Quantification of Diffuse Myocardial Fibrosis and Its Association with Diastolic Dysfunction in Patients with Diastolic Heart Failure Using Cardiovascular Magnetic Resonance

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Introduction

Heart failure (HF) is a clinically defined syndrome and can occur across the entire range of ejection fraction (EF) in the left ventricle (LV). Patients with HF can be roughly categorized into systolic heart failure (SHF) and diastolic heart failure (DHF) based on the EF evaluation. There is growing evidence that SHF and DHF are distinct disease entities, having different aetiology, epidemiology and response to treatment (1). Specifically, diagnosis of DHF in patients with HF requires demonstration of relatively preserved systolic function and evidence of diastolic dysfunction. Various clinical and experimental studies have demonstrated the importance of diffuse myocardial fibrosis as a cause of diastolic dysfunction (2, 3). To date, it remains unclear whether diffuse myocardial fibrosis is associated with impaired diastolic function in patients with DHF. In this study, we used myocardial T1 mapping and Cine MRI to quantify, respectively, diffuse myocardial fibrosis and diastolic function of the LV. We aimed to verify that patients with DHF had increased diffuse myocardial fibrosis and that the fibrosis was associated with the impairment of diastolic function.

Materials and Methods

Sixty-seven patients with heart failure (HF) and 22 patients without heart failure (control) were enrolled in this study. Myocardial T1 mapping were acquired before and 10 minutes after the infusion of 0.1mmole/kg of Gd-DTPA on a 3T MR system (Siemens, Erlangen, Germany). Myocardial T1 mapping was obtained from merged images by using an EKG-triggered modified Look Locker Inversion Recovery (MOLLI) pulse sequence. The MOLLI protocol used two inversion-recovery blocks to acquire 7 images over 12 heart beats (TR/TE/FA=1.9ms/1.0ms/35°, inversion time increment=80ms, matrix=256x192, slice thickness=6mm, spatial resolution=1.28mm and GRAPPA acceleration factor=2). Five short-axis planes were acquired to cover the whole LV. Cine MRI was performed using a segmented balanced steady-state gradient echo pulse sequence (TR/TE/FA=3.0ms/1.5ms/46°, matrix=256x208, slice thickness=8mm, gap=2mm, spatial resolution=1.21mm) with a retrospective ECG R-wave trigger. Multiple short-axis slices were prescribed from the mitral orifice to the LV apex. A total of approximately 10 to 12 short-axis slices were obtained, depending on cardiac sizes. For T1 mapping, the cavity and myocardium of the LV were segmented manually in the central area of the LV cavity and the septal myocardium on each image. The averaged T1 values of the segmented regions were then computed. After subtraction with measurements from pre-contrast, the change of relaxation rate (1/T1) in the LV cavity and in the myocardium was obtained. The extracellular volume fraction (ECV) values were calculated using the ratio of the change in relaxation rate in the myocardium to that in the LV cavity, and corrected for the heart rate and hematocrit. We averaged each ECV value over five short-axis slices for each subject, and compare them among each group. LV functional indices including end-diastolic volume (LVEDV), end-systole volume (LVESV), EF, peak ejection rate (PER), peak filling rate (PFR), time for deceleration (Tdec) and LV mass were measured from Cine images. Data was presented in mean ± SD. HF patients were assigned to DHF group (N=40) if patients with EF >50% measured from Cine MRI and LV diastolic dysfunction documented by tissue duplex echocardiography. The rest of HF patients were assigned to SHF group (N=27). Intergroup differences in the ECV, LV functional indices were tested for significance by the Kruskal-Wallis one-way analysis of variance (ANOVA) test and post-hoc analysis using the Mann-Whitney U test for comparison of the medians between groups. The correlation between ECV and PFR was tested by Pearson correlation. A value of $p < 0.05$ was considered significant.

Results

For group comparison, the ECV in SHF group was significantly higher than that in DHF group (33.8 ± 4.3% vs. 29.2 ± 2.5%, $p < 0.001$) and control group (33.8 ± 4.3% vs. 27.6 ± 2.2%, $p < 0.001$). In addition, patients with DHF also showed significantly higher ECV than controls (29.2 ± 2.5% vs. 27.6 ± 2.2%, $p = 0.044$) (Fig 1). LV functional indices and mass were all significantly different in SHF as compared to DHF and control groups (Table 1). Correlation analysis demonstrated that DHF group had significant correlations between ECV with EF ($r = -0.437$, $p = 0.005$), PER ($r = -0.358$, $p = 0.023$) and PFR ($r = -0.319$, $p = 0.045$). There was no correlation between ECV and any LV functional indices in SHF and control groups.

Conclusion

In this study we used myocardial T1 mapping to investigate the ECV in patients with HF. Our data shows that the ECV is increased in patients with HF in contrast to age-matched patients without HF. For the patients with HF, greater ECV is seen in SHF than in DHF, suggesting that patients with SHF have more diffuse myocardial fibrosis than in DHF patients. For differences in LV function, our present study shows that both SHF and DHF have significantly decreased PFR but only SHF has significantly decreased PER as compared to controls. These findings support that DHF has relatively preserved systolic function and impaired diastolic function in the LV. Correlation analysis demonstrates a significant association between ECV with EF, PER and PFR in DHF. These findings suggest that diffuse myocardial fibrosis is increased in patients with DHF and the increment of ECV not only impairs LV diastolic function but also affects the systolic function of the LV.

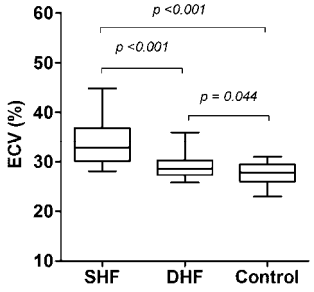

Fig 1. Group comparison among the patients with SHF, DHF and control subjects in the myocardial ECV.

	SHF (n = 27)	DHF (n = 40)	non-HF (n = 22)
EDV, ml	189 ± 101*†	91 ± 28	84 ± 21
ESV, ml	133 ± 94*†	21 ± 14	18 ± 8
EF, %	33 ± 11*†	78 ± 9	79 ± 6
PER, s^{-1}	-1.60 ± 0.57*†	-3.73 ± 0.85	-3.63 ± 0.68
PFR, s^{-1}	1.29 ± 0.64*†	3.14± 0.89†	3.81 ± 0.81
Tdec, % of RR	8.2 ± 4.0*†	11.2 ± 3.3†	14.6 ± 2.9
LVM, gm	177 ± 87*†	117 ± 34†	95 ± 25
MVR	0.93 ± 0.29*†	1.39 ± 0.52†	1.16 ± 0.28

*p < 0.05 compared with DHF, †p < 0.05 compared with non-HF group

Table 1 LV function and mass for patients with/without heart failure (HF)

References

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