50th Annual Meeting of the Association for European Paediatric and Congenital Cardiology
June 1 - 4, 2016

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

Germanakis I. (1) , Bagaki A. (1), Kotsaka X. (2), Anastasakis A.(2)
Pediatric Cardiology Unit, Dpt of Pediatrics, Faculty of Medicine, University of Crete, Greece (1);
Cardiac Code Unit, Athens, Greece (2)

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 Ministry of Education and Health Region authorities, was preliminary applied in a sample of primary schools of a Mediterranean island (Crete) in selected geographical isolated areas with presumably increased SCD incidence. Participation was voluntary, following informed written parental consent at local health stations.

•After completion of a **standardized history questionnaire** by parents, children underwent **clinical evaluation** (dynamic heart auscultation, weight, height and BP measurement) as well as **12-lead ECG** recording. 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 **11,4yrs** (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/ hypertension (n=6). Fig. 1

•**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 (Fig. 2), respectively

•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), including his father (QTc=460) and one sister (QTc=490). Fig. 3

•Further **molecular DNA testing** was negative in the first child, while it revealed a **novel KCNH2 heterozygous mutation** (NP_000229.1:p.Ser606Tyr) in the child and affected family members in the second case. Fig. 4

• In silico analysis using Polyphen-2 and SIFT suggested that the Ser606Tyr mutation might be harmful. The family was advised to receive b-blocker prophylactic treatment.

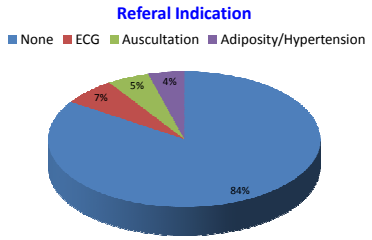

Fig 1. Diagnostic yield of CV screening program

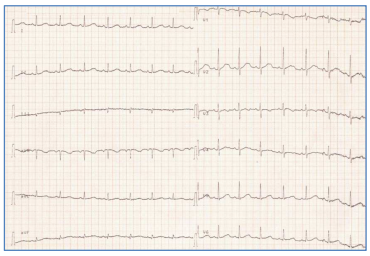

Fig 2. ECG-based school screening: QTc prolongation

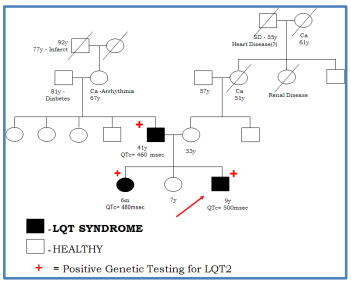

Fig 3. Family ECG screening and LQT2 cases

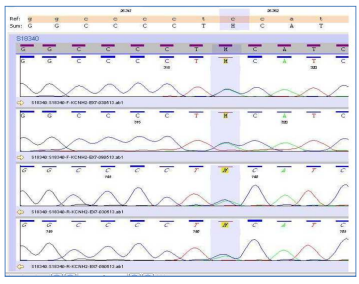

Fig 4. Novel KCNH2 heterozygous mutation

Conclusions

Genetic testing in certain cases **multiplies the value of ECG screening** due to genetic family screening and the identification of normal mutation carriers n the family.

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

Authors declare that there is no conflict of interest
The study has been approved by the Greek Ministry of Education and the 7th Health Region of Crete.