The impact of *cascade screening* in familial hypercholesterolemia diagnosis

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Introduction

Familial hypercholesterolemia (FH) is a genetic disorder of cholesterol metabolism caused by mutations in LDLR, APOB and PCSK9 genes. It's characterized by an increase of total and LDL cholesterol levels leading to premature cardiovascular disease. According to the frequency of the disease in most European countries (1:500 individuals) it is estimated that in Portugal exists about 20.000 cases of FH, but this disease is severe under-diagnosed in our country. *Cascade screening* (CS) is as method for identifying individuals at risk of a genetic condition by a process of family tracing through molecular studies, allowing the rapid identification of new FH cases within a family.

Purpose

The aim of this study is to understand the importance of CS in the identification of FH cases that, otherwise, could fail to be diagnosed.

Methods

The Portuguese FH Study performs the genetic identification of FH patients through the molecular study of *LDLR, APOB* and *PCSK9*. Biochemical characterization of index/relatives includes total cholesterol (TC), direct LDLc, HDLc, ApoAI, ApoB, Lp(a) and sdLDL measurement.

Results

A total of 496 FH individuals have been genetic identified, including 289 relatives through the CS method (Fig. 1). TC, LDLc, sdLDL and ApoAI levels are statistically lower in relatives identified in CS than in index patients in both groups, adult patients (data not shown) and in children (Fig. 2).

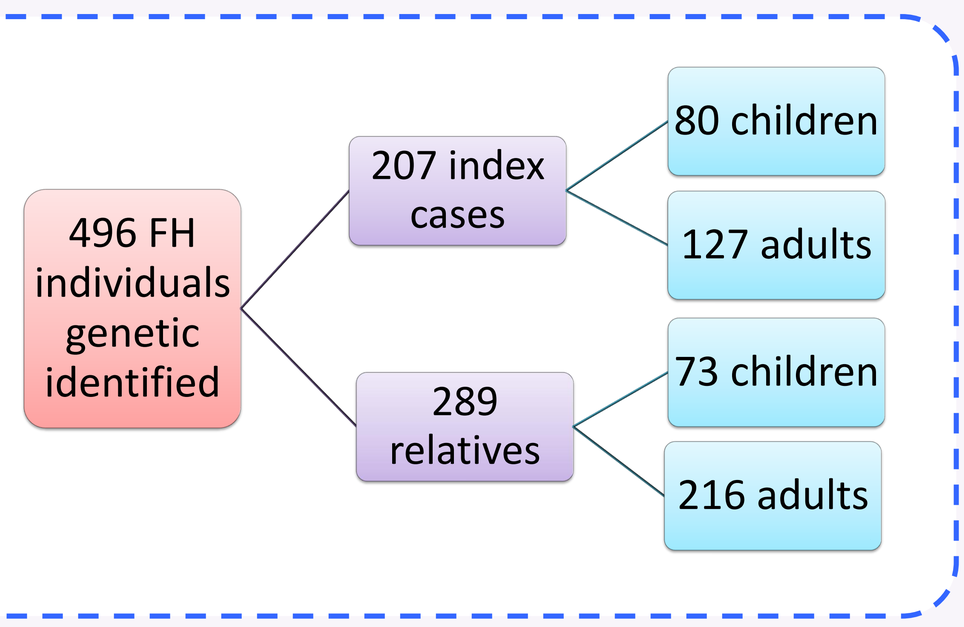

Fig.1. Distributon of genetically identified FH cases

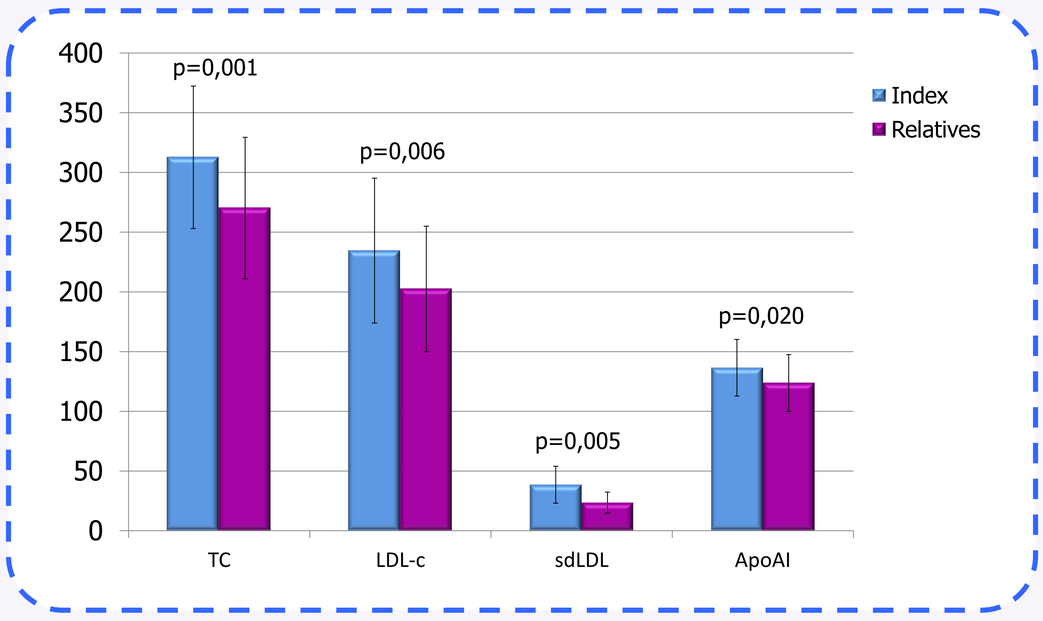

Fig.2. Comparisson of TC, LDL, sdLDL, APOAI values between index and relatives in children group.

Among the 73 children identified in CS 43,1% and 22,8% did not fulfill the criteria for TC and LDLc, respectively, according to Simon Broome criteria. Based on biochemical characterization the clinical identification of these children would be probably missed.

Discussion and Conclusion

These results suggest that Cascade Screening is a cost effective method for the identification of new FH patients, especially children, because their phenotype, most of the times, does not allow clinical identification.
Cascade Screening may also allow premature detection of the disease and the reduction of morbidity and mortality by implementation of adequate counseling and therapeutic measurements in early ages.

Acknowledgements: Alexandra Gomes and Ana Margarida Medeiros were funded by Portuguese Society of Cardiology; Ana Catarina Alves was funded by FCT SFRH / BD / 27990 / 2006; Project grant from Portuguese Society of Cardiology 2006-2009 and 2010-2012