Tissue Cardiovascular Magnetic Resonance Demonstrates Regional Diastolic Dysfunction in Remote Tissue Early After Inferior Myocardial Infarction

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ABSTRACT

Purpose: To investigate regional diastolic and systolic function using tissue cardiovascular magnetic resonance (CMR), early after transmural myocardial infarction of the inferior wall due to single proximal right coronary artery disease. Materials and Methods: Velocity encoded CMR was used to measure early diastolic transmitral flow velocity (E), and regional, longitudinal, myocardial systolic (Sa) and early diastolic (Ea) velocities (tissue CMR) in 15 patients with a recent transmural inferior myocardial infarction and in 15 age and LV-mass index matched control subjects. An unpaired two-tailed t test was used to assess significance of continuous variables. Results: Global systolic (ejection fraction 46 ± 7% versus 57 ± 4%, p = 0.000052) and global diastolic LV function (average Ea of infarcted or inferior, remote or anterior, adjacent or septal and lateral myocardium 6.8 ± 1.7 cm/s versus 10.4 ± 1.5 cm/s, p = 0.0000012) were impaired in patients as compared to controls. Regional systolic and diastolic LV velocities were impaired in infarcted and adjacent tissue in patients. However, in remote or anterior tissue, systolic velocities were preserved (Sa 6.6 ± 2.0 cm/s versus 6.8 ± 1.4 cm/s, p = 0.70), but diastolic velocities were impaired in patients as compared to controls (Ea 7.2 ± 2.3 cm/s versus 10.2 ± 2.5 cm/s, p = 0.0026). Conclusions: Regional diastolic velocities early after inferior myocardial infarction are impaired in the infarcted, adjacent and remote tissue, but regional systolic velocities are preserved in remote tissue.

INTRODUCTION

Impairment of global diastolic left ventricular (LV) function following myocardial infarction is related to LV remodeling (1) and is a predictor of cardiac death (2). Diastolic dysfunction is an early marker of disease. In myocardial infarction of the inferior wall, regional LV diastolic function, the relation between regional and global diastolic function, and the relation between regional diastolic and systolic function is largely unknown. Myocardial infarction of the anterior wall causes impaired regional function in both infarcted, adjacent and remote myocardium (3, 4). Myocardial infarction of the inferior wall exhibits a smaller functional loss when compared to similar sized myocardial infarction of the anterior wall (5, 6). Therefore, we hypothesized that in myocardial infarction of the inferior wall, regional diastolic velocities of the remote tissue are impaired, while regional systolic velocities are preserved. Velocity encoded cardiovascular magnetic resonance (CMR) with low (30 cm/s) velocity encoding (tissue CMR) allows measurement of regional myocardial velocities (7–9).

The purpose of the present study was to investigate regional diastolic and systolic function using tissue CMR, early after transmural myocardial infarction of the inferior wall due to single vessel proximal right coronary artery disease.


METHODS

Subjects and study design

The study protocol was approved by the medical ethical committee, and all patients gave written informed consent before participation. Patients with a first acute q-wave myocardial infarction of the inferior wall and single proximal, dominant right coronary artery disease were included in the present study. All patients underwent percutaneous coronary intervention of the culprit lesion within 6 hours of the acute event and received treatment with beta-blockers and angiotensin-converting enzyme inhibitors. Patients with a contraindication for CMR, irregular heart rate, hypertension or diabetes mellitus were excluded. The data were compared with age and LV-mass index matched control subjects.

CMR measurements

CMR studies were performed using a Sonata MR scanner and a 12 channel Body Array surface coil (Siemens, Erlangen, Germany). The entire heart was imaged in the short-axis orientation with a breath-hold cine steady-state free precession technique (TrueFISP imaging) (9).

Late gadolinium enhancement (LGE) was studied 15 minutes after intravenous bolus injection of 0.2 mmol/kg gadolinium-DTPA (Magnevist, Schering, Berlin, Germany). The entire heart was imaged in short-axis orientation using a TrueFISP sequence (10).

Transmitral flow was acquired using a retrospective electrocardiographically triggered Flash phase-contrast CMR technique with a velocity sensitivity of 130 cm/s, as described before (9). In order to cover late diastolic filling, acquisition was performed throughout the cardiac cycle with a retrospective period of 1.2. Imaging parameters included the following: 30/3.2 (repetition time ms/echo-time ms), 5-mm section thickness, 240 × 256 matrix, 380 × 380 mm field of view, 1.6 × 1.5 mm in-plane spatial resolution and 30° flip angle. Two signals were averaged and temporal resolution was 16 to 18 ms.

Regional LV velocities were assessed by repeating this phase-contrast CMR sequence with a velocity encoding of 30 cm/s (tissue CMR) and the slice positioned during early diastole at 2/3 of the long-axis of the interventricular septum perpendicular to tissue movement as described previously (9) and encompassing the infarct area.

CMR image analysis

Offline analysis of short-axis images was performed using MASS analytical software (Medis, Leiden, The Netherlands). From the volume-versus-time curves, LV peak filling rate and time to peak filling rate were calculated (11). LV wall motion was assessed visually by two observers (B.P and H.J.L., 8 years and more than 15 years of experience in cardiac CMR, respectively) working together in consensus. Each segment was scored in a 17-segment model (12) using a 4-point scale (1 = normal wall motion, 2 = hypokinesia, 3 = akinesia, 4 = dyskinesia) (13). For each patient a wall motion score index was calculated as the sum of scores divided by the number of total segments.

The transmural extent of LGE was scored using the 17-segment model (13). Transmurality in each segment was visually assessed (B.P. and H.J.L. in consensus) on a 5-point scale: 0 = no hyperenhancement; 1 = 1–25% hyperenhanced; 2 = 26–50% hyperenhanced; 3 = 51–75% hyperenhanced, and 4 = 76–100% hyperenhanced (14). For each patient, a myocardial transmurality index was calculated as the sum of segmental scores divided by the number of segments. A transmurality index in the right coronary artery territory or inferior transmurality index was assessed separately as the sum of LGE score divided by 5 segments assigned to the right coronary artery (basal and mid inferior segments, basal posteroseptal, basal posterior and apical inferior segments). The extent of myocardial damage was traced and calculated using MASS analytical software package and expressed as percentage of total LV mass (Medis, Leiden, The Netherlands) (15).

From the transmitral flow curves, early (E) and late (A) LV filling velocity and E/A ratio was determined (9). Analysis of longitudinal myocardial tissue velocities was done offline by one author (B.P.). A standardized circular region of interest (ROI) of 20 pixels was placed at different locations in the LV myocardium (Fig. 1). The measured myocardial regions were: inferior (= infarcted); lateral and septal (= adjacent); and anterior (= remote). The ROI was traced on the modulus image, adjusted in each phase for cardiac motion and was transferred to the paired phase image, using the FLOW analytical software package (Medis, Leiden, The Netherlands). For each ROI, peak systolic velocity (Sa) and peak early diastolic velocity (Ea) was measured (Fig. 1). Regional velocities were measured in the same standardized ROI position in control subjects. In addition, average early diastolic longitudinal tissue velocity of infarcted, adjacent and remote myocardium or average Ea was calculated as a measure of global diastolic LV function.

Statistical analysis

Data are presented as mean ± SD. An unpaired two-tailed t test was used to compare parameters between patients and control subjects. Significance was set at p < 0.05. All statistical analyses were performed by using computer software (SPSS for Windows, version 12.0; SPSS, Chicago, Illinois, USA).

RESULTS

Fifteen consecutive patients (male/female: 12/3) were included. Maximal creatine kinase MB was 224 ± 147 ng/mL. CMR was performed at 6 ± 3 days (range 2–12 days) after acute myocardial infarction.

Fifteen control subjects (male/female: 10/5) were normal at clinical examination, without a history of cardiovascular disease and without any complaints. The age of patients (52 ± 5 years) and healthy subjects (48 ± 6 years) was matched (p = 0.10). Subjects were normotensive, patients with a mean blood pressure of 89 ± 8 mm Hg, and healthy subjects with a mean
blood pressure of 89 ± 13 mm Hg (p > 0.99). Heart rate was 67 ± 9 beats/min and 74 ± 15 beats/min (p > 0.18) for patients and control subjects, respectively.

**Global left ventricular morphology and function**

The culprit lesion was located in the proximal segment of the right coronary artery and after percutaneous intervention TIMI 3 flow was obtained. All patients had a transmural myocardial scar located in the LV inferior wall (including basal and mid segments of the inferior wall) (Table 1). Parameters of global LV systolic and diastolic function are shown in Table 1.

Global systolic LV function was depressed in the patients as compared to control subjects (ejection fraction: 46 ± 7% versus 57 ± 4%, p = 0.000052). Global diastolic LV function was impaired in patients as compared to controls, as indicated by impaired LV filling (peak filling rate: 301 ± 98 mL/s versus 430 ± 63 mL/s, p = 0.00026; time to peak filling rate: 238 ± 138 ms versus 152 ± 25 ms, p = 0.032), impaired average Ea (6.8 ± 1.7 cm/s versus 10.4 ± 1.5 cm/s, p = 0.0000012), and increased E/posteroseptal Ea (12.5 ± 4.0 versus 8.8 ± 5.3, p = 0.00030). E/A was not different between patients and controls.

**Regional left ventricular function**

Regional systolic velocities were reduced in patients as compared to controls, in the infarcted myocardium (inferior Sa: 5.5 ± 1.4 cm/s versus 7.5 ± 1.9 cm/s, p = 0.002), and adjacent myocardium (Table 2). Regional systolic velocities were preserved in the remote myocardium (remote Sa patients: 6.6 ± 2.0 cm/s versus remote Sa controls: 6.8 ± 1.4 cm/s, p = 0.70).

Regional diastolic LV velocities were impaired in patients in infarcted myocardium (Ea: 5.7 ± 2.0 cm/s versus 9.2 ± 2.8 cm/s,
Table 1. Scar Tissue, Global Systolic and Diastolic Left Ventricular Function

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients with Myocardial Infarction (n = 15)</th>
<th>Control Subjects (n = 15)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmurality index</td>
<td>0.88 ± 0.3</td>
<td>0</td>
<td>0.0000006</td>
</tr>
<tr>
<td>Inferior transmurality index</td>
<td>3.0 ± 1</td>
<td>0</td>
<td>0.00000054</td>
</tr>
<tr>
<td>Scar tissue (%)</td>
<td>27 ± 8</td>
<td>71 ± 11</td>
<td>0.080</td>
</tr>
<tr>
<td>Mass index (g/m²)</td>
<td>81 ± 17</td>
<td>71 ± 11</td>
<td>0.019</td>
</tr>
<tr>
<td>End-diastolic volume/BSA (mL/m²)</td>
<td>86 ± 20</td>
<td>72 ± 8</td>
<td></td>
</tr>
<tr>
<td>End-systolic volume/BSA (mL/m²)</td>
<td>48 ± 6</td>
<td>31 ± 5</td>
<td>0.0019</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>46 ± 7</td>
<td>57 ± 4</td>
<td>0.000052</td>
</tr>
<tr>
<td>Stroke index (mL/m²)</td>
<td>39 ± 7</td>
<td>40 ± 4</td>
<td>0.48</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>2.8 ± 0.4</td>
<td>3.6 ± 0.8</td>
<td>0.0028</td>
</tr>
<tr>
<td>Wall motion score index</td>
<td>1.5 ± 0.3</td>
<td>1</td>
<td>0.0000089</td>
</tr>
<tr>
<td>Peak filling rate (mL/s)</td>
<td>301 ± 98</td>
<td>430 ± 63</td>
<td>0.00026</td>
</tr>
<tr>
<td>Time to peak filling rate (ms)</td>
<td>238 ± 138</td>
<td>152 ± 25</td>
<td>0.032</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>74 ± 21</td>
<td>76 ± 19</td>
<td>0.83</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>56 ± 14</td>
<td>51 ± 8</td>
<td>0.23</td>
</tr>
<tr>
<td>E/A</td>
<td>1.4 ± 0.4</td>
<td>1.5 ± 0.5</td>
<td>0.34</td>
</tr>
<tr>
<td>Average Ea (cm/s)</td>
<td>6.8 ± 1.7</td>
<td>10.4 ± 1.5</td>
<td>0.0000012</td>
</tr>
<tr>
<td>E/posteroseptal Ea</td>
<td>12.5 ± 4.0</td>
<td>8.8 ± 5.3</td>
<td>0.00030</td>
</tr>
</tbody>
</table>

All values are mean ± SD. Parameters of scar tissue, global systolic and diastolic function were determined by magnetic resonance. A = peak mitral velocity at atrial contraction; BSA = body surface area; E = peak transmitral velocity in early diastole, Ea = early diastolic tissue velocity; average Ea represents average Ea of all regions (infarcted, adjacent and remote).

DISCUSSION

In the present study, clinical application of tissue CMR demonstrated that early after reperfused transmural myocardial infarction of the inferior wall, regional longitudinal diastolic velocities were impaired in the infarcted, adjacent and remote tissue, whereas regional longitudinal systolic velocities were preserved in remote tissue.

Table 2. Regional Systolic and Diastolic Left Ventricular Function

<table>
<thead>
<tr>
<th>Region</th>
<th>Patients</th>
<th>Controls</th>
<th>Patients</th>
<th>Controls</th>
<th>(Difference) between regional Ea and average Ea (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior</td>
<td>5.5 ± 1.4</td>
<td>7.5 ± 1.9</td>
<td>5.7 ± 2.0</td>
<td>9.2 ± 2.8</td>
<td>−16 ± 18</td>
</tr>
<tr>
<td>Lateral</td>
<td>7.3 ± 1.7</td>
<td>8.8 ± 2.0</td>
<td>8.0 ± 3.2</td>
<td>12.6 ± 3.0</td>
<td>16 ± 31</td>
</tr>
<tr>
<td>Septal</td>
<td>5.6 ± 1.2</td>
<td>8.5 ± 2.3</td>
<td>6.3 ± 1.8</td>
<td>9.8 ± 2.6</td>
<td>−5 ± 24</td>
</tr>
<tr>
<td>Anterior</td>
<td>6.6 ± 2.0</td>
<td>6.8 ± 1.4</td>
<td>7.2 ± 2.3</td>
<td>10.2 ± 2.5</td>
<td>6 ± 17</td>
</tr>
<tr>
<td>Average</td>
<td>6.3 ± 1.0</td>
<td>8.6 ± 1.3</td>
<td>6.8 ± 1.7</td>
<td>10.4 ± 1.5</td>
<td>NA</td>
</tr>
</tbody>
</table>

All values are mean ± SD. E = peak transmitral velocity in early diastole; Ea = peak early diastolic tissue velocity; average Ea represents average Ea of all regions (infarcted, adjacent and remote); Sa = peak systolic tissue velocity. NA = non applicable.

Unpaired two-tailed Student t test control subjects versus patients. Percent difference with average Ea was not significant between control subjects and patients.
Recently, quantification of regional myocardial function by measurement of myocardial velocities and by measurement of myocardial deformation or strain has been made possible. Myocardial velocities can be measured by tissue Doppler imaging and tissue CMR (7–9). Myocardial strain can be measured by a tissue Doppler imaging-based modality: strain Doppler echocardiography or strain rate imaging (16, 17) and by CMR tagging (18). The analysis of remote myocardial function has mainly been focused on anterior myocardial infarction (5, 19), demonstrating reduced longitudinal velocities using tissue Doppler imaging (20), impaired strains (3, 21) and strain rates (22, 23) in the remote myocardium using strain rate imaging and CMR tagging.

In this study, regional longitudinal function was assessed in the early phase after myocardial infarction of the inferior wall. For this purpose, longitudinal myocardial velocities were measured using tissue CMR.

In the presently studied patients with myocardial infarction of the inferior wall, regional longitudinal systolic LV velocities (Sa) were preserved in the remote myocardium. In myocardial infarction of the anterior wall however, tissue Doppler imaging data have shown reduced myocardial velocities (20), and CMR tagging data have shown impaired longitudinal LV shortening in the noninfarcted myocardium (3, 4). In the presently studied patients with myocardial infarction of the inferior wall, only longitudinal diastolic LV velocities (Ea) of both the adjacent and the remote myocardium were found impaired. Longitudinal ventricular motion is mainly determined by the oblique clockwise oriented myocardial fibers in the subendocardium (24, 25). The circumferentially wrapped cardiac fibers in the middle layer and the oblique anticlockwise oriented cardiac fibers in the subepicardial layer mainly contribute to circumferential and radial function (26). During LV filling the ventricle expands radially and longitudinally. Diastolic dysfunction is known to be a sensitive and early marker of myocardial disease (22, 27). In contrast to the subepicardial myocardium, the function of the subendocardial myocardium is especially sensitive and prone to ischemia (28, 29). Therefore, impairment of longitudinal diastolic velocities in the adjacent and remote myocardium may be an early sign of myocardial dysfunction. Although myocardial infarction of the inferior wall exhibits a smaller functional loss as compared to similar sized myocardial infarction of the anterior wall, impact on the remote region may be apparent from regional diastolic dysfunction.

Regional myocardial velocities are, however, not only determined by the function of the segment under investigation but also by traction and tethering from other myocardial segments and by translational motion of the entire heart (16). Motion of the heart base is basically the resultant sum of longitudinal motion between apex and base of the heart. Therefore, reduction of velocities in these basal segments does not always mean reduction in function of these segments. In the presently studied patients, reduction of myocardial velocities in the remote region during diastole might represent myocardial tethering. Myocardial deformation (strain) and rate of deformation (strain rate) are less influenced by cardiac translation and motion due to tethering from other segments. Assessment of strain rate in future research by using CMR tagging may overcome the limitations of velocity measurement (17).

Within hours of cardiomyocyte injury, infarct expansion results in wall thinning and ventricular dilatation causing elevation of systolic and diastolic wall stress (30). Increased wall stress stimulates adaptive hypertrophy and alterations in both the infarcted and surrounding non-infarcted ventricular myocardium architecture in order to distribute wall stresses more evenly. Late remodeling (beyond 72 hours) is characterized by distortion of the LV shape and hypertrophy in the remote myocardium. Increased remodeling and strain alterations in the non-infarcted myocardium have been related to the extent of microvascular obstruction within infarcted regions (31). Therefore, both the tethering effect of the infarcted myocardium and regional alterations in wall stress (5, 31, 32), together with reduced coronary vasodilation (31) might explain reduction of function in the adjacent and remote myocardium. Due to smaller impact on global LV function in patients with myocardial infarction of the inferior wall, only moderate LV remodeling (5, 6) and therefore moderately increased LV end diastolic volumes were found in the present study.

Global diastolic dysfunction and impaired relaxation was apparent in patients from the functional LV volumes showing a reduced LV peak filling rate and a prolonged LV time to peak filling rate. Posteroseptal Ea and average Ea which represent the net velocity changes of the heart during early diastole in LV long-axis dimension relate to the rate of myocardial relaxation (33). The transmitral flow pattern, including E/A ratio (1.5 ± 0.5 versus 1.4 ± 0.4 in patients, p > 0.05), however, was similar between control subjects (34, 35) and patients. Since posteroseptal Ea and average Ea were found to be reduced, the “normal” transmitral flow pattern in patients was most likely pseudonormal (9, 33).

In addition, dysfunction of the early diastolic longitudinal LV motion of both infarcted and non-infarcted myocardium might have contributed to global LV diastolic dysfunction. There was a mild increase in the relative contribution of the remote region to global early diastolic long-axis velocity (= average Ea). The remote region is relatively small, and this contribution was not statistically significantly different. Therefore, relative segmental contribution to global diastolic LV function in patients was similar to the segmental distribution in control subjects. Since early diastolic long axis LV motion precedes transmitral flow and influences LV filling (36), depressed longitudinal LV motion of infarcted, adjacent and remote myocardium affects LV filling due to decreased elastic recoil and impaired diastolic suction (37).

**CONCLUSIONS**

Assessment of regional velocities after myocardial infarction is feasible using tissue CMR. Regional diastolic velocities early after inferior myocardial infarction are impaired in the infarcted, adjacent and remote tissue. However, regional systolic velocities are preserved in remote tissue. Therefore, impairment of regional diastolic velocities can be an early marker of dysfunction in remote tissue after inferior myocardial infarction.
REFERENCES


