Early Enhancement with Gadobutrol Can Visualize Diffuse Myocardial Fibrosis in Dilated Cardiomyopathy : A Cardiovascular Magnetic Resonance Study

O. Strohm[1], M. S. Cocker[1], and M. G. Friedrich[1]

[1]Stephenson CMR Centre at the Libin Cardiovascular Institute, University of Calgary, Calgary, Alberta, Canada

Background

Progressive ventricular dilatation and interstitial fibrosis in Dilated Cardiomyopathy (DCM) result in increased volume of distribution for Gadolinium-based contrast agents, which are utilized for contrast-enhanced cardiovascular magnetic resonance imaging. T1-weighted early enhancement (EE) is considered to be a surrogate marker of myocardial inflammation and hyperemia in the setting of inflammatory cardiomyopathies, as it reflects early contrast uptake. In tissue that has interstitial fibrosis, such as that found in DCM, there is increased space for contrast distribution. As such, EE may be utilized as a marker of diffuse fibrosis in the setting of DCM.

Hypothesis

We hypothesize that in patients with DCM, EE will be elevated and will relate to depressed ventricular function.

Methods

We assessed 27 patients with DCM (age 45+14 years, 18 male) using standard EE and late gadolinium enhancement (LGE) sequences with Gadobutrol (Gadovist®, Bayer Healthcare Canada), on a 1.5 Tesla MRI system (Avanto, Siemens Healthcare, Germany). ECG-triggered, non-breath hold, EE images were obtained in axial and short-axis orientations (matrix 256X256, slice thickness 15 mm, TE 26 ms, TR= 1RR, with identical parameters before and after injection of a bolus of 0.1 mmol/kg Gadobutrol (Gadovist®, Bayer Healthcare, Canada). An EE ratio was calculated, where myocardial and skeletal muscle contrast uptake post-Gadobutrol was compared to that of pre-Gadobutrol, followed by normalization of myocardial to skeletal muscle contrast uptake, as previously described. LGE was obtained with optimized TI for myocardial suppression (PSIR, matrix 256x192, TE 3.3 ms, TR=1RR) 8-10 minutes after a second injection of 0.1 mmol/kg Gadobutrol. Myocardial fibrosis was quantified as % of total LV-mass above a threshold of 2 SD from the mean of remote non-enhancing myocardium, using automated computer detection.

Abbreviations for cardiac parameters for function:
LVEDVI – Left-ventricular end-diastolic volume indexed-to-height; LVESVI – Left-ventricular end-systolic volume indexed-to-height; EF – ejection fraction.

Results

EE was increased in 14 patients (mean ratio was 6.7, normal range <4.0). The presence of EE was associated with reduced EF (33.5+14.5 vs. 49.6+18.6 %, p=0.03), while there were no differences in LVEDVI or LVESVI (p>0.05). The presence of LGE was associated with increased LVEDVI (124+38 vs. 83+18 ml/m, p=0.02), LVESVI (85+42 vs. 39+11 ml/m, p=0.02), and reduced EF (35.0+16.6 vs. 52.2+12.4%, p=0.03).
Non-ischemic fibrosis was seen in 17 patients, where the average extent of fibrosis was 22+11%, and did not correlate with measures of ventricular function.

Discussion

Diffuse interstitial fibrosis is a feature of DCM, but its assessment with standard LGE may be challenging, given the fact that to generate contrast between injured and healthy myocardium, "nulling" is required. The injury pattern in DCM is diffuse, so by nulling what is considered to be 'healthy' myocardium, diffuse fibrosis is also nulled, and thus may not be visible on LGE images in DCM. We have found that diffuse interstitial fibrosis can be identified with EE, and relates to contractile function in DCM.

Conclusion

Our data indicates that EE can identify diffuse, interstitial fibrosis in patients with dilated cardiomyopathy. Further studies are needed to assess whether EE can be utilized to monitor the progression of myocardial injury in DCM, as well as in other cardiomyopathies that have diffuse fibrosis, such as Fabry's disease.
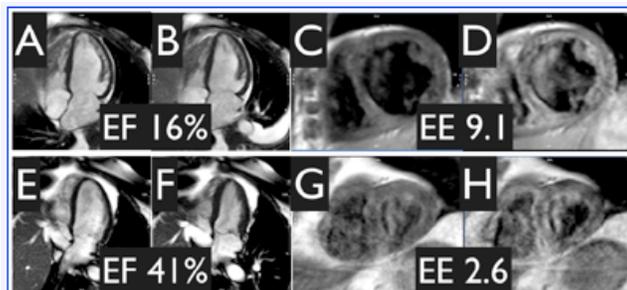

Figure 1: Patient with reduced EF and increased early enhancement ratio (EE) - upper row; patient with reduced EF and normal EE - lower row. Diastolic (A,E) and systolic (B,F) cine phases; pre-contrast (C,G) and post-contrast (G,H) EE