Editorial

Quantification of Myocardial Fibrosis by Cardiac Magnetic Resonance Imaging: Advances, Impacts, and Perspectives

Isabela Bispo Santos da Silva Costa[1]

Universidade de São Paulo, Instituto do Câncer do Estado de São Paulo,[1] *São Paulo, SP – Brazil*

Cardiac magnetic resonance imaging (CMR) has been established as a fundamental tool for the diagnosis and management of cardiomyopathies, especially due to its accuracy in tissue characterization, identification, and quantification of myocardial fibrosis.[1,2] Late gadolinium enhancement (LGE) allows accurate assessment, identifying areas of myocardial fibrosis, and it serves to characterize, locate, and quantify them.[3] In recent years, the role of LGE in the risk stratification of patients with hypertrophic cardiomyopathy (HCM) and other genetic cardiomyopathies has been the subject of several studies that aimed to correlate the presence and extent of myocardial fibrosis with the risk of sudden cardiac death (SCD) and major cardiovascular events.[4-6]

Different techniques are currently used to acquire, analyze, and quantify LGE by CMR. The presence of LGE is based on the differential tissue retention of gadolinium, which is preferentially absorbed in areas of fibrosis, where scar tissue is altered due to the presence of collagen.[3] LGE acquisition techniques nowadays are fast, safe, and can be performed without requiring long respiratory pauses, as was the case in the past, with progressively better resolution and image definition. To quantify areas of fibrosis, different software programs that allow adequate quantification in a semi-automated manner are currently available.

Kiaos et al., in a recent meta-analysis with 11 studies evaluating the quantification of myocardial fibrosis and risk of sudden death in patients with HCM offered a robust and comprehensive view of this correlation, leading to new reflections and perspectives in clinical practice.[7] In this study, they analyzed almost 5,550 patients with a mean follow-up of 5.2 years and mean patient age of 51 years. The rate of sudden death events was 4.4%, and LGE was present in 61% of patients. The published data showed a statistically significant association between the presence of LGE and an increased risk of adverse events, including SCD. The odds ratio of the association between the extent of LGE and SCD was 4.93 (95% confidence interval: 3.75 to 6.47), reinforcing that the extent of fibrosis measured by LGE has been shown to be a strong predictor of SCD in these patients.[7]

Keywords

Endomyocardial Fibrosis; Magnetic Resonance Imaging; Cardiomyopathies.

Mailling Address: Isabela Bispo Santos da Silva Costa •
Universidade de São Paulo, Instituto do Câncer do Estado de São Paulo. Av. Dr. Arnaldo, 251. Postal code: 01246-000. São Paulo, SP – Brazil
E-mail: isabelabispo@yahoo.com.br

DOI: https://doi.org/10.36660/abcimg.20240114i

In this meta-analysis, fibrosis was quantified in 4 different manners. In 7 studies, LGE was measured using the technique > 6 standard deviations (SD) from normal myocardium and quantified as a percentage of left ventricular mass. Two studies quantified LGE manually. One study quantified LGE with the 4 SD technique, and one study used the 2 SD technique. It is important to highlight that, despite the different methodologies used, the study authors assessed that there was no statistically significant difference in the prediction of SCD between these 4 methods used ($p = 0.443$).[7]

Classic studies on quantification of LGE on CMR to predict the risk of SCD in HCM used the 2 SD technique, and, based on this, the 15% cutoff point was validated in the literature[8] and indicated in the leading guidelines on the topic as a prognostic marker.[1,2] The European guidelines on cardiomyopathies published in 2023 maintain the recommendation to first estimate the risk of SCD using SCD-HCM risk calculators. For patients in the low to intermediate risk category, the presence of extensive LGE (≥ 15%) can be used in shared decision-making with patients about prophylactic implantation of an implantable cardioverter-defibrillator.

Magalhaes et al.,[1] in the Brazilian cardiology guidelines published this year, reinforced that the presence of myocardial fibrosis greater than 15% of the left ventricular mass is a prognostic predictor in HCM and that LGE can be quantified using dedicated software or estimated visually. In addition to quantifying myocardial fibrosis, the guideline reaffirms other prognostic factors visualized by CMR that can assist clinicians in risk stratification of patients with HCM, namely: left ventricular ejection fraction less than 50%, left ventricular wall thickness greater than 30 mm, and presence of apical aneurysm. Other poor prognostic factors mentioned included left atrial enlargement and the presence of outflow tract obstruction. The Brazilian guideline lists CMR as class of recommendation I, level of evidence A in patients with suspected HCM for investigation of myocardial fibrosis for risk stratification and differential diagnosis with other heart diseases with hypertrophic phenotypes.[1]

These data provide us with clinical implications that patients with HCM and extensive fibrosis identified by LGE may benefit from closer monitoring and, in some cases, from the indication for an implantable cardioverter-defibrillator, which may be essential for the prevention of sudden death in high-risk patients. Moreover, quantification of fibrosis may assist in longitudinal follow-up, allowing the assessment of disease progression and the efficacy of interventions, aiding in the definition of septal reduction therapy.[2,9] However, in initial studies with the cardiac myosin inhibitors (mavacamten and aficamten) used in HCM, they seem not to have any benefits in relation to reducing myocardial fibrosis.[10,11]

Accordingly, it is clear that quantification and characterization of myocardial fibrosis play an important role in these patients. With technological advances, the incorporation of new methodologies, the integration of artificial intelligence, and advanced image analysis, there are future prospects that these data will become increasingly accurate, and analyses will be faster every day. Artificial intelligence has the potential to optimize fibrosis quantification and reduce interobserver variability, allowing more patients to benefit from personalized risk analysis. Furthermore, the development of contrast-enhanced CMR techniques with higher resolution may further improve the accuracy of LGE, especially in cases with less extensive fibrosis.

References

1. Magalhães TA, Carneiro ACC, Moreira VM, Trad HS, Lopes MMU, Cerci RJ, et al. Cardiovascular Computed Tomography and Magnetic Resonance Imaging Guideline of the Brazilian Society of Cardiology and the Brazilian College of Radiology - 2024. Arq Bras Cardiol. 2024;121(9):e20240608. doi: 10.36660/abc.20240608.
2. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, et al. 2023 ESC Guidelines for the Management of Cardiomyopathies. Eur Heart J. 2023;44(37):3503-626. doi: 10.1093/eurheartj/ehad194.
3. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, et al. Relationship of MRI Delayed Contrast Enhancement to Irreversible Injury, Infarct Age, and Contractile Function. Circulation. 1999;100(19):1992-2002. doi: 10.1161/01.cir.100.19.1992.
4. Todiere G, Nugara C, Gentile G, Negri F, Bianco F, Falletta C, et al. Prognostic Role of Late Gadolinium Enhancement in Patients with Hypertrophic Cardiomyopathy and Low-to-Intermediate Sudden Cardiac Death Risk Score. Am J Cardiol. 2019;124(8):1286-92. doi: 10.1016/j.amjcard.2019.07.023.
5. Habib M, Adler A, Fardfini K, Hoss S, Hanneman K, Rowin EJ, et al. Progression of Myocardial Fibrosis in Hypertrophic Cardiomyopathy: A Cardiac Magnetic Resonance Study. JACC Cardiovasc Imaging. 2021;14(5):947-58. doi: 10.1016/j.jcmg.2020.09.037.
6. Kamp NJ, Chery G, Kosinski AS, Desai MY, Wazni O, Schmidler GS, et al. Risk Stratification Using Late Gadolinium Enhancement on Cardiac Magnetic Resonance Imaging in Patients with Hypertrophic Cardiomyopathy: A Systematic Review and Meta-analysis. Prog Cardiovasc Dis. 2021;66:10-6. doi: 10.1016/j.pcad.2020.11.001.
7. Kiaos A, Daskalopoulos GN, Kamperidis V, Ziakas A, Efthimiadis G, Karamitsos TD. Quantitative Late Gadolinium Enhancement Cardiac Magnetic Resonance and Sudden Death in Hypertrophic Cardiomyopathy: A Meta-analysis. JACC Cardiovasc Imaging. 2024;17(5):489-97. doi: 10.1016/j.jcmg.2023.07.005.
8. Chan RH, Maron BJ, Olivotto I, Pencina MJ, Assenza GE, Haas T, et al. Prognostic Value of Quantitative Contrast-enhanced Cardiovascular Magnetic Resonance for the Evaluation of Sudden Death Risk in Patients with Hypertrophic Cardiomyopathy. Circulation. 2014;130(6):484-95. doi: 10.1161/CIRCULATIONAHA.113.007094.
9. Fernandes F, Simões MV, Correia EB, Marcondes-Braga FG, Coelho-Filho OR, Mesquita CT, et al. Guidelines on the Diagnosis and Treatment of Hypertrophic Cardiomyopathy - 2024. Arq Bras Cardiol. 2024;121(7):e202400415. doi: 10.36660/abc.20240415.
10. Saberi S, Cardim N, Yamani M, Schulz-Menger J, Li W, Florea V, et al. Mavacamten Favorably Impacts Cardiac Structure in Obstructive Hypertrophic Cardiomyopathy: EXPLORER-HCM Cardiac Magnetic Resonance Substudy Analysis. Circulation. 2021;143(6):606-8. doi: 10.1161/CIRCULATIONAHA.120.052359.
11. Masri A, Cardoso RN, Abraham TP, Claggett BL, Coats CJ, Hegde SM, et al. Effect of Aficamten on Cardiac Structure and Function in Obstructive Hypertrophic Cardiomyopathy: SEQUOIA-HCM CMR Substudy. J Am Coll Cardiol. 2024;84(19):1806-17. doi: 10.1016/j.jacc.2024.08.015.

This is an open-access article distributed under the terms of the Creative Commons Attribution License