Rev Port Cardiol. 2020;39(11):623–624

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Arrhythmogenic risk of late gadolinium enhancement in patients with hypertrophic cardiomyopathy: Burden and location?

Risco arritmogénico de realce tardio pelo gadolínio em doentes com miocardiopatia hipertrófica: quantidade e localização?

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Available online 6 November 2020

Hypertrophic cardiomyopathy (HCM) is a common genetic disease, and is one of the leading causes of sudden cardiac death (SCD), particularly in young athletes.[1] Myocardial fibrosis and scar formation are frequently observed in patients with HCM.[2] Quantitative late gadolinium enhancement (LGE) has emerged as a tool for risk stratification in HCM, as the presence and extent of LGE have been associated with increased risk of SCD. Quantitative LGE (through the use of various threshold methods) and semi-quantitative methods have been proposed to quantify the extent of LGE.[3–5]

In HCM, LGE is most commonly observed in the septal wall, usually but not always limited to hypertrophied segments in a variety of patterns that are not related to vascular territories. This is in contrast to ischemic cardiomyopathy, in which the subendocardial area related to the culprit artery is most frequently affected.[3,6,7] Histopathological analysis results from postmortem or post-surgical samples in HCM patients have shown that LGE areas are indicative of myocardial scarring or interstitial fibrosis, and so the proposed mechanism has been hypothesized to be related to microvascular ischemia rather than stenosis of epicardial coronary arteries.[8,9]

In this issue of the *Journal*, Barbosa and colleagues observe that the location of LGE, in addition to its extent, are important features associated with increased risk of ventricular arrhythmias in HCM patients. They hypothesize that areas of increased mechanical stress are more prone to LGE development, and that such areas may play an arrhythmogenic role.[10]

There is a paucity of evidence linking LGE location and increased arrhythmogenic risk in HCM patients. The exception is LGE that is isolated to the right ventricular insertion point. This has been shown not to be correlated with SCD, as here it in fact represents areas of expanded extracellular space rather than replacement fibrosis.[11] Amano et al.[12] have shown that in addition to the total number of LGE segments, the presence of LGE in non-septal segments may also be related to arrhythmias and could add important information beyond fibrosis extent. Nojiri et al.[3] showed that the basal anteroseptal, mid anteroseptal, mid inferoseptal and apical septal segments, in that order, are the segments most often involved in HCM patients with preserved left ventricular ejection fraction, and also that mid-wall area involvement is more prevalent than subepicardial or subendocardial involvement. Based on the study's findings, and dividing the heart into 18 segments and 3 layers, they defined a scoring model up to 48 points and proposed that a higher score (i.e. higher LGE) is correlated with a higher rate of cardiac events including heart failure or ventricular tachycardia.

DOI of original article:
https://doi.org/10.1016/j.repc.2020.03.017
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https://doi.org/10.1016/j.repc.2020.10.002

Of interest, Basso et al.[13] showed that in patients with mitral valve prolapse, LGE at the papillary muscles and basal inferior segment were associated with arrhythmia. They hypothesized that mechanical stretch by the prolapsing leaflet (and the subsequent development of LGE in the aforementioned segments) could act as a trigger of electrical instability. Maurer et al.[14] suggested that there is an association between increased myocardial wall stress and increased metabolic demand, mostly in locations corresponding to the basal inferior and lateral segments. Excitation-contraction coupling plays an important role in cardiac physiology. In addition, mechanical stress could be a trigger for electrical activity and instability, termed mechano-electrical feedback, as in commotio cordis, which is more pronounced in non-uniform cardiac muscle.[15,16]

The association between the location of LGE in HCM patients and clinical risk factors and subsequent premature cardiac death demonstrated by Barbosa et al.[10] represents an important first step. Nevertheless, there is a wide range and overlap in the extent of LGE within patient subgroups. Due to the small number of patients (n=61) and of events (n=15) in their study, it is difficult to independently attribute the increased arrhythmogenic risk to the location of LGE, rather than to the presence (or more likely, the overall burden) of LGE. It is also important to remember that using two or more clinical risk factors has just 45% sensitivity and 23% positive predictive value to predict sudden cardiac death in HCM patients.[17] However, the important data presented by Barbosa et al. indicate that further research into the prognostic value of LGE location in HCM patients is warranted.

Conflicts of interest

The author has no conflicts of interest to declare.

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