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EDITORIAL COMMENT

Left ventricular non-compaction: Challenges in the etiopathogenesis and risk stratification of sudden cardiac death in clinical practice

Não compactação ventricular esquerda: desafios na etiopatogénese e na estratificação de risco de morte súbita na prática clínica

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In their study published in this issue of the *Journal*,[1] Oliveira et al. elegantly described a family of patients with left ventricular non-compaction (LVNC), illustrating the challenges in clinical practice regarding etiological investigation and risk stratification of sudden cardiac death in these patients.

A family history of LVNC has been described in about 30% of cases[2] and a pathogenic mutation has been found in nearly one-third.[3] Although LVNC is a genetically heterogeneous cardiomyopathy, sarcomere mutations represent more than half of the known genetic causes, especially in adults, and *MYH7* is one of the most commonly mutated genes.[2] Nevertheless, the causal relation between genetic variants and the LVNC phenotype remains to be ascertained in the majority of cases. This case report underlines the importance of a specialized cardiomyopathy team in the systematic genetic and clinical screening of family relatives and the interpretation of the clinical significance of genetic variants in LVNC. Moreover, the previous report of this *MYH7* mutation in a case of hypertrophic cardiomyopathy further supports the notion that the same mutation may be associated with different cardiomyopathy phenotypes.

The etiopathogenesis of LVNC is largely unknown. Recently, cellular models, such as induced pluripotent stem cell lines derived from LVNC patients, have been developed and may prove useful to clarify the molecular, genetic, and functional aspects of the condition.[4]

Risk stratification of sudden cardiac death in LVNC is also a complex matter, particularly in the primary prevention setting, given the lack of robust evidence supporting clinical practice. Although the optimal risk stratification strategy is not clear, it will probably lie in a multiparametric assessment, in which left ventricular function appears to play a major role, as patients with reduced left ventricular systolic function have been found to be at a 4.6-fold higher risk for major adverse cardiac events (MACE).[5] The role of genetic testing for risk stratification in LVNC is still a matter of debate and a deeper understanding of genotype-phenotype correlations in LVNC is necessary. The identification of pathogenic mutations has been associated with a higher risk of MACE. However, it is noteworthy that

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sarcomere mutations have been associated with a lower risk of such events compared to other genetic causes.[3] By contrast, other studies have not found genetic variants to be predictors of the risk of MACE.[5] Therefore, as illustrated in the case presented by Oliveira et al.,[1] decisions on cardioverter-defibrillator implantation may be complex in current clinical practice and individualized clinical judgment by a specialized cardiomyopathy team is pivotal for accurate patient risk stratification.

Conflicts of interest

The author has no conflicts of interest to declare.

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