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MORTE CARDIACA IMPROVVISA

O17 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", known to occur in ~2% of elite male athletes, may result in SCD, which in turn may be genetically based; thus, genetic analysis may help to identify potentially pathological cardiac abnormalities. Aim: We performed phenotype-guided genetic analysis in athletes who, pre-participation, showed ECG and/or cardiac echo "borderline" abnormalities, to discriminate subjects at a greater risk of SCD. Subjects and 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 were: a) borderline ECG repolarization abnormalities; b) benign ventricular arrhythmias; c) left ventricular wall thickness in the grey zone of physiology versus pathology (maximum wall thickness 12-15 mm in females; 13-16 mm in males). Based on the suspected phenotype, we screened subjects for: the LMNA gene, 8 sarcomeric genes, 5 desmosomal genes, and cardiac calcium, sodium and potassium channel disease genes. Results: Genetic analysis was completed in 37 out of 49 athletes, 22 competitive and 27 noncompetitive 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), or Brugada syndrome (BrS, n. 1). We identified 11 mutations in 9 athletes (an ARVD athlete was a compound heterozygote for the PKP2 gene and an HCM athlete was a 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 from ~800 normal chromosomes and were predicted "probably damaging" by in silico analysis. Patch clamp analysis in channelopathies indicated that some mutations were associated with abnormal biophysical behavior of the corresponding mutant protein. Conclusion: Genetic analysis may help distinguish between physiology and pathology in athletes with suspected familial or sporadic heart disease.