Journal of the American College of Cardiology
Vol. 58, No. 11, 2011

Published by Elsevier Inc.
ISSN 0735-1097/$36.00

CORRESPONDENCE

Letters to the Editor

Late Gadolinium Enhancement and Higher Risk of Arrhythmias

Fibrosis or Increased Ventricular Wall Stress?

Current criteria indicating implantable cardioverter-defibrillator (ICD) therapy for primary prevention of sudden cardiac death are poor, and non–evidence-based ICD implantations are more likely to have worse outcomes. Therefore, Iles et al. (1) examined late gadolinium enhancement (LGE) by using cardiac magnetic resonance imaging to predict appropriate device therapy in patients with ischemic and nonischemic cardiomyopathy. The study relies on the assumptions that myocardial fibrosis is the substrate of LGE and that fibrosis is associated with arrhythmias.

Well-documented links between fibrosis and LGE exist in patients who have experienced myocardial infarction in whom nonviable cardiomyocytes are replaced by collagen. This contiguous subendocardial or transmural area can be detected by a bright LGE pattern. Histological changes are very different in patients with dilative cardiomyopathies. Histopathological studies have shown that the myocardial remodeling can be associated with an increased collagen volume fraction, and in transmural left ventricular sections, the extent of fibrosis increased from epicardium to endocardium and from the right to the left side of the septum (2). LGE occurs as midwall (septal) streak (1) or is irregularly diffuse. Thus, in dilative cardiomyopathies, causes beyond fibrosis should be taken into account for LGE.

In the study by Iles et al. (1), all patients with ischemic cardiomyopathy exhibited LGE, and the ICD discharge rate was 14%, whereas it was 29% in patients with nonischemic cardiomyopathy and LGE. Also, based on the absence of differences in left ventricular ejection fraction and end-diastolic volume index, it was concluded that fibrosis predicts appropriate ICD therapy. However, it remains to be assessed whether indeed fibrosis or an increased wall stress was responsible for LGE and ICD therapy. Using echocardiography-based ventricular mass and geometry data, we suggest calculating wall stress and examining the contention that patients with ICD therapy exhibit increased wall stress.

In accordance with a role of wall stress for LGE, our recent study on 300 patients with dilative cardiomyopathy showed that a rise in wall stress (3) was associated with LGE (4). Most likely, higher wall stress is associated with an increased capillary leakage, and thus favors contrast medium emission into the interstitial space. Also, its venous clearance can be prolonged by an impaired redistribution. The link of LGE with arrhythmias would follow from experimental studies in which myocardial stretch and neurohumoral reactions predispose patients to arrhythmias involving, for example, stretch-activated cation channels.

The proposed subanalysis also could clarify whether LGE per se is an independent prognostic predictor or a dependent surrogate marker. Thus, in a study of 141 patients with dilated cardiomyopathy, the prognostic value of LGE regarding survival was found only by univariate, but not by multivariate, analysis (5). Increased wall stress thus could be the underlying mechanism of a worse prognosis and should be evaluated also as indicator for ICD therapy.

***Peter Alter, MD**
***Heinz Rupp, PhD**

*Internal Medicine Cardiology
Philipps University
Baldingerstrasse
35033 Marburg
Germany
E-mail: alter@staff.uni-marburg.de or
rupp@staff.uni-marburg.de

doi:10.1016/j.jacc.2011.03.061

REFERENCES

1. Iles L, Pfluger H, Lefkovits L, et al. Myocardial fibrosis predicts appropriate device therapy in patients with implantable cardioverter-defibrillators for primary prevention of sudden cardiac death. J Am Coll Cardiol 2011;57:821–8.
2. Unverferth DV, Baker PB, Swift SE, et al. Extent of myocardial fibrosis and cellular hypertrophy in dilated cardiomyopathy. Am J Cardiol 1986;57:816–20.
3. Alter P, Rupp H, Rominger MB, Klose KJ, Maisch B. A new methodological approach to assess cardiac work by pressure-volume and stress-length relations in patients with aortic valve stenosis and dilated cardiomyopathy. Pflugers Arch 2008;455:627–36.
4. Alter P, Rupp H, Adams P, et al. Occurrence of late gadolinium enhancement is associated with increased left ventricular wall stress and mass in patients with non-ischaemic dilated cardiomyopathy. Eur J Heart Fail 2011. In press, doi:10.1093/eurjhf/hfr082.
5. Hombach V, Merkle N, Torzewski J, et al. Electrocardiographic and cardiac magnetic resonance imaging parameters as predictors of a worse outcome in patients with idiopathic dilated cardiomyopathy. Eur Heart J 2009;30:2011–8.

Reply

Drs. Alter and Rupp propose that late gadolinium enhancement (LGE) in nonischemic cardiomyopathy may be the result of increased myocardial wall stress with resultant increased capillary permeability and reduced venous return.

In our study (1), patients without LGE did not experience implantable cardioverter-defibrillator discharges, suggesting that this group may be at lower risk for malignant ventricular arrhythmia. LGE previously was demonstrated to correlate well with ischemic regional fibrosis (2) and also in limited human studies in nonischemic pathological conditions (3). Therefore, we postulated the likely mechanism for implantable cardioverter-defibrillator discharges in advanced cardiomyopathy to be the presence of regional scar acting as an arrhythmogenic substrate. However, regardless of the mechanism, a lack of LGE was associated with a