Late Gadolinium Enhancement in Sarcoidosis
Ventricular Wall Stress Should Not Be Overlooked

To the Editor:

With great interest, we read in CHEST (October 2014) the study by Nagai et al.,1 who examined the occurrence of late gadolinium enhancement (LGE) by cardiovascular MRI (CMR) in patients with sarcoidosis. In sum, 13% of 61 patients exhibited perimyocardial, transmymocardial, or intramyocardial LGE. Noteworthy was that thinning of the interventricular septum, as measured by echocardiography, was revealed as an independent predictor of LGE. Thus, the question of the pathophysiologic rationale behind linking LGE to a thinned septum is addressed to the authors. Since no prognostic influences of LGE were found, the question on the morphologic or functional substrate also arises.

The appearance of LGE is caused by prolonged, interstitial contrast-agent deposition used for CMR image acquisition. LGE is known to accurately delineate scarring following myocardial infarction. In contrast, the diagnostic accuracy is less defined in other cardiac diseases. Intramyocardial, often distributed, spots of LGE are typically found in myocarditis, although the finding is neither obligatory nor specific. Additional sequences (eg, edema sensitive) are required for further classification.2 In dilated cardiomyopathy, LGE frequently occurs as a septal midwall pattern or at the hinge points of the septum. It has been deduced from postinfarct findings that LGE also would delineate fibrosis in dilated cardiomyopathy, which remains debatable. Studies on histology showed that the extent of myocardial fibrosis involves a gradient that increases from subepicardial to subendocardial layers not matching a midwall pattern. Due to the increased load of the affected regions, the question arises whether functional determinants are involved.

It was shown in 300 patients with cardiomyopathy that occurrence of LGE is associated with increased ventricular wall stress.3 Wall stress is predominantly determined by ventricular volumes, mass, and the transmural pressure gradient.4 In the study by Nagai et al.,1 it was pointed out that thinning of the interventricular septum was an independent predictor of LGE. Thus, it can be assumed that septal thinning was associated with reduced myocardial mass, which leads to increased wall stress. It is suggested that the authors1 provide CMR-based myocardial mass and calculate ventricular wall stress. It should be examined whether increased wall stress is related to LGE in sarcoidosis. Increased ventricular wall stress is associated with an increased arrhythmia risk by activation of stretch-associated ion channels, increased oxygen consumption, and unfavorable remodeling. Accordingly, it should be evaluated whether increased wall stress is a causative risk factor and associated with adverse events.

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References
Response

To the Editor:

We appreciate the correspondence from Dr Alter and colleagues on our article in CHEST.1 Whether left ventricular (LV) volumetric and functional determinants, measured by cardiovascular MRI (CMR), could influence the long-term prognosis of patients with systemic sarcoidosis is a topic of interest, and we analyzed volumetric and functional CMR variables in our study.1 These variables, including LV ejection fraction, LV end-systolic volume, and LV end-diastolic volume, were comparable between patients who experienced adverse events and those who did not, with the exception of LV mass (121.3 ± 32.2 g vs 82.3 ± 18.2 g, respectively, for patients who experienced events and those who did not; P < .001). In addition, there were no significant differences in these variables between the late gadolinium enhancement (LGE)-positive and LGE-negative groups. These findings suggest that, in our study, CMR-measured LV volume and systolic function were not directly associated with LGE and adverse events. However, it should be noted that adverse events occurred in only four patients.

Previous studies showed that > 20% of patients with systemic sarcoidosis had positive LGE, cardiac events occurred in > 10% of patients, and LGE was hypothesized to predict future cardiac events, even in patients with preserved LV systolic function.2-4 Contrary to these findings, our rates of positive LGE and cardiac events were lower, and, importantly, LGE did not predict adverse events.1 These differences can be explained by disease severity, including the extent of LGE. Patients in our study had lower frequencies of receiving immunosuppressants and having ECG abnormalities, no cardiac symptoms or impaired LV systolic function, and smaller extent of LGE compared with those in a previous study.3 Ise et al5 previously reported that smaller extent of LGE (% LGE mass < 20%) could predict a lower rate of cardiac events. Taking these findings together, the clinical implication of adding LV wall stress analysis would be limited in our population with latent and less severity and preserved LV systolic function. We believe that a larger cohort with a higher event rate (eg, greater disease severity, impaired LV function, and larger extent of LGE) is needed to investigate the association between LV volume and functional variables and long-term prognosis in patients with systemic sarcoidosis.

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References