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GENETIC PRE-PARTICIPATION SCREENING IN SELECTED ATHLETES: A NEW TOOL FOR THE PREVENTION OF SUDDEN CARDIAC DEATH?

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Background: Sudden cardiac death (SCD) of athletes is a topical issue. "Borderline cardiac abnormalities", which occur in ~2% of elite male athletes, may result in SCD, which may have a genetic base. Genetic analysis may help identify pathological cardiac abnormalities. We performed phenotype-guided genetic analysis in athletes who, pre-participation, showed ECG and/or echo "borderline" abnormalities, to discriminate subjects at a greater risk of SCD.

Methods: We studied 24 elite athletes referred by the National Federation of Olympic sports; and 25 subjects seeking eligibility to practice agonistic sport referred by the Osservatorio Epidemiologico della Medicina dello Sport della Regione Campania. Inclusion criteria: a) ECG repolarization borderline abnormalities; b) benign ventricular arrhythmias; c) left ventricular wall thickness in the grey zone of physiology versus pathology (max wall thickness 12-15 mm in females; 13-16 mm in males). Based on the suspected phenotype, we screened subjects for the LMNA gene, for 8 sarcomeric genes, 5 desmosomal genes, and cardiac calcium, sodium and potassium channel disease genes.

Results: Genetic analysis was completed in 37/49 athletes, 22 competitive and 27 non-competitive athletes, showing "borderline" clinical markers suggestive of hypertrophic cardiomyopathy (HCM, n. 24), dilated cardiomyopathy (n. 4), arrhythmogenic right ventricular dysplasia/catecholaminergic polymorphic ventricular tachycardia (ARVD/CPVT, n. 11), long QT syndrome (LQTS, n. 4), sick sinus syndrome (SSS, n. 5), Brugada syndrome (BrS, n. 1). We identified 11 mutations in 9 athletes (an ARVD athlete was compound heterozygote for the PKP2 gene and an HCM athlete was double heterozygote for the MYBPC3 and TNNT2 genes): 3 known mutations related to LQTS, HCM and ARVD, respectively, and 8 novel mutations, located in the SCN5A, RyR2, PKP2, MYBPC3 and ACTC1 genes. The new mutations were absent in ~800 normal chromosomes and were predicted "probably damaging" by in silico analysis. Patch clamp analysis in channelopathies indicated for some mutation abnormal biophysical behavior of the corresponding mutant protein.

Conclusion: Genetic analysis may help distinguish between physiology and pathology in athletes with clinically suspected heart disease.