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From population ECG screening to molecular diagnosis of channelopathies: preliminary experience in pediatrics.

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Introduction: There is a lack of data regarding efficacy of cardiovascular (CV) screening programs including ECG when applied in young children, for early detection of unrecognized genetic conditions associated with high risk for sudden cardiac death (SCD). We evaluated the performance of a CV screening program, including 12-lead ECG recording, when applied in selected populations of Mediterranean children.

Methods: A CV screening program for primary schools, approved by Minstry of Health, was applied in a sample of primary schools of a Mediterranean island, in geographical isolated areas with reported increased SCD incidence. Participation was voluntary following parental consent. After completion of a standarized history questionnaire by parents, children underwent clinical evaluation and 12-lead ECG recording, at local health stations. A stepwise referral pattern was established, including pediatric cardiology evaluation and molecular DNA confirmatory testing, whenever the possibility of inherited arrhythmogenic CV disease was increased.

Results
220 primary school children, (84 male, 116 female), median age 11,4 (range 7.5-12yrs) have been evaluated during two years (2014-15). 22 children (10%) had an indication for further diagnostic or lifestyle modification for CV risk factors, including ECG abnormalities (n=9), abnormal heart auscultation (n=7) and adiposity/hypetension (n=6). ECG abnormalities included WPW (n=1), VES (n=2), probable LVH (n=2), and QTc prolongation (n=2) both boys, with QTc 475 and QTc 490. Children with ECG abnormalities underwent further evaluation including ambulatory ECG monitoring and regular follow up. Family ECG screening was positive in one child with prolonged QTc (490ms, wide T wave), regarding his father (QTc=460) and one sister (QTc=490). Further molecular DNA testing was negative in the first child, while it revealed a novel KCNH2 heterozygous mutation (NP_000229.1:p.Ser606Tyr) in child and affected family members in the second case. In silico analysis using Polyphen-2 and SIFT suggested that the Ser606Tyr mutation might be harmful, and the family was advised to receive b-blocker prophylactic treatment.

Conclusions: A stepwise approach from ECG population screening to molecular diagnostics can detect and genetically characterize subclinical cases of inherited CV disease, associated with arrhythmogenic SCD also in pediatrics.