Circumferential strain using MR tagging can assess subclinical myocardial abnormality in patients with apparently preserved systolic function

Poster No.: C-2181
Congress: ECR 2014
Type: Scientific Exhibit
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Keywords: Tissue characterisation, Imaging sequences, Diagnostic procedure, MR-Functional imaging, MR, Cardiac
DOI: 10.1594/ecr2014/C-2181

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Aims and objectives

Since myocardial fibrosis strongly influences the systolic function of left ventricle (LV) [1] and it can be the substrate of ventricular arrhythmias [2], late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging (CMR) has widely used to assess myocardial fibrosis in various myocardial diseases. However, frequently, no LGE was detected in patients with cardiac events such as heart failure with preserved ejection fraction (HFpEF) and ventricular arrhythmias. Since LGE relies on the difference in signal intensity between replacement fibrosis and normal myocardium, its sensitivity is limited for the assessment of diffuse interstitial fibrosis [3]. At the myocardial level, patients with HFpEF demonstrate elevated interstitial myocardial collagen content, and greater cardiomyocyte hypertrophy [4]. Moreover, hypertrophic and fibrotic myocardial tissues are pro-arrhythmic substrates in vitro [5]. More sensitive and accurate method for assessing myocardial damages in the patients with cardiac events, despite of normal ventricular systolic function, is desired.

Recently, strain using magnetic resonance tagging (MR tagging) is used to evaluate the regional abnormal myocardial shortening which is barely visible to the naked eyes [6]. The strain involves a change in the distance between two distinct tag points during the cardiac cycle. According to the direction of the main myofibers, three types of myocardial motion (radial, circumferential, and longitudinal) can be evaluated (Fig. 1 on page 3a). In the short-axis plane, radial strain ($\text{Err}$) reflects wall thickening toward the center of LV and circumferential strain ($\text{Ecc}$) is tangential to the epicardial wall (Fig. 1 on page 3b). $\text{Err}$ is usually well appreciated visually, while $\text{Ecc}$ cannot be indicated apparently. A previous study suggested that the occult cardiovascular dysfunction in the presence of normal global function can be demonstrated by the $\text{Ecc}$ using MR tagging [7]. In addition, $\text{Ecc}$ has been reported as a powerful predictor of cardiac events in patients with HF [8]. We hypothesized that $\text{Ecc}$ using MR tagging can estimate subclinical myocardial damages in patients with apparently preserved systolic function, which could not be detected by LGE.
Fig. 1: a. Illustration of the three types of myocardial strain. b. Illustration of how circumferential and radial strain are obtained from short axis section.

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Methods and materials

**Study population:** Ten patients (mean age 43 ± 22 years; 6 males and 4 females) with cardiac events, who underwent clinical CMR studies between August and December 2013, were analyzed. 4 patients (40%) had the history of heart failure and 6 patients (60%) suffered ventricular arrhythmias. Clinical characteristics of patients were presented in Table 1 on page 6. The LV contraction of all patients were apparently preserved (mean LVEF 59 ± 6%, range 50.1 to 68%). No patient had coronary artery disease or biopsy evidence of secondary myocardial disease. We also examined 5 healthy volunteers as control subjects.

**CMR protocol:** All CMR examinations were performed using a standardized clinical protocol on a 3-T system (Magnetom Verio, Siemens, Erlangen, Germany) with a 32-channel surface coil. Cine images were acquired with prospective electrocardiogram (ECG)-gating, using true-FISP sequence (TE 1.53 ms, TR 37.73 ms, flip angle 50 degree, slice thickness 5 mm, gaps 5 mm, in plane resolution 1.7×1.3 mm) with multiple breath hold in contiguous short-axis slices and 3 standard long-axis slices. We also acquired LGE using a segmented inversion-recovery (IR) prepared true-FISP sequence with ECG-triggering at 10 min. after the administration of 0.10 mmol/kg body weight of gadolinium-DTPA. Other imaging variables consisted of 84 segments, TE 1.13 ms, TI 350 ms, flip angle 40 degree, field-of-view 360×270 mm, slice thickness 8mm, gaps 2mm, and in plane resolution 1.9×1.5mm.

**Myocardial tagging images:** Tagged cine images were acquired in the short axis of the basal, middle, and apical LV (Fig. 2 on page 7), with ECG-triggered fast gradient echo sequence before administration of gadolinium. Imaging variables consisted of 6 mm grid-type tag spacing, TR 47.7ms, TE 2.54 ms, flip angle 10 degree, field-of-view 340×255 mm, slice thickness 6mm and in plane resolution 1.3×1.3 mm.

**CMR image analysis:** For quantification of LV volumes and global function, we manually traced the LV endocardial contours in end-systolic and end-diastolic frames of cine imaging with the dedicated software (Argus system®, Siemens, Erlangen, Germany). The LGE positive was defined as myocardial enhancement at 10 min. delayed images assessed visually by 2 experienced radiologists.

**Myocardial strain analysis:** Tagged cine images were analyzed with post processing workstation (Zio station 2 software, Ziosoft Inc., Japan) [9]. After manually tracing of epicardium and endocardium, Ecc and Err were automatically calculated and a superimposed color parametric map of each short-axis plane was generated (Fig. 2 on page 7). Mean peak Ecc and Err were evaluated in 16 segments (6 segments at
the basal and middle levels, and 4 segments at apical level), according to the American Heart Association classification. Fig. 3 on page 8a represented the mean peak $Ecc$ of 16 segments in a normal control. Fig. 3 on page 8b was the graph of $Ecc$ curves in each segment.
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Table 1 Baseline Characteristics of the Study Population (n = 10)

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<table>
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<tbody>
<tr>
<td>Age (years)</td>
<td>43 ± 22</td>
</tr>
<tr>
<td>Male (%)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>History of Cardiac Event:</td>
<td></td>
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<tr>
<td>Heart Failure (%)</td>
<td>4 (40)</td>
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<tr>
<td>Ventricular Arrhythmia (%)</td>
<td>6 (60)</td>
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<tr>
<td>CMR Parameters:</td>
<td></td>
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<tr>
<td>LVEF (%)</td>
<td>59 ± 6</td>
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<tr>
<td>LVEDVI (ml/m²)</td>
<td>73 ± 15</td>
</tr>
<tr>
<td>LVESVI (ml/m²)</td>
<td>31 ± 6</td>
</tr>
<tr>
<td>LV mass (g/m²)</td>
<td>48 ± 10</td>
</tr>
<tr>
<td>Mean peak $E_cc$ (%)</td>
<td>-11.7 ± 3.0</td>
</tr>
<tr>
<td>Mean peak $Err$ (%)</td>
<td>4.1 ± 3.9</td>
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Table 1: Baseline characteristics of the study population (n = 10).

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**Fig. 2:** Myocardial strain analysis using MR tagging. Color map illustrated high strain values in red and weak strain values in yellow.

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Fig. 3: 33-year-old normal control (LVEF=60.5%). a. Peak circumferential strain according to the 16-segment American Heart Association model. b. Circumferential strain curves in each segment.

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Results

In patients with cardiac events, LGE was found in only 5 segments of 1 patient. Compared with segments of control subjects, segments of patients with cardiac events demonstrated significantly weaker peak Ecc (-13.8 ± 2.0% vs. -11.7 ± 3.0%, p<0.0001). More interestingly, there was a significant difference in peak Ecc between the control segments and the segments without LGE (p<0.0001) (Fig. 4 on page 13). In addition, peak Err in patients with cardiac events was also decreased to 4.1 ± 3.9% (5.7 ± 4.3% in controls, p=0.003) and the segments without LGE were significantly lower in peak Err than control segments (p=0.012) (Fig. 4 on page 13). Based on receiver operating characteristic curve analysis, a cut-off Ecc value of -12.7% had positive predictive value (PPV) of 100% and negative predictive value (NPV) of 71% for detecting patients with cardiac events (area under the curve (AUC) =0.86), while a cut-off Err value of 4.9% had PPV of 88% and NPV of 67% (AUC=0.83).

Fig. 5 on page 14 showed the representative images of Ecc analysis of the patient with ventricular tachycardia. The peak Ecc of lateral wall and inferoseptum were regionally impaired while no bright LGE was detected in any segments.
Fig. 1: a. Illustration of the three types of myocardial strain. b. Illustration of how circumferential and radial strain are obtained from short axis section.

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Fig. 4: Difference in myocardial strain between control segments, and segments with or without late gadolinium enhancement (LGE). Both circumferential strain and radial strain were significantly weaker in the segments without LGE than control segments; however, the variation of circumferential strain was sufficiently small to the variation of radial strain.

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Fig. 5: 27-year-old patient with ventricular tachycardia (LVEF = 58.2%). The peak circumferential strain of lateral wall and inferoseptum (yellow arrow and asterisk) were regionally impaired while no bright LGE was detected in any segments.

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Conclusion

Despite apparently preserved LV systolic function and unenhanced myocardium on LGE, impairment of Ecc and Err was found in patients with HFP EF and ventricular arrhythmias. However, the difference in Ecc was more significant with small variation. A recent study of two-dimensional strain imaging by echocardiography suggested that the mean peak Ecc was associated with early impairment of LV function more than the mean peak Err [10]. Similar to the previous studies, our result indicated that Ecc could be more sensitive parameter to reflect the subclinical disease than Err. Since the number of our study population was relatively low, further investigation is required in larger population.

In conclusion, Ecc using MR tagging has a potential to detect early myocardial damages, which cannot be detected by conventional CMR analysis.
References


