Genetic variants determining of the cardiovascular and skeletal muscle adaptation to exercise in Lithuanian elite athletes

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Introduction. Among the individual components of cardiovascular (renin-angiotensin) system, the genes encoding angiotensinogen (AGT) gene, angiotensin-II receptor type I (AGTR1 gene), angiotensin-II receptor type II (AGTR2 gene) and nitric oxide synthase 3 (encoded by NOS3 gene) together with environmental factors play important role in cardiovascular and skeletal muscle adaptation to exercise (Ahmetov, Fedotovskaya, 2015; Barh, Ahmetov, 2019; Hellsten, Nyberg, 2016; Yvert et al., 2018; Zmijewski et al., 2018). The aim of this case-control and genotype-phenotype associations study was to investigate the polymorphisms of AGT Thr207Met (rs4762), AGTR1 A1166C (rs5186), AGTR2*501A>C (rs11091046) and NOS3-786T>C (rs2070744) in Lithuanian elite athletes.

Methods. A total of 205 elite athletes (endurance (n = 85), sprint/power (n = 56) and mixed (n = 64) groups) and 265 healthy untrained Lithuanian citizens (controls) were genotyped for AGT(T>C), AGTR1 (A>C) and AGTR2 (A>C) variants by restriction fragment length polymorphism methods. For NOS3 (T>C) athletes and controls were genotyped by real-time polymerase chain reaction method. Anthropometric measurements and muscle strength (grip strength, short-term explosive muscle power (STEMP), anaerobic alactic muscle power (AAMP)), and maximum oxygen uptake (VO2max) were measured. Statistical analysis was performed using Rv3.2.

Results. The phenotypic measurements were different and specific to each sports groups (p < 0.05). Our study results support the evidence that there is a differences between genders in sports, since males athletes had on average better anaerobic power and aerobic capacity indices than female athletes. Case-control association analysis results showed that significant differences in AGT genotypes distribution were observed between mixed athletes and controls (CC/CT/TT: 48.4/50/1.6% vs 64.5/32.1/3.4%, p=0.025). The AGT gene T allele was higher in sprint/power-oriented (26%) and mixed athletes (26.6%) compared to endurance-oriented (19%) and controls (19%). The AGT CC genotyped endurance-oriented athletes had significantly higher VO2max than CC genotyped sprint/power athletes (p = 0.00004). Regarding the AGTR1 variant, genotypes distribution significantly differed between sprint/power-oriented athletes group and controls (AA/AC/CC: 32.1/55.4/12.5% vs 54/35/11%; p = 0.008). The AGTR1 C allele frequency is more prevalent in sprint/power athletes (55.4%) compared with endurance (39%), mixed (28%) and controls (25%) (p < 0.05). The findings indicated that the AGTR1 heterozygous AC genotype is more prevalent in sprint/power athletes (55.4%) compared with endurance (39%), mixed (28%) and controls (35%). AGTR1 AC genotyped athletes had significantly higher STEMP than AA genotyped athletes (p = 0.036). The other gene considered in this study was the AGTR2 and its polymorphism. The AGTR2 genotypes distribution significant differed between women endurance athletes and women controls (CC/CA/AA: 67.9/17.9/14.2% vs 38.6/45.5/15.9%; p = 0.035). The AGTR2 C allele is more prevalent in women endurance athletes (76.8%) compared to sprint/power-oriented athletes (50%) and controls (61.4%) (p = 0.028). Regarding the NOS3 variant, genotypes distribution significant differed between sprint/power-oriented athletes group and controls (TT/TC/CC: 55.4/44.6/0% vs 43.3/47.1/9.6%; p = 0.006).

Conclusions. Our findings provide support for an association of AGT(rs4762), AGTR1 (rs5186), AGTR2(rs11091046) and NOS3 (rs2070744) genetic variants with athletic status in Lithuanian athletes: the AGT T allele, AGTR1 C and NOS3 T alleles are associated with sprint and power ability while AGTR2 C allele are associated with women endurance ability. AGTR1C allele (AC and CC genotype) confers ability to achieve better muscle efficiency in short-term, maximum-effort requiring physical activity and AGT CC genotyped athletes have better aerobic capacity. Many beneficial
applications of genetic testing in sport practice will emerge upon full understanding of genetic variants in cardiovascular adaptation on exercise. **Keywords:** cardiovascular adaptation, genetic variants, phenotypic measurements.

REFERENCES