Analysis of Genetic Markers for Cardiovascular Disorders in a Portuguese population with Familial Hypercholesterolaemia

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Estudo Português de Hipercolesterolemia Familiar

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Introduction

Familial Hypercholesterolaemia is a genetic disorder characterized by an increase in TC and LDLC leading to premature atherosclerosis (ATH) and cardiovascular disorders (CVD) but not all FH patients develops premature CVD.

Early identification of FH patients at an even increased risk of developing CVD is important. Genetic markers could improve risk stratification for this patients

Inflammation has been considered to be involved in the pathogenesis of CVD and genetic and oxidative stress markers may also contribute to ATH and CVD outcome.

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Material and Methods

41 FH patients with CVD

91 FH patients without CVD

49 healthy individuals

Biochemical Caracterization

Total Cholesterol	hsPCR
LDL-Cholesterol	Ceruloplasmin
HDL-Cholesterol	Haptoglobin
Triglycerides	Interleukin6
ApolipoproteinA1	Tumor Necrosis Factor-α
ApolipoproteinB	Nitric Oxid
Lipoprotein(a)	oxLDL

Genetic Caracterization

LPL D9N	IL6 -174G/C
LPL N291S	TNFα -308G/A
LPL S447X	MTHFR 677C/T
APOAV -1131T/C	NOS E298D
APOCIII 3238C/G	

Results - I

• Biochemical and genetic results were obtained from 41 FH patients with CVD, 91 without CVD and 49 healthy individuals.

• FH patients with CVD presented increased TC ($p<0,001$) and LDLC ($p=0,001$) and apoB ($p<0,001$) levels and decreased apoA1 ($p=0,021$) levels in relation to the FH group without CVD (Figure 1a);

• In the FH group with CVD it was observed the highest oxLDL (Figure 1b) and the lowest NO (Figure 1c) concentrations when comparing with the group of FH patients without CVD and the control group.

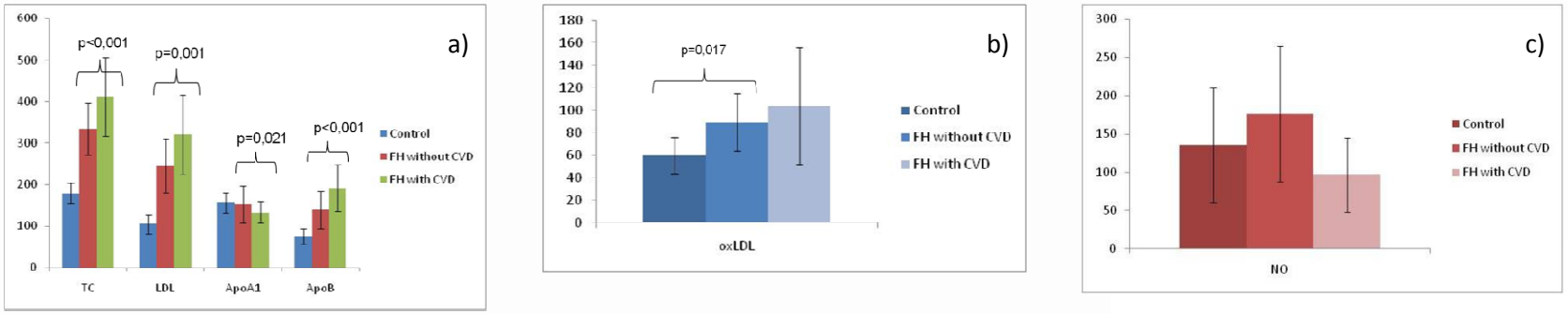

Figure 1 – Comparison between control, FH without CVD and FH with CVD groups of a) TC, LDL, ApoA1 and ApoB levels, b) oxLDL and c) NO concentrations.

Results - II

• APOAV-1131C alelle and APOCIII3238C/G genotype were associated with higher TG levels (p=0,013; p=0,019) in the FH group without CVD. No association was found in the group of FH patients with CVD (Figure 2a, 2b).

• MTHFR677T allele was associated with high TC levels (p=0,006) in the FH group with CVD. No association was found in the group of FH patients without CVD (Figure 2c).

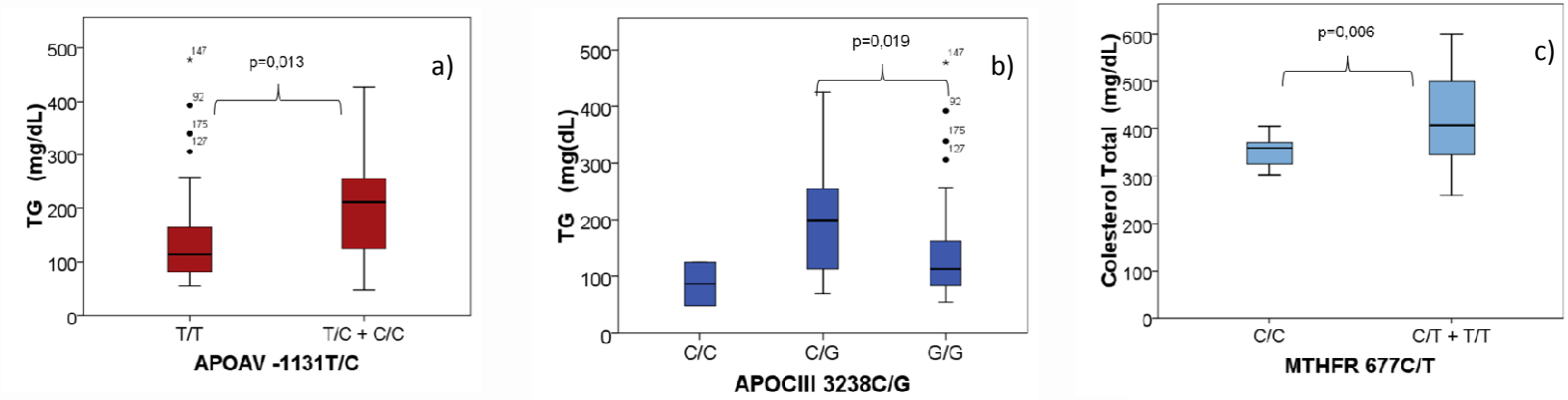

Figure 2 – Comparison of the allelic combination and TG or TC levels for three different polymorphisms a) APOAV -1131T/C in FH without CVD group, b) APOCIII3238C/G in FH without CVD group and c) MTHFR677C/T in FH with CVD group.

Discussion and Conclusions

The results obtained confirmed the envolvement of the lipid metabolism and oxidative stress in CVD

The results obtained from the **markers of lipid metabolism** are consistent with the levels usually found in individuals that present a genetic defect in cholesterol metabolism as FH and with CVD.

oxLDL concentrations are increased in the FH with CVD group and it is known that oxidative modification of LDL is important in the pathophysiology of ATH.

NO is a vasodilator which has been considered to have an atheroprotective function and we observed the lowest concentrations in the group of FH with CVD.

From the genetic analysis we found association between **APOAV-1131T/C and APOCIII3238C/G polymorphisms** and increased TG levels in FH without CVD group. These polymorphisms are usually associated with TG in hypertriglyceridemic patients. Polymorphism **MTHFR677C/T** showed association with elevated TC levels in the FH with CVD group. This polymorphism has been related to elevated ATH and CVD risk.

Although lipid metabolism markers are evident between the groups analyzed, inflammatory and genetic markers need further studies to improve our knowledge of their role in CVD outcome.