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Original scientific article

INFLUENCE OF *ACE* AND *ACTN3* GENES POLYMORPHISMS ON CARDIOVASCULAR ADAPTATION IN FEMALE FOOTBALL PLAYERS

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The aim of study was to investigate distribution of *ACE* and *ACTN3* gene polymorphisms in young female footballers and to test association of common gene polymorphisms with body composition, arterial blood pressure and ECG screening variables. A group of 45 white, healthy, adolescent female elite footballers (FG) and 60 sedentary female controls (CG) enrolled in this study. HRM method has been developed to differentiate between variant alleles of *ACE* and *ACTN3* genes. No significant difference was found in the *ACE* and *ACTN3* genotypes or allele frequencies distribution between FG and CG ($p>0.05$). Also, neither insertion in the ACE gene, nor nonsense mutation in the *ACTN3* gene had a significant effect on resting BP and ECG parameters. Cardiovascular adaptation to intensive physical activity in FG is manifested as lowered resting systolic and diastolic blood pressure (lower 18 and 11 percentiles, respectively). Footballers with *ACE DD* and *ACTN3 XX* polymorphisms had higher values of Sokolow-Lyon voltage for LV hypertrophy, but without statistically significance ($p=0.61$ and 0.2, respectively). Interpretation of the effect of specific genes with presumed large effect on sport performance, should be cautious, especially in team sports with a mixed type of physical activity, such as football.

Key words: ACE, ACTN3, elite female football players, gene polymorphisms, cardiovascular adaptation

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INTRODUCTION

Elite sport performance is a complex trait, composed of many different components: from morpho-physiological, biochemical to psychological. All of these components are the results of the complex interplay between different extrinsic factors (e.g., quality and quantity of training), and a plethora of genes (DI CAGNO *et al*., 2013). Despite genetics of sports was in the scientific focus for many years now, it is still not clear enough which of genetic markers contributes the most to the elite sport performance (AHMETOV *et al*., 2010). In support to this fact, there is a considerable number of studies that have emphasized associations of specific genetic polymorphisms with elite athletic performance (DI CAGNO *et al*., 2013; AHMETOV *et al*., 2010; MA *et al*., 2013). The concept of association between genetic traits and elite sport performance is even more important bearing in mind the fact that the heritability of athlete status was estimated at approximately 66% (DE MOOR *et al*., 2007).

Talent identification nowadays has become a scientific endeavor. However, predictors of performance in various sports are not easily scientifically determined (EGOROVA *et al*., 2014).

Unlike most other group sports where weaknesses in certain areas of physical performance can often be compensated by strengths in others, football is far different. Namely, football players not only have significant individual differences in anthropometric and physiological characteristics, but also they may not need to have an extraordinary capacity within any of the fields of physical performance, but must possess a reasonably high level within all areas. Because of previously mentioned fact, genotyping for performance-associated DNA polymorphisms at an early age, before the development of anthropometric and physiological characteristics, could be useful in predicting later success in elite sport performance (REILLY *et al.*, 2000).

The angiotensin I-converting enzyme (*ACE*) and alpha-actinin-3 (*ACTN3*) genes are of particular interest as candidate genes for elite performance phenotypes (MA *et al*., 2013; AHMETOV *et al*., 2011). *ACE* is important component of the renin-angiotensin-aldosterone system. It's main role is to generate angiotensin II, the vasoconstrictor hormone, and also to degrade the vasodilator kinins. Insertion of a 287 bp fragment in exon 16 of the *ACE* gene is associated with lower *ACE* activity, both in tissues and in circulation. Many studies have shown that the *ACE* insertion polymorphism is associated with better endurance performance in elite athletes (MA *et al*., 2013; SABER-AYAD *et al*., 2014; GUNEL *et al*., 2014). *ACTN3* gene, codes for α-actinin-3 protein, belonging to the superfamily of actin-binding proteins, expressed almost exclusively in type 2 fast twitch muscle fibers (VINCENT *et al*., 2007) and responsible for rapid and strong muscle contractions, mainly in sprint and power activities (CLARKSON *et al*., 2005). ACTN3 gene is also expressed in the pulmonary artery smooth muscle suggesting the possible role of this protein in the function of the cardiovascular system (DESCHAMPS *et al*., 2015). Very common genetic variation in the *ACTN3* gene leads to arginine (R) replacement with a stop codon (X) at amino acid position 577 (R577X, rs 1815739). Although it is well known that *ACTN3* variation, which leads to α-actinin-3 protein deficiency, does not lead to muscular functional impairment, there is a number of studies confirming positive association between high power muscle contractions and the presence of the R allele (VINCENT *et al*., 2007; CLARKSON *et al.*, 2005; ROTH *et al*., 2008). Additionally, it is also documented that the presence of 577X allele may contribute to better endurance performance (VINCENT *et al*., 2007; ROTH *et al*., 2008).

Recent studies pointed to significant dissimilarities in the effect of *ACE* and *ACTN3* polymorphisms on athletic performance in different sexes. Namely, some studies demonstrated a significantly greater increase in strength in female athletes with *ACTN3* 577R577X allele compared with male athletes (CLARKSON *et al*., 2005). Moreover, although there are a number of studies concerning sex difference explanations in relation to different gene polymorphisms in elite female athletes, by the best of authors' knowledge to date there are no studies attempting to establish the impact of multiple genotype combinations on cardiovascular adaptation in female football players?

In order to address this issue, in this study of Serbian young female football players we focused on gene variants involved in the regulation of circulatory homeostasis and muscle contraction (*ACE* and *ACTN3*). Therefore, the aim of this study was to investigate the distribution of *ACE* and *ACTN3* gene polymorphisms in young female footballers, as well as to test individually and in combination the association of common gene polymorphisms with body composition, arterial blood pressure and ECG screening variables.

MATERIALS AND METHODS

Subjects

With the use of a cross-sectional design method, in order to determine the allele and genotype frequencies, this study included 45 female football players (17.8±1.2 age) and 60 sedentary female controls (control group, CG) (35.2±7.9 age), living in Serbia. Controls were admitted on the criterion of not being connected with any particular sport and not having a regular exercise program, as well as being free from any kind of chronic diseases.

Athletes involved in this study were subject to the following inclusion criteria: 1) international level 2) 15 or more hours of training per week, 3) non-smokers, and none of them was taking any medication at the time of testing and 4) absence of any disease. All participants were informed about the investigation before giving written informed consent to participate. All procedures were approved by the ethics committee the University of Belgrade School of Medicine, and were conducted in accordance with the declaration of Helsinki for human studies of the World Medical Association.

According to the *ACE* I/D polymorphism, tested subjects were classified as: *ACE* DD, *ACE* DI, *ACE* II genotypes, and according to the *ACTN3* R577X polymorphism as: *ACTN3* RR, *ACTN3* RX *ACTN3* XX genotypes.

Anthropometric data

Before testing all athletes were asked to take a light dinner (before 8 pm) on the day before; not to eat food or drink caffeine beverages on the test-day. The body weight (BW) and body fat percentage (BF%) were measured on a scale with 0.01 kg readability (InBody 370, InBody, Seoul, Korea), with participants wearing minimal clothes and being barefoot.

The body height (BH) was measured with a stadiometer with 0.1 cm readability (Seca 214 Portable Stadiometer, Cardinal Health, USA) according to the described standardized procedures (15). The body mass index (BMI) was calculated as the ratio of the body mass (kilograms) divided by body height (meters) squared.

Blood pressure measurement

Resting blood pressures (BPr) were measured at each annual pre-participation physical evaluation, at the same time as complete pre-participation screening. After giving 15 minutes of rest in sitting posture, brachial systolic (SBP) and diastolic blood pressure (DBP) were measured using a mercury sphygmomanometer with an appropriately sized cuff. Three consecutive BP recordings at 5 minutes intervals were taken and the average of these values was included for the present study. Gender-specific percentile values were calculated for both SBP and DBP.

Electrocardiographic parameters

We compared several electrocardiographic parameters on the 12-lead ECG (Schiller Cardiovit AT101, Schiller, Baar, Switzerland). To screen for pre-excitation syndrome and bundle branch blocks, we measured the QRS durations. For the screening of long QT and short QT syndrome, the corrected QT intervals were checked. For left ventricular hypertrophy (LVH), Sokolow–Lyon criteria was used: S wave in lead V1 + R wave in lead V6 >3.5 mV (15). The electrocardiographic parameters were measured in a blinded manner using serial numbers.

DNA extraction and genotyping

Using sterile swabs, buccal cells samples were collected from all the tested subjects, upon obtaining their written consent, in accordance with the principles of World Medical Association's Declaration of Helsinki. Genomic DNAs from buccal samples were extracted manually, using the commercial kit (PureLink genomic DNA, Invitrogen). Concentration and purity of DNA samples were assessed spectrophotometrically. All DNA samples were normalized to 1 ng of DNA per 1 microliter. Regions of *ACNT3* and *ACE* genes containing studied polymorphisms (rs1815739 and rs1799752, respectively) were amplified by PCR, using 1 nanogram of DNA sample, previously published flanking primers (CIESZCZYK *et al*., 2010) at a final concentration of 0.3 μM, and MeltDoctor™ HRM Master Mix (Thermo Fisher Scientific) in a total volume of 20 microliters. PCR amplification and melting of the PCR products were performed in ViA 7 machine (Applied Biosystems), running QuantStudio Real Time PCR software, ver. 3.2 (Applied Biosystems). After 40 cycles of amplification (10 seconds of denaturation at 95°C and 30 seconds of annealing/extension at 55°C), PCR products were denatured at 95°C for 10 seconds, annealed for 1 minute at 55°C, and then melted by increasing the temperature from 55 to 95°C, at a rate of 0.02°C/sec. Drop in fluorescence of the dye detached from the melted DNA was continuously monitored. Melting profiles were assessed using HRM Software Module for ViiA™ 7 System (Applied Biosystems™), able to call variants based on the differences in the shape of the melt curves and the differences in the Tm values of amplicons. Accuracy of the variant calls obtained by HRM analysis was checked by comparing the results to those obtained for a subset of samples (AHMETOV *et al*., 2011) genotyped by conventional methods (gel electrophoresis for I/D polymorphism in ACE gene, or RFLP analysis for R577X mutation in *ACTN3* gene). Perfect concordance between genotyping results obtained using different methods proved 100% specificity of this, in house developed, HRM method for accurate genotyping of these polymorphisms.

Statistical analyses

Statistical analysis was performed using SPSS software version 15.0 (SPSS, Inc., Chicago, Illinois). Continuous data are expressed as mean ± SD. Categorical data are expressed as frequencies. One-way analysis of variance (ANOVA) with multiple Bonferroni *post hoc* tests and The Kruskal-Wallis H test was used to access differences between groups. For these analyses, additive models for the allele D in the *ACE* gene and allele R in the *ACTN3* gene were assumed (19). Statistical significance was set for a 2-tailed p value <0.05.

RESULTS

Young female football players recruited from the Serbian National Youth Football Team were selected from football players who were used to participating in irregular football playing for 3–4.5 h/week for minimally 5 years prior to joining the Serbian National Team. After their recruitment, they were under a regular training program including both endurance and strength components for about 15 h/week (3 h static exercises + 12 h dynamic training/week).

Genotype distributions of two gene polymorphisms in the experimental and control group were in Hardy–Weinberg equilibrium. The *ACE* I/D and *ACTN3* R577X genotype frequencies in a simple of female athletes and control group are shown in Table 1 and 2. There are no statistically significant differences between the two groups in *ACE* I/D and *ACTN3* R577X genotype frequencies (X^2=0.45, 2.539, respectively).

Table 1. Allele frequencies and genotype distribution of ACE genotype in young female football players and control group

	Genotype			Allele frequency		
	DD (n, %)	ID (n, %)	II (n, %)	I allele	D allele	p
Female football players (n=45)	19 (42)	18 (40)	8 (18)	34 (38)	56 (62)	ns
Control group (n=60)	25 (41)	22 (36)	13 (23)	48 (40)	72 (60)	ns

Values are presented as number (frequency). *ACE*, angiotensin I-converting enzyme; ns, not significant

Table 2. Allele frequencies and genotype distribution of ACTN3 genotype in young female football players and control group

	Genotype			Allele frequency		
	RR (n, %)	RX (n, %)	XX (n, %)	R allele	X allele	p
Female football players (n=45)	9 (20)	26 (58)	10 (22)	44 (49)	46 (51)	ns
Control group (n=60)	13 (21)	26 (43)	21 (34)	52 (43)	68 (57)	ns

Values are presented as number (frequency). *ACTN3*,α-actinin 3; ns, not significant

Table 3 and 4 represent anthropometric and resting cardiovascular parameters of the experimental group according to *ACE* and *ACTN3* polymorphisms. There was no difference in body height (p = 0.20), body weight (p = 0.66), body mass index (p = 0.85), resting heart rate (p=0.20), SBP (p = 0.60) and DBP (p = 0.32) between examined groups.

Table 3. Influence of ACE I/D genotypes on clinical characteristics of the young female football players

Variables	*ACE* DD (n=19)	*ACE* ID (n=18)	*ACE* II (n=8)	p
Age (yrs)	17.95±1.13	17.67±1.24	17.75±1.49	ns
Years of training (yrs)	7.4±2,69	8.35±2.55	7.38±2.07	ns
Height (cm)	168.75±6.41	166.01±7.3	162.71±3.49	ns
Weight (kg)	59.69±7.45	59.62±5.85	55.57±2.57	ns
BMI (kg/m^2)	20.91±1.85	21.61±1.65	20.97±1.28	ns
BMI percentiles (%)	45.71±23.07	53.74±18.11	46.60±17.45	ns
HR (bpm)	66.87±11.97	65.06±10.99	66±12.65	ns
SBP (mm Hg)	100.67±8.83	99.41±8.45	100.63±9.03	ns
DBP (mm Hg)	61.33±7.19	59.41±5.27	63.75±6.41	ns
SBP percentiles (%)	21.05±19.27	17.22±18.47	17.54±16.74	ns
DBP percentiles (%)	33.73±20.32	27.78±17.25	38.66±12.15	ns
HR (bpm)	66.87±11.97	65.06±10.99	66.00±12.65	ns
PR interval (s)	0.14±0.02	0.17±0.11	0.14±0.02	ns
QRS complex width (s)	0.08±0.005	0.08±0.01	0.08±0.01	ns
QTc (ms)	0.41±0.02	0.41±0.03	0.40±0.01	ns
Sokolow-Lyon voltage for LV hypertrophy (mm)	24.20±5.07	21.06±7.49	22.13±5.46	ns

Abbreviation: BMI = body mass index, HR = heart rate, bpm = beats per minute, SBP = systolic blood pressure, DBP = diastolic blood pressure, QRS: ECG wave representing ventricular depolarization; QTc: QT interval corrected to the heart rate, LV, left ventriculum, Sokolow-Lyon = SV1+ RV5 or V6. * Weekly training includes 12 h of dynamic and 3 h of static training, ns, not significant

Also, there was no difference in PR interval (p=0.43 and 0.81, respectively), QRS complex (p=0.39 and 0.17, respectively) and QTc interval duration (p=0.49 and 0.2, respectively) between examined *ACE* and *ACTN3* polymorphisms (Table 3, 4). Additionally, only one football player with *ACE* ID and *ACTN3* RR polymorphism reached the Sokolow-Lyon voltage criterion for LV hypertrophy (SV1+ RV5 or V6 ≥ 35 mm).

Generally, although female footballers with *ACE* DD and *ACTN3* XX polymorpisms had higher values of Sokolow-Lyon voltage for LV hypertrophy, it didn't reach statistically significance (p=0.61 and 0.2, respectively).

Table 4. Influence of ACTN3 R/X genotypes on clinical characteristics of the young female football players

Variables	*ACTN3* RR (n=9)	*ACTN3* RX (n=26)	*ACTN3* XX (n=10)	p
Age (yrs)	18.11±1.17	17.73±1.34	17.7±0.95	ns
Years of training (yrs)	8±2,94	7.74±2.16	7.8±3,15	ns
Height (cm)	166.94±6.72	167.65±6.63	162.13±5.46	ns
Weight (kg)	59.59±6.49	59.69±6.31	55.54±5.15	ns
BMI (kg/m^2)	21.36±1.81	21.18±1.52	21.17±2.22	ns
BMI percentiles (%)	44.88±25.75	49.71±18.95	49.67±22.14	ns
HR (bpm)	65.30±7.76	67.61±13.73	61.29±5.44	ns
SBP (mm Hg)	102.00±8.88	100.00±8.66	97.86±8.01	ns
DBP (mm Hg)	60.71±6.07	60±5.44	63.5±8.18	ns
SBP percentiles (%)	18.88±19.98	17.36±19.53	20.75±18.72	ns
DBP percentiles (%)	38.35±21.48	27.80±12.72	36.42±25.17	ns
HR (bpm)	65.3±7.76	67.61±13.73	61.29±5.44	ns
PR interval (s)	0.15±0.02	0.16±0.09	0.14±0.02	ns
QRS complex width (s)	0.08±0.005	0.08±0.001	0.08±0.01	ns
QTc (ms)	0.39±0.01	0.41±0.02	0.41±0.03	ns
Sokolow-Lyon voltage for LV hypertrophy (mm)	21.14±8.78	21.78±5.92	24.90±5.06	ns

Abbreviation: BMI = body mass index, HR = heart rate, bpm = beats per minute, SBP = systolic blood pressure, DBP = diastolic blood pressure, QRS: ECG wave representing ventricular depolarization; QTc: QT interval corrected to the heart rate, LV, left ventriculum, Sokolow-Lyon = SV1+ RV5 or V6. * Weekly training includes 12 h of dynamic and 3 h of static training, ns, not significant

DISCUSSION

It is well known that the renin-angiotensin-aldosterone system plays an important role in response to physical training (CIESZCZYK *et al.*, 2010). Although its role in the heart function has been established, many previous investigations showed varied and sometimes paradoxical results regarding the effect of I/D gene polymorphism in cardiovascular adaptation to physical training.

According to the literature data, *ACE* D allele is associated with superior sprint and other anaerobic performances in elite athletes (DI CAGNO *et al.*, 2013; GUNEL *et al.*, 2014). Conversely, the disruption of the ACE gene with 279bp insertion is associated with lower *ACE* activity, which results in improved aerobic capacity during exercise (HRUSKOVICOVA *et al.*, 2006). Additionally, *ACTN3* R577X polymorphism is shown to be associated with power-oriented sport disciplines (HOGARTH *et al.*, 2016) in a way that functional protein, predominantly expressed in fast twitch muscle fibers, is required for high intensity short term muscle contractions.

The results of the present study indicate that the distributions of *ACE* and *ACTN3* genotypes were similar in two examined groups. Genotype DD of *ACE* gene was the most common in both groups (42% in footballers and 41% in controls), followed by ID genotype (40% and 36%) and II, which showed the least frequency (18% and 23%). For *ACTN3* genotype frequency, results were similar and also without any significant differences between examined groups. RX genotype was the most common, both in footballers and control group (58% and 43%), followed by XX genotype (22% and 34%) and RR, which showed the least frequency (20% and 21%). These results are in accordance with literature data which pointed that alpha-actinin 3 deficiency is not consistently favorable in endurance athletes population. Namely, Gomez-Gallego and associates have indicated that RR/RX elite cyclists showed not only higher ventilatory treshold, but also higher peak power, which all are advantageous for endurance sports, compared to XX mates (GOMEZ-GALLEGO *et al*., 2009). Additionally, the study on Russian elite rowers showed that the R577 allele is not only over-represented in this population, but also well-appointed for competition results (AHMETOV *et al*., 2010). Namely, the perseverance of R allele in elite endurance athletes probably indicate the physiological requirement of endurance sports wherein in some situations powerful muscle contractions are progressively crucial.

Our results are in accordance with previous studies made in Egyptian population (22). On the other hand, in contrast to our results, there is a number of studies suggesting an association between particular *ACE* and *ACTN3* gene variants and endurance or power characteristics in different sport disciplines (WOODS *et al*., 2003; TANRIVERDI *et al*., 2005; AHMETOV *et al*., 2010). These data disagreements could be explained by the fact that both strength and power are important phenotypic traits in football and that this sport discipline is not a pure-endurance or pure-power sport as is endurance running or weight lifting in which running economy or power lifting is a phenotype trait favored by the *ACE* II or *ACTN3* RR genotype, as a key performance determinant.

Additionally, although DD genotype is associated with higher potential for muscle hypertrophy compared with the II genotype, II combination might confer improved cardiovascular function, and thus could be favorable for endurance sports, such as running. On the other hand, the II genotype could be detrimental to other more power-oriented sports (HOGAN, 2009).

Although our study also investigated association between the *ACE* and *ACTN3* polymorphisms and some body composition determinants and the most important ECG parameters, our results did not reach statistical significance. Cardiovascular adaptation to intensive physical activity in our group of adolescent female elite football players is manifested as lowered resting systolic and diastolic blood pressure (lower 18 and 11 percentiles, respectively). These parameters of cardiovascular system adaptations to physical activity in two football players with the „extreme endurance“ genotype combination (*ACE* II-*ACTN3* XX) were even slightly lower (in 1 percentile for SBP) compared to age and height matched sedentary peers.

Our genotyping results suggest that, if present, the influence of the examined genetic variants on the cardiovascular adaptation is not of a large magnitude. It remains to be determined not only if parameters of cardiovascular system adaptation remain regardless of whether these

footballers continued to engage in intense physical activity, but also whether these adaptive changes are under influence of examined genetic variants.

Also, the specific differences in cardiovascular adaptation to intensive exercise is not only genotype-specific, but also could be explained by different adaptive functional sympatholytic pattern according to the sport type (HEARON *et al.,* 2016). Namely, scientific results point on the continuum of vascular response that varies directly with the intensity of the muscle activity (MAYET *et al*., 1996). Additionally, we should not forget the potential extra-sarcomeric role of alfa-actinin 3. Namely, its expression is also observed although at a lower level, in pulmonary artery smooth muscle cells, indicating its potential role in the maintenance of vascular tone (DESCHAMPS *et al*., 2015).

Our results are in accordance with previously reported study conducted by Mayet et al., who investigated ECG differences between endurance athletes, football players and controls. They pointed on the fact that although some body composition and ECG parameters such are QTd might be increased, the results sometimes do not reach statistical significance (MAYET *et al*., 1996; ZDRAVKOVIC *et al*., 2010; ZDRAVKOVIC *et al*., 2017). Our results are expected not only because of the limited number of study subjects, but also because our study involved unique group of adolescent, still young female athletes, especially because of the fact that the pediatric ECG interpretation is heavily dependent on age. Also, increased left ventricular wall thickness is not common in female adolescent period and consequently ECG-related changes are less likely to be expected (ZDRAVKOVIC *et al*., 2010; ZDRAVKOVIC *et al*., 2017).

Also, one more very important fact is that, although *ACE* I/D and *ACTN3* R/X polymorphisms have shown to be altered in frequency in elite athletes compared to controls, in our study there is no evidence for cumulative performance benefits (ZDRAVKOVIC *et al*., 2010; SANTIAGO *et al*., 2010). Our results support the theory that elite sport performance is a polygenic trait, molded by multiple genes working together, with a relatively minor contribution of each examined polymorphism to the unique athletic phenotype. Ongoing scientific efforts are aimed to the discovery of novel genetic markers, which, through epistatic interaction with ACE and ACTN3, might better explain the actual effect of these genes. Additionally other single nucleotide polymorphisms (SNP) in these genes are found to be associated with its final protein products (GRENDA *et al*., 2014).

Moreover, when arguing about the idea that genetic factors are the main determinants of elite sport performance, there are several very important facts. First, elite sport performance is a result of a artificial selection process, that includes strict and continuous training process in a extremely small fraction of the population. Secondly, the fact that someone have the most „unfavorable“ genotype combination does not necessarily limit elite sport performance, because a large portion of the variance in sport performance can be explained by gene-environment interaction.

The importance of our study lies in its pioneering attempt to link specific genes variations with early talent identification in female football. Also, it could be important not only for coaches who can specifically adapt trainings for athlete according to specific genetic constitution, but also for physicians who are taking care of athletes' health.

Follow-up of our study population may throw light on the significance and explanation of the study results.

CONCLUSIONS

It is clear that although elite athletic performance is polygenic, with the combined effect of hundreds of genetic factors, interacting between themselves and with sport and training regime, many other factors such as technique, kinematics or motivation, among others, remain to be identified. Interpretation of the effect of specific genes with a presumed large effect on sport performance (e.g., *ACE* and *ACTN3*), should be cautious, especially in team sports with a mixed type of physical activity, such as football.

Study limitations

A possible limitation of the study is the relatively small sample size of the studied group of athletes, which on the other hand might be understandable keeping in mind their unique competition level. Many previous studies suggested that different gender and ethnicity could explain heterogeneity between studies. Also, our results concerning association between specific *ACE* and *ACTN3* genotypes and cardiovascular response to intensive physical activity, could be explained by the fact that physiological adaptation to high intensity sport is multi-functional, and therefore could not be accurately predicted by the variations in only two genes.

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UTICAJ POLIMORFIZAMA *ACE* I *ACTN3* GENA NA ADAPTACIJU KARDIOVASKULARNOG SISTEMA KOD FUDBALERKI

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Izvod

Cilj ove studije je bio da se utvrdi distribucija polimorfizama ACE i ACTN3 gena kod fudbalerki adolescentskog doba, kao i da se testira njihova povezanost sa parametrima telesne kompozicije, arterijskog krvnog pritiska i EKG parametara. U studiju je uključeno 45 zdravih vrhunskih fudbalerki, bele rase (FG) i 60 fizički neaktivnih ispitanica (CG). HRM metod je korišćen u cilju detekcije varijanti polimorfizama ACE i ACTN3 gena. Nije pokazana statistički zanačajna razlika u učestalosti genotipova ispitivanih ACE i ACTN3 genotipova, kao ni u distribuciji frekvencija alela među ispitivanim grupama ($p>0.05$). Takođe, niti insercija niti nonsense mutacija ACTN3 gena nisu imale značajan efekat na vrednosti arterijskog krvnog pritiska umiru, kao i na ispitivane EKG parametre. Adaptacija kardiovaskularnog sistema na intenzivnu i kontinuiranu fizičku aktivnost u FG se manifestovala nižim vrednostima sistolnog i dijastolnog arterijskog krvnog pritiska u miru (vrednosti niže od 18, odnosno 11. percentila, respektivno). Fudbalerke sa *ACE DD* i *ACTN3 XX* polimorfizmom su imale više vrednosti Sokolow-Lyon voltažnog kritertijuma za hipertrofiju leve komore, ali bez statističke anačajnosti uočene razlike ($p=0.61$ and 0.2, respektivno). Tumačenje efekta specifičnih genskih polimorfizama na sportske performance treba uvek raditi uz maksimalan oprez, pogotovo u slučaju kada se radi o timskim sportovima koji podrazumevaju mešoviti tip fizičke aktivnosti, kao što je slučaj u fudbalu.

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