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EDITORIAL COMMENT

Genetics and myocardial infarction

Genética e enfarte do miocárdio

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Genetic information is being increasingly used as part of individual clinical care, and genomic medicine is having an impact in several medical fields, especially in rare and undiagnosed diseases but also in oncology, pharmacology, and cardiology, among others. The ability to use genomic information to improve health is a direct result of the Human Genome Project (HGP), but translation of new discoveries into use in patient care can take years. Since completion of the HGP the focus has been on understanding how variations in an individual's DNA may affect disease and health, clarifying disease etiologies and prognosis, identifying variants that confer disease susceptibility, and improving the efficacy and safety of pharmacological treatments.

Discoveries in cardiovascular genetics are increasingly moving from bench to bedside and becoming more and more relevant to the clinical management of patients.[1] This field encompasses a wide variety of inherited cardiac conditions, including monogenic diseases such as various channelopathies and cardiomyopathies, and, although still at a very early stage, some disorders with a more complex inheritance pattern.[2]

Myocardial infarction (MI) is a complex multifactorial disorder caused by the interaction of environmental and genetic factors. It is the most severe type of coronary artery disease (CAD) and one of the leading causes of death worldwide. Several risk factors for MI have been identified, particularly hypertension, dyslipidemia, diabetes and smoking.[3] Various studies have also addressed the importance of genetic factors, but despite the progress in cardiovascular genetics, data on the genetic background of MI are still limited and somewhat inconsistent.[4] Clinical and population-based studies have long shown that a positive family history for MI is a major cardiovascular risk factor. However, the heterogeneity of CAD and its clinical complications introduce significant complexity in genetic studies,[5] and the range of genes underlying the heritable component of MI is not fully known. The Coronary ARtery DIsease Genome wide Replication and Meta-analysis plus The Coronary Artery Disease (CARDIoGRAMplusC4D) consortium is an example of a collaborative effort to combine data from multiple large-scale genetic studies to identify risk loci for CAD and MI.[6] Current knowledge of genetic variants affecting risk of CAD is largely based on analysis of common single-nucleotide polymorphisms (SNPs) in genome-wide association studies.[6] Several genetic loci have been associated with CAD and it appears that genetic susceptibility to this common disease is largely determined by common SNPs of small effect size.[6] In the context of CAD and MI, as for other disorders with complex inheritance patterns, it is also important to consider epigenetic mechanisms that regulate the expression of these genes, and interactions between multiple genes and between these genes and environmental factors, as well as isolated genetic risk factors.

Knowledge of the genetic factors associated with the risk of MI is of particular importance for clinical management.

Coronary atherosclerosis underlies the occurrence of MI in the majority of cases, and factors such as plaque vulnerability and the extent of thrombotic reaction to plaque disruption may predispose to MI in the presence of CAD.[6] It is accepted that the rupture of a vulnerable atherosclerotic plaque, local activation of thrombotic mechanisms with or without severe underlying stenosis, local thrombosis formation and arterial lumen closure are the mechanisms most often underlying acute MI.

In the current issue of the *Journal*, Pina-Cabral et al.[7] analyze the potential role of eight polymorphisms in four genes coding for platelet receptors, *GP1BA*, *ITGB3*, *ITGA2* and *P2RY12*, as risk factors for MI. It is known that platelet G protein-coupled receptors are critical regulators of platelet function, and it has been hypothesized that increased platelet activity at the site of atherosclerotic plaque rupture may result in MI.[8]

Pina-Cabral et al.'s study has several limitations that are clearly stated by the authors, including the low numbers of patients and polymorphisms studied and heterogeneity between the control and MI groups, which limit the conclusions of the study. Despite its limitations, the paper assesses these polymorphisms in a Portuguese population and underlines the importance of fully understanding the genetic factors and molecular mechanisms behind the pathogenesis of MI, highlighting the need for further studies addressing genetic risk factors for MI.

Previously, genetic testing was based on conventional techniques like Sanger sequencing, analyzing genes one by one, but recent advances in DNA sequencing technologies have made it possible to investigate large numbers of disease genes simultaneously.[9] These new sequencing methods, known as next-generation sequencing (NGS), are able to maximize the number of bases sequenced in the least amount of time, generating a wealth of data that can be used to understand complex phenotypes. These techniques are providing researchers and clinicians with a variety of tools to probe genomes in greater depth, leading to an enhanced understanding of how genome sequence variants underlie phenotype and disease.[10] Not surprisingly, clinical screening tools for whole-exome or genome sequencing are now entering the clinical domain, and the results they generate are beginning to be used by different medical specialties, including cardiology. With this in mind, as a final remark, it is important to emphasize that as genetic testing advances and NGS technologies become more accessible and affordable, training in cardiovascular genetics will be critical to ensure that the cardiological community is able to provide effective high-quality care for patients and families.[2]

Conflicts of interest

The author has no conflicts of interest to declare.

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