PORTUGUESE FAMILIAL HYPERCHOLESTEROLEMIA STUDY

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on behalf of the investigators of the Portuguese FH Study

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Portuguese FH Study

Introduction

Familial hypercholesterolemia (FH) is an autossomal dominant disorder associated with high levels of plasma cholesterol and premature coronary heart disease (pCHD), with a frequency of 1/500. The major aim of the Portuguese FH Study is to identify the genetic cause of disease in patients with clinical diagnosis of FH so patients can receive counselling and treatment in time to prevent the development of pCHD.

Methods

The clinical criteria used is from the Simon Broome Register, UK (TC>290mg/dl LDLc >190mg/dl, hypercholesterolaemia in all generations and/or pCHD) and the genetic diagnosis was performed by the analysis of 18 fragments of the *LDLR*, 2 of the *APOB* and 5 of the *PCSK9.* These fragments are amplified by PCR and analysed by dHPLC and sequenced. MLPA was also performed to identify potential rearrangements. The biochemical parameters, total cholesterol (TC), LDLc, HDLc, triglycerides, ApoAI and ApoB were determined for all patients by immunoturbidimetric methods and the LDL was measured directly, in automated equipment. All data were analyzed using SPSS software (version 17.0) using ANOVA andTukey. For all tests $p<0.05$ was considered statistically significant.

Results

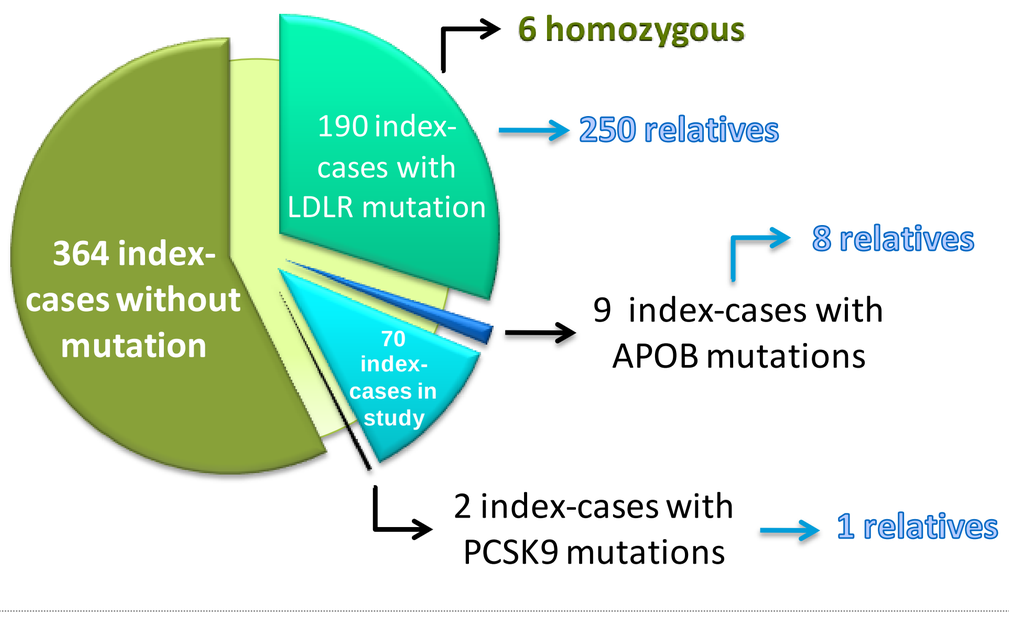

Figure 1. General results form the Portuguese FH Study

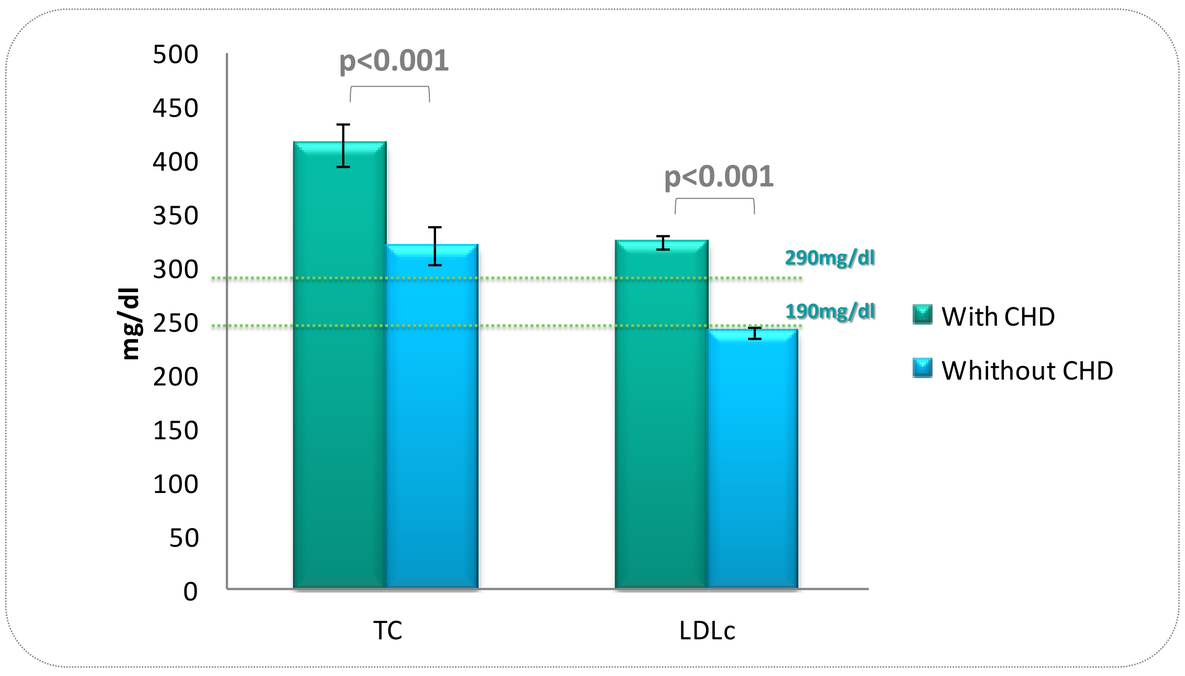

Figure 2. Biochemical parameters (Total cholesterol and LDL cholesterol) in FH patients genetically identified. Comparison of biochemical values in FH patients with pCHD vs. whitout CHD.

- Portuguese FH Study identified a genetic defect in 461 patients: 124 children, 337 adults (index patients) and 58 children, 201 adults (relatives).
- Represent only 2,3% of the FH cases estimated to exist in Portugal.

- Majority of index patients had a genetic defect in LDLR and 23% of the adults had pCHD. From the 259 relatives with FH identified by cascade screening, 14% of the adults had pCHD and 76 individuals in these families died from pCHD.

- FH patients have sdLDL mean values (54.94±7.09mg/dl) statistically higher (p=0.005) than patients with no mutations (sdLDL=35.28±3.07mg/dl). This analysis was performed in a small number of patients (71/565) because most of the patients are in treatment when referenced to the PFHS.

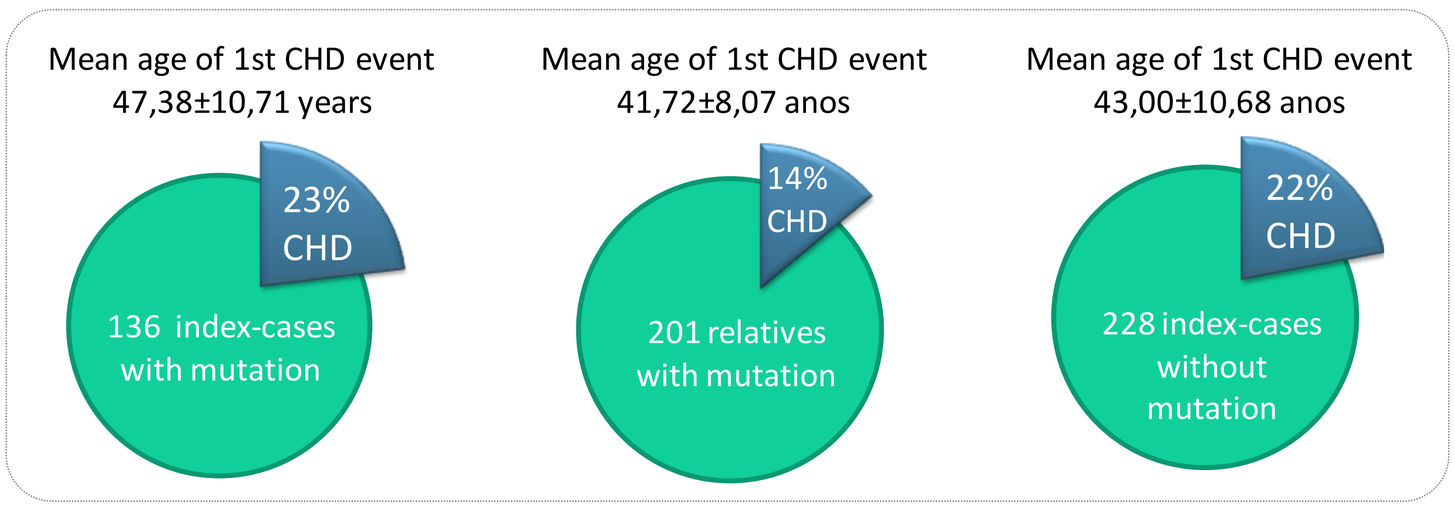

Figure 3. Mean age of 1st CHD event and percentage of CHD in the different groups: index-cases and relatives with mutation, and index-cases with no mutations identified in the FH genes

Conclusion

The genetic diagnosis of FH confirms the clinical diagnosis based on plasma cholesterol levels and provides unequivocal diagnosis and early identification of relatives. The counselling of these patients should result in appropriate treatment and adoption of a healthier lifestyle, in order to reduce their risk of CHD and decrease avoidable deaths.
Patients without a detectable mutation can have different type of mutation in the 3 genes studied but most probably will have a mutation in an undescribed gene, since all exhibit a phenotype of clinical FH. Efforts are being made by our group to discover another genes involved in the lipid metabolism that can cause FH

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