Genetic polymorphisms and Coronary Artery Disease in the Portuguese population: the GENEMACOR Study

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INTRODUCTION

Multiple studies have showed an association between genetic polymorphisms and the risk of coronary artery disease (CAD). Initially, studies focused mainly in variants acting in pathophysiological axis of CAD or its risk factors. Genome-Wide Association Studies (GWAS) revealed other genes that, besides having an unknown mechanism, are statistically significant. Both of this complementary approaches could further reveal the genetic basis of CAD. To data, there are no studies in the Portuguese population.

OBJECTIVES

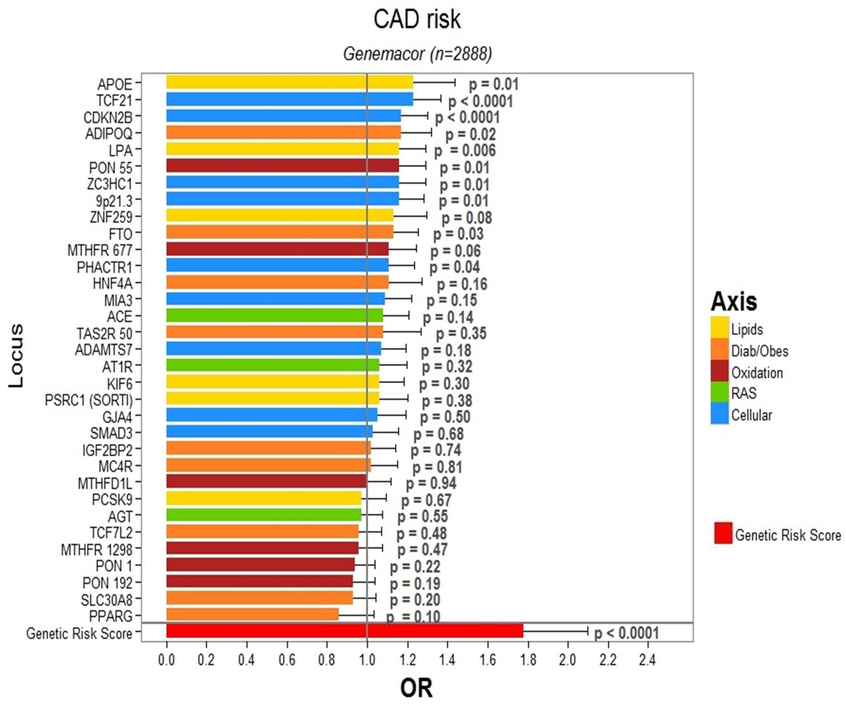
- Investigate the main risk factors and genetic variants associated with CAD risk in our population.
- Assign the genetic variants by the main pathophysiological axis.

METHODS

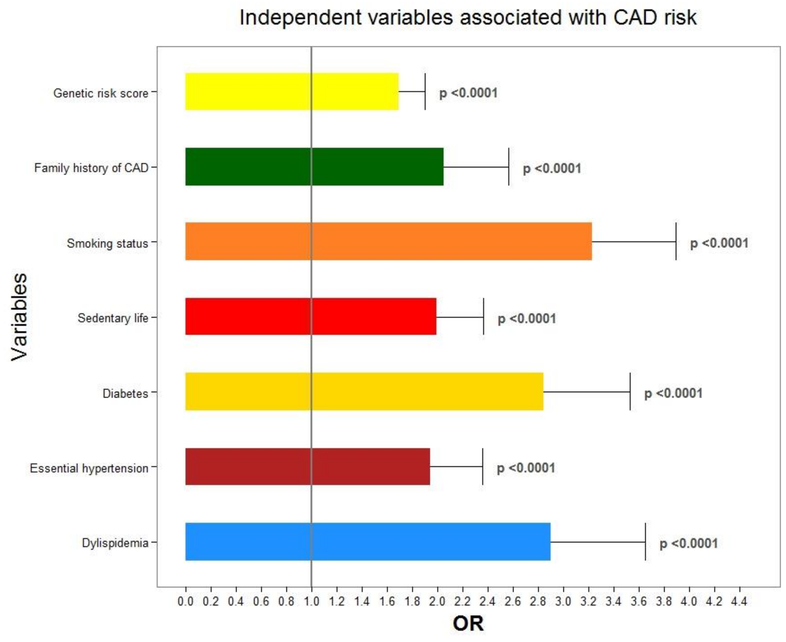
We performed a case-control study with 1566 consecutive coronary patients (mean age 53.3 ± 8.0 years, 79.1% male) and 1322 controls selected from GENEMACOR Study (GENE-MADEIRA-CORONARY DISEASE), a straight-forward registry with a prospective follow-up cohort, designed to investigate the main cardio vascular risk factors of CAD, in this Island. Traditional risk factors (TRF) and biochemical markers were evaluated. Genetic variants associated to CAD were genotyped and deviation from Hardy Weinberg equilibrium were assessed. A weighted genetic risk score (GRS) was determined by the product of the ORs of each of 33 genetic variants. Two multivariate logistic regressions were performed firstly with all variants and secondly with TRF and GRS.

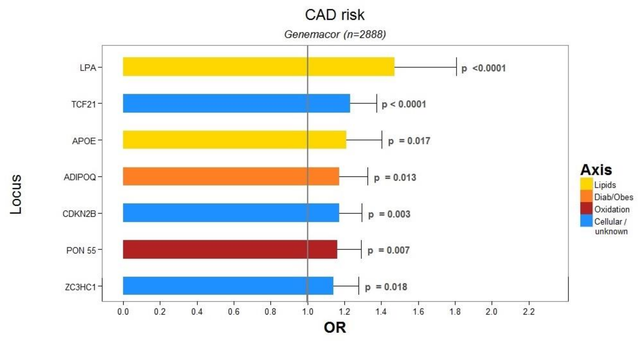
RESULTS

The variants rs3798220 (LPA T/C), rs12190287 (TCF21 G/C), rs429358 (APOE), rs266729 (ADIPOQ C/G), rs4977574 (CDKN2B A/G), rs458560 (PON55 L/M) and rs11556924 (ZC3HC1 T/C) were significantly associated with CAD (p<0.05). GRS was also found to show a significant CAD risk (OR=1.69; p<0.0001).



CAD risk (OR) of the 33 genetic variants and GRS in our population





Genetic variants significantly associated with CAD risk by logistic regression analysis

CONCLUSIONS

In our population, the genetic polymorphisms significantly related to CAD risk were: LPA and APOE associated with lipids metabolism; TCF21 associated with cellular mechanisms; ADIPOQ associated with obesity; CDKN2B and ZC3HC1 with cellular/unknown mechanism and PON55 associated with oxidation. GRS was found to be an independent risk factor for CAD.

"All authors declare no conflits of interest"

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