotypes were higher than both ACE DI (10.8 mm; 9.7 mm; 231.9 g; 125.3 g/m^2) and ACE II genotypes (9.0 mm; 8.6 mm; 185.0 g; 107.5 g/m^2) in male athletes. Left ventricular septal and posterior wall thicknesses often increase in male athletes, but not in female athletes.[7]

It was shown that there were significant differences in IVS thickness and in LVPW thickness between control subjects and endurance-trained athletes. The overall mean LVM of the control subjects was significantly lower than the overall mean LVM of the endurance-trained athletes.[8] According to the findings of Montgomery *et al.*, individuals with the ACE DD genotype show a significantly increased LVM in response to physical training, compared to those with the II genotype and the ID genotype.[9]

Our results suggest that genetic background may influence the development of LVH. Our study cannot identify the mechanism by which the DD genotype of the ACE gene may affect cardiac hypertrophy. We suggest that male athletes with a DD genotype may have a higher risk for ventricular hypertrophy. This will require investigation in a longitudinal study. The DD genotype may serve as a critical marker for left ventricular hypertrophy in male athletes.

Conflict of interest

None declared.

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