Cardiac magnetic resonance infarct heterogeneity: is it ready to be used on patients for the prevention of sudden cardiac death?

Bobak Heydari and Raymond Y. Kwong*

Brigham and Women’s Hospital, Boston, USA

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Numerous advancements in the treatment of acute myocardial infarction (MI), from reperfusion therapy to coronary care units, have markedly reduced 30-day patient mortality. Despite optimal therapy, a significant proportion of patients remain at high risk for sudden cardiac death (SCD), particularly in the first 6 months. The absence of herald symptoms and the catastrophic outcomes from arrhythmia-related SCD have led to the investigation of the prophylactic role of implantable cardioverter-defibrillators (ICDs) following acute MI. Two large-scale, randomized clinical trials (DINAMIT, IRIS) of early ICD implantation failed to demonstrate a benefit in all-cause mortality, despite a reduction in arrhythmia-related deaths. These studies highlight that despite the availability of an effective therapy for the prevention of SCD, we still lack the clinical risk-stratifying tools to identify patients at highest risk who may benefit from ICD therapy.

Unlike other post-infarct complications that are related to the extent of myocardial injury and left ventricular (LV) systolic failure, the development of arrhythmia-related SCD often occurs in patients with medium-to-small infarcts. Electrophysiological studies (EPS) have implicated heterogeneity of depolarization and dispersion of repolarization within the border zones of the infarcted myocardium as key substrates in arrhythmia-related SCD. It is postulated that these ‘peri-infarct zones’ (PIZs) represent an admixture of fibrotic and viable cardiomyocytes that provide a necessary electrophysiological setting for precipitation of fatal arrhythmias.

Yan et al. assessed the prognostic role of PIZ quantified by late gadolinium-enhancement cardiac magnetic resonance (CMR) imaging in patients with chronic ischaemic heart disease. The PIZ was found to be the strongest adjusted variable of post-infarct mortality beyond indices of LV remodelling and ejection fraction (EF). Concordant to these findings, other clinical studies reported supportive results that implicated PIZ as a region with arrhythmogenic potentials. Schmidt et al. investigated the PIZ in 47 patients with chronic ischaemic heart disease referred for EPS prior to ICD implantation for primary prevention. They reported that PIZ was the only significant marker of inducible monomorphic ventricular tachycardia (VT) at the time of EPS evaluation, whereas LVEF was not. Roes et al. studied 91 patients referred for ICD implantation following for a median of 8.5 months and reported that PIZ was the strongest adjusted predictor of appropriate ICD therapy for spontaneous VT. Collectively, these studies suggest that characterization of infarct architecture by CMR contains information that is linked to myocardial substrates associated with ventricular arrhythmias and even mortality in patients with chronic coronary artery disease.

In the previous issue of the European Heart Journal - Cardiovascular Imaging, Robbers et al. reported their assessment of the prognostic role for the PIZ in patients with acute MI. They examined a subgroup of 162 patients with ST-elevation MI from the HEBE trial. All patients underwent successful revascularization with percutaneous intervention. Overall, the cohort was one with medium size infarction and moderate LV dysfunction (mean infarct size of 32%, and LVEF of 43%). The primary outcome measure of arrhythmic risk was evaluated by documenting non-sustained or sustained VT during a 24-h Holter examination performed 1 month following revascularization. The study investigators reported that, in adjusted analysis, the only independent predictors of arrhythmic risk were ventricular fibrillation at the time of MI and proportion of PIZ.

These results contribute to an emerging body of evidence, suggesting that the evaluation of myocardial infarct architecture may have important prognostic implications beyond present clinical parameters, and may be evaluable early in the post-infarct period. Although this study utilized a surrogate marker for SCD, they reported no difference in the incidence of non-sustained or sustained VT for patients stratified by an LVEF of 40%. This further substantiates the poor sensitivity of clinical risk stratification by LVEF alone. Furthermore, they found a higher rate of VT in patients with a smaller total infarct size, lending further credence to the hypothesis that infarct characteristics, as opposed to the extent of myocardial injury, may be a more sensitive determinant of arrhythmic risk.

Occurrence of non-sustained or sustained VT on 24-h Holter monitoring was used as the primary study outcome. Eighteen percent of patients experienced VT, among which most if not all...
were non-sustained. No patient experienced VF. Despite early observational studies suggesting that non-sustained VT is a risk factor for SCD, the impact of such a surrogate endpoint early in the post-MI period on therapeutic decision-making is questionable.10 The EMIAT trial reported that, among patients with an LVEF of ≤30%, mortality was elevated if non-sustained VT was detected.11 However, the positive predictive value of non-sustained VT for post-MI SCD remains limited,12 and the landmark CAST trial found an increase in mortality when an anti-arrhythmic therapy was used to suppress asymptomatic non-sustained ventricular complexes.13 Currently, detection of asymptomatic non-sustained ventricular complexes does not serve as a target for any therapeutic intervention.

Limitations of this study include the method used to quantify the PIZ and the unknown influence of the different assigned protocols of bone marrow mononuclear cellular infusions on the subsequent risk of ventricular arrhythmias. To date, studies examining the prognostic importance of infarct characteristics by CMR have used different criteria to differentiate PIZ from a infarct core, including a threshold of 2 and 3 SDs,6 or the full-width at half-maximum method.7 A combination of these methods was recently validated histologically in an animal model of MI.14 Robbers et al. used a novel criteria not previously validated, identifying the PIZ with a threshold of 25–50% of maximal signal intensity within the infarct. It presently remains unclear which criteria is optimal for characterization of infarct heterogeneity or can be used to guide relevant clinical trials of ICDs or other novel therapies. Ultimately, a histological validation study in humans, or clinical trial evaluating the prognostic importance of one method to establish a standard criterion, would be highly valuable to the advancement of this field. It should also be noted that CMR studies, such as this one, performed in the acute period following acute MI are biased towards the null due to exclusion of the highest risk patients. These patients are likely to undergo therapy that excludes their eligibility for a CMR study, such as insertion of ventricular assist devices, or immediate ICD implantation. Therefore, the prognostic results of this study are only applicable to ‘stable’ patients following acute MI.

Nevertheless, the study by Robbers et al. provides intriguing evidence that myocardial tissue architecture assessed by CMR in the acute post-infarction period is linked to myocardial arrhythmogenic substrates. Further study evaluating the histopathological correlation of PIZ, serial assessment to evaluate changes during convalescence, and the use of novel T1 mapping techniques by CMR to assess myocardium remote from infarction may not only provide important prognostic information, but also characterize inflammatory, apoptotic, and maladaptive pathophysiological processes following acute MI. This information may help to further elucidate the pathogenesis of arrhythmia and adverse LV remodelling that predispose to heart failure and may provide novel treatment targets for the prevention of SCD.

Please note: This editorial refers to the manuscript, Myocardial infarct heterogeneity assessment by late gadolinium enhancement cardiovascular magnetic resonance imaging shows predictive value for ventricular arrhythmia development after acute myocardial infarction by Robbers et al. (doi:10.1093/ehjci/jet111) which was printed in the December 2013 issue of European Heart Journal - Cardiovascular Imaging.

Conflict of interest: None declared.

References