

## Editorial

T<sub>2</sub>-weighted Cardiovascular Magnetic Resonance Imaging to Delineate Ischemic Myocardium at Risk: Fact or Fiction?Secuencias de resonancia magnética cardiaca en T<sub>2</sub> para delimitar el miocardio isquémico en riesgo: ¿realidad o ficción?

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*"Fiction is the lie through which we tell the truth"*

Albert Camus

One of the fundamental principles behind urgent revascularization of the culprit coronary vessel in patients with acute myocardial infarction (AMI) is to salvage ischemic but still viable myocardium and thereby reduce final infarct size and improve survival.<sup>1</sup> Cardiovascular magnetic resonance (CMR) imaging can quantify salvaged myocardium by comparing edema extent in T<sub>2</sub>-weighted sequences (myocardium at risk [MAR]) with infarcted myocardium in T<sub>1</sub>-weighted late gadolinium enhancement images.<sup>2</sup> Accordingly, CMR parameters of myocardial injury are widely used as measures of reperfusion efficacy and prognostic markers after AMI in both routine clinical practice and as a surrogate endpoint in clinical trials.<sup>3,4</sup> However, the accurate delineation of MAR is crucial to correctly estimate myocardial salvage. Whether or not the regions with high T<sub>2</sub> signal intensity in CMR imaging correspond to the true MAR is hotly debated within the CMR community.<sup>5,6</sup> Some authors doubt the histopathological validation of T<sub>2</sub> edema imaging for MAR assessment,<sup>7</sup> whereas others criticize the limited diagnostic robustness of standard T<sub>2</sub>-weighted short-tau inversion recovery (STIR) sequences<sup>8</sup> in particular. Other authors recently reported a temporal pattern of myocardial edema in animal models with important implications for the optimal timing of CMR assessment of MAR after successful reperfusion.<sup>9,10</sup>

In the article published in *Revista Española de Cardiología*, Fernández-Friera et al.<sup>11</sup> provide novel evidence regarding the accuracy of T<sub>2</sub>-weighted STIR imaging for MAR quantification according to AMI territory. The authors used an experimental model with 40-minute balloon occlusion of the left anterior descending, left circumflex, and right coronary arteries in 4 pigs

each and applied 3 different methods to assess MAR: a) perfusion CMR imaging during selective intracoronary injection of gadolinium at the subsequent coronary occlusion site before infarction induction; b) black-blood T<sub>2</sub>-weighted STIR CMR imaging 7 days after occlusion/reperfusion; and c) Evans Blue staining with postmortem histopathological workup. The results revealed good concordance between perfusion CMR imaging and histopathology. Moreover, T<sub>2</sub>-weighted STIR imaging showed a strong correlation with both perfusion CMR imaging and histopathology in the left anterior descending and right coronary artery territories. However, the correlation was poor in the left circumflex territory.

Study limitations are related to the rather small sample size (n = 12) and missing data regarding the final infarct size. The latter is required to exclude transmural infarction of the entire MAR and to definitely reject the hypothesis that T<sub>2</sub> hyperintensity reflects infarcted myocardium.<sup>7</sup> However, transmural infarction seems unlikely because the balloon occlusion persisted for only 40 minutes.

The authors should be congratulated on their work, which highlights 2 major aspects in this important research field: perfusion CMR imaging with intracoronary gadolinium injection enables accurate in vivo assessment of MAR in experimental studies and, more importantly, T<sub>2</sub>-weighted STIR imaging reliably delineates MAR in anterior and inferior AMI. These findings support the concept of MAR determination with CMR imaging by identifying the region of edema and are in line with previous experimental results.<sup>12</sup> However, the negative results in the left circumflex territory need further consideration because this technique should theoretically be applicable to all coronary territories. The small sample size of only 4 pigs undergoing left circumflex occlusion and the inherent study limitations could have contributed to these results. Another explanation might be provided by signal loss due to through-plane cardiac motion, a known drawback of T<sub>2</sub>-weighted CMR imaging that is especially noticeable in the inferior and lateral wall.<sup>13,14</sup> Consistently, the signal intensity change between edematous and remote myocardium in the study by Fernández-Friera et al.<sup>11</sup> was most pronounced in the left anterior descending territory and significantly lower in pigs with occlusion of the right and particularly the left circumflex coronary arteries.

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Limitations of the STIR technique are subject to repeated discussions, and some authors even question the reliability of CMR edema imaging. The low signal-to-noise ratios and small differences in contrast-to-noise ratios between injured and remote myocardium can impede the acquisition of high-quality images in some individuals.<sup>12</sup> Patient-related factors such as tachyarrhythmias or an inability to sustain long breath-holds further impact image quality. Moreover, image interpretation can be impaired by an inadequately suppressed blood signal causing a bright rim at the endocardial border (“slow flow artifact”) as well as a lack of standardized sequence parameters and cutoff values for normal vs abnormal tissue. Adequate slice thickness (at least 8 to 10 mm) and technical advances (eg, surface-coil intensity correction or the use of body coils) help to overcome some of these drawbacks of T<sub>2</sub>-weighted STIR imaging.<sup>13</sup> However, efforts are directed at implementing alternative, more robust, sequences for CMR edema imaging. Contrast-enhanced steady-state free precession imaging seems to achieve higher diagnostic quality than T<sub>2</sub> sequences.<sup>8</sup> Furthermore, T<sub>1</sub>- and T<sub>2</sub>-mapping are very promising techniques to directly detect myocardial edema without the need for reference regions of interest.<sup>15,16</sup>

The time course of myocardial edema following AMI might represent another determinant of the validity of CMR-based quantification of MAR. Contrary to the assumption that the edematous reaction remains stable for several days to weeks, recently published experimental studies suggest a bimodal pattern with both early and delayed waves of edema.<sup>9,10</sup> These data raise questions about the optimal timing of edema imaging and challenge the results of previous clinical studies that assumed a stable reaction and determined MAR at diverse time points after AMI. However, the currently available human data do not support a dynamic course of myocardial edema extent during the first week after AMI.<sup>8,17,18</sup> Importantly, the duration of the edematous reaction after AMI seems to vary among different mammalian species, including humans.<sup>13</sup> Furthermore, experimental animal models do not account for minimal residual blood flow, stuttering course, collateral circulation, or ischemic preconditioning, which are all important factors in human AMI. Therefore, validation of experimental data in human studies is crucial.

In summary, the study by Fernández-Friera et al. underlines the accurate determination of MAR with T<sub>2</sub>-weighted STIR imaging for anterior and inferior AMI and largely supports the attractive concept of CMR edema imaging to delineate MAR. Future research efforts should aim to develop explanatory models and solutions for the poor correlation in the left circumflex territory and to validate the recently acquired experimental data regarding myocardial edema after AMI in human studies. Novel CMR sequences provide a promising approach to improve edema imaging and should be implemented in routine clinical practice and research to allow a

comprehensive characterization of reversible and irreversible myocardial injury after reperfusion.

## CONFLICTS OF INTEREST

None declared.

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