Tissue Doppler strain-mapping in the assessment of the extent of chronic myocardial infarction: validation using magnetic resonance imaging

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Aims The distribution of myocardial strain values can be visualized by colour-coded strain images. We examined for the first time if this strain-mapping function can be used to study the extent of prior myocardial infarction.

Methods and results Echocardiography and cardiac magnetic resonance imaging with delayed contrast enhancement were performed in 26 patients with chronic myocardial infarction. Two-dimensional strain images of the left ventricle were obtained in all standard apical views. Myocardial segments (n = 416) were assigned a score ranging from one to four based on the strain-coded colour of the segment, with higher scores representing worse myocardial function. Strain-mapping scores and quantitative strain values averaged, respectively, 1.3 ± 0.6 and 2 ± 16.4 ± 7.6% in segments without infarction, 1.7 ± 1.0 and 2 ± 15.0 ± 8.6% in non-transmural infarctions, and 2.8 ± 1.2 and 2 ± 6.5 ± 8.6% in transmural infarctions. Strain-mapping had a sensitivity of 60% and a specificity of 95% in detecting segments with transmural myocardial infarction. Corresponding values for echocardiographic wall motion analysis were 50 and 96%. Strain-mapping was possible in 80% of the segments and inter-observer agreement was substantial (κ = 0.63).

Conclusion Strain-mapping is a clinically applicable method for the assessment of regional myocardial function in post-myocardial infarction patients. Strain-mapping has reasonable feasibility and is more sensitive in detecting infarction damage than routine wall motion analysis.

KEYWORDS
Myocardial strain; Tissue Doppler imaging; Myocardial infarction; Cardiac magnetic resonance imaging; Delayed contrast enhancement

Introduction

Assessment of irreversible myocardial injury is important in clinical practice in patients who have suffered an ischaemic event. Cardiac magnetic resonance imaging with delayed contrast enhancement (DE-CMR) is the best reference technique for the evaluation of myocardial viability in chronic ischaemic heart disease, as it allows direct visualization of the transmural extent of necrotic non-viable tissue.1–3 Echocardiography is more readily available for the assessment of myocardial function than cardiac magnetic resonance imaging (CMR), but traditional wall motion analysis suffers from poor sensitivity in detecting myocardial contraction abnormalities.

Strain imaging is a relatively new echocardiographic method for the evaluation of regional myocardial function. Strain imaging has been validated in both animal models using sonomicrometry4 and in human trials with tagged magnetic resonance imaging.5 Strain measures deformation of a myocardial segment over time and is calculated using tissue velocity data. By convention, lengthening is expressed as a positive strain value and shortening as a negative value.6,7

Representation of myocardial strain values as colour-coded strain images is available as a real-time imaging mode in modern echocardiographic systems.8 Shortening of the myocardium is encoded in red and lengthening in blue. Infarcted myocardium shows no or reduced systolic strain, which is displayed in grey. Online analysis of these two-dimensional colour maps allows an easy and rapid estimation of regional myocardial function, in the authors’ experience.
However, strain-mapping has not previously been validated in a clinical study.

The objective of the present study was to investigate whether strain-mapping could be used in the assessment of the extent of myocardial damage in post-myocardial infarction patients using DE-CMR as reference. Previous studies suggest that quantitative strain analysis can distinguish between non-infarct and infarct segments as well as determine the transmural extent of infarction. Strain-mapping offers the advantages of strain imaging in being a quantitative and objective method in comparison with standard wall motion analysis, and in addition might serve the clinician as a useful screening tool of regional myocardial function.

Methods

Patients

Twenty-six patients admitted for acute coronary syndrome to the coronary care unit of Helsinki University Central Hospital were recruited prospectively to this study. Inclusion criteria were prolonged chest pain within 48 h of recruitment with associated ischaemic ECG changes and/or elevated cardiac enzymes (CK-MB > 7 μg/L and/or TnT > 0.03 μg/L). Exclusion criteria were atrial fibrillation, pacemaker rhythm, bundle branch block, and the need for ventilatory support. The 22 invasively treated patients were revascularized 5–10 months before the imaging for this study: 17 patients had percutaneous coronary intervention within the first day of admission and five patients had CABG 1–121 days after the acute event. Four of the patients with ST-elevation MI were treated with thrombolysis alone. Baseline characteristics are presented in Table 1.

The 26 patients included in the study underwent echocardiography with standard B-mode and strain imaging 6–12 (7.7 ± 1.4) months after the index event. None of the patients suffered from new ischaemic events before imaging. Cardiac magnetic resonance imaging with delayed contrast enhancement was possible in 24 of the 26 patients (one patient got an ICD after inclusion, one patient refused). The time interval between echocardiography and DE-CMR was 12 ± 7 days. The patients gave their written informed consent. The study was approved by the ethics committee of the Helsinki University Central Hospital and complies with the Declaration of Helsinki.

Echocardiography

Echocardiographical data were acquired by second generation coded harmonic imaging using a Vivid 7 ultrasound scanner (GE Medical Systems, Horten, Norway) and a 1.5–4.0 MHz phased array transducer (M3S). Images were analysed off-line on a personal computer using EchoPAC software provided by GE. Two-dimensional images of the heart were obtained in all standard apical views (two-chamber, three-chamber, and four-chamber views), and for B-mode analysis in short axis views as well. For the analysis of regional myocardial function, the left ventricle was divided into 16 segments according to the model defined by the American Heart Association and the American Society of Echocardiography. Regional myocardial systolic function was assessed by longitudinal strain analysis from Tissue Doppler registrations and by wall motion analysis in B-mode assigning each segment a wall motion score (WMS) from 1 to 4 according to the recommendations (1, normokinesia; 2, hypokinesia; 3, akinesia; 4, dyskinesia). Tissue Doppler loops were recorded from the apical views by limiting the imaging sector to one myocardial wall at a time (sector angle 30°). The tissue velocity scale was adjusted to avoid aliasing (pulse repetition frequency 1.00–1.5 kHz). The frame rate varied between 202 and 248 frames per second. Patients were asked to stop breathing if needed in order to hold the myocardial wall in the centre of the imaging sector during three consecutive heartbeats. Segments were excluded from analysis if the angle between the ultrasound beam and the myocardial wall exceeded 30°. Segments with artefacts or bad quality grey-scale data were also excluded.

For strain-mapping analysis, tissue Doppler data were displayed as two-dimensional colour-coded strain images. We analysed these colour maps using two different strain scales (±15 and ±30%) with positive strain values encoded in blue and negative strain values encoded in grey if less negative than −6 or −12% using scale ±15 or ±30%, respectively, and red if more negative. Each segment was assigned a score from 1 to 4 according to the colour exceeding 50% of the segment (Figure 1A and B). Strain-mapping score 1 (representing strain values < −12%) was assigned to red segments using scale ±30%, score 2 (strain −6 to −12%) to segments that were grey using scale ±30% and red using scale ±15%, score 3 (strain 0 to −6%) to grey segments using scale ±15%, and score 4 (strain >0%) to blue segments. We chose these strain scales based on previous studies assuming that strain values less negative than −12% should be abnormal, and strain values less negative than −6% should be severely abnormal.

Quantitative strain values were obtained by placing the sample volume in the middle of each segment (Figure 1C). The default strain length of 12 mm was used. The strain profiles of three consecutive heartbeats were averaged and the end-systolic strain value was reported. End-systole was defined by aortic valve closure.

Cardiac magnetic resonance imaging

Cardiac magnetic resonance imaging was performed on a 1.5 T scanner (Sonata, Siemens Medical Solutions, Erlangen, Germany). Cardiac magnetic resonance imaging with delayed contrast enhancement (Figure 1D) was used as the reference technique for determining the location and the transmural extent of the myocardial infarction. Cine magnetic resonance imaging was used for wall motion analysis. The location of the myocardial infarction as defined by the presence of delayed contrast enhancement (DE) was determined independently by two observers. In addition, one of the observers assessed the maximal transmural extent of the

<table>
<thead>
<tr>
<th>Table 1 Patient baseline characteristics</th>
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<tbody>
<tr>
<td><strong>Patients</strong></td>
</tr>
<tr>
<td>Number: 26</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td>61 ± 9.6 (range 44–78)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
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<tr>
<td>27 ± 4.8</td>
</tr>
<tr>
<td><strong>History of CAD</strong></td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td><strong>Previous MI</strong></td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td><strong>DM II</strong></td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td><strong>Dyslipidaemia</strong></td>
</tr>
<tr>
<td>20</td>
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<tr>
<td><strong>Electrocardiograph</strong></td>
</tr>
<tr>
<td>59 ± 9%</td>
</tr>
<tr>
<td><strong>Q-waves in ECG</strong></td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td><strong>Maximal CK-MBm (µg/L)</strong></td>
</tr>
<tr>
<td>170 ± 144 (range 32–612)</td>
</tr>
<tr>
<td><strong>Culprit artery</strong></td>
</tr>
<tr>
<td>LAD: 15</td>
</tr>
<tr>
<td>RCA: 9</td>
</tr>
<tr>
<td>LCX: 2</td>
</tr>
</tbody>
</table>

Data are presented as number or mean ± SD.

aCalculated by Simpson’s rule.

bApparent in coronary angiogram in 24 patients, two determined on the basis of changes in ECG and echocardiogram only. CAD, coronary artery disease; DM II, diabetes mellitus type II; ECG, electrocardiogram; MI, myocardial infarction; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.
infarction and two experienced radiologists performed the visual assessment of the myocardial wall motion blinded from the results from the DE analysis.

Cardiac magnetic resonance imaging with delayed contrast enhancement was performed 10–15 min after a bolus injection of 0.2 mmol/kg of contrast agent (gadodiamide, Omniscan TM, GE Healthcare). A stack of left ventricular short axis images was scanned using a breath-hold T1-weighted segmented inversion-recovery turbo-FLASH sequence. Inversion time to null the signal from normal myocardium was 250–300 ms, repetition time 8.6 ms, echo time 4.3 ms, matrix 256 x 256, section thickness 8 mm, and intersection gap 20% were used. The cine magnetic resonance image series were obtained with retrospectively ECG-gated segmented steady-state free precession imaging and the following parameters: echo time 1.51 ms, repetition time 3.0 ms, flip angle 52°, matrix 256 x 256, field of view 240 x 340 mm, section thickness 6 mm, and temporal resolution 44–47 ms.

Cardiac magnetic resonance image analysis was performed using the same 16-segment model as for echocardiography. The extent of the scar in each segment was assessed as the percentage of DE of the wall thickness. Global infarction percentage was calculated by averaging the scar extent in all segments of the left ventricle. The segments were divided into five groups according to the transmural extent of DE: 0; 1–25; 26–50; 51–75; and 76–100%. The segments were also assigned a WMS depending on the degree of wall motion disturbance: 1, normokinesia; 2, hypokinesia; 3, akinesia; and 4, dyskinesia. Non-transmural infarcts were defined as segments with DE 1–50% showing normo- or hypokinesia by wall motion analysis (n = 32) and transmural infarcts as segments with DE >50% showing hypo-, a- or dyskinesia (n = 32).

**Statistical analysis**

Continuous parameters are expressed as mean ± SD. Strain values were tested for normal distribution and compared by the use of analysis of variance (ANOVA) with Bonferroni procedure for multiple comparisons. Strain-mapping scores were compared by the use of the Kruskal-Wallis H-test and Mann-Whitney U-test with Bonferroni correction of P-values. Correlation analysis between global strain-mapping scores, global strain scores, and global infarction percentage was performed using two-tailed Pearson’s correlation. A P-value of <0.05 was considered statistically significant. Inter-observer agreement for strain-mapping was tested by the coefficient of agreement ‘kappa’, calculated over the segments of 10 randomly chosen patients analysed independently by two observers. All statistical calculations were done by SPSS 14.0 statistical software.

**Results**

**Cardiac magnetic resonance images**

Left ventricular infarction was demonstrated with DE-CMR in 21 of 24 patients imaged. The average number of infarction
segments was 4.0 ± 3.2 per patient (range 1–12). A total of 384 segments were analysed for the presence of infarction by DE-CMR by two independent observers. The results of the two observers were concordant in 366 (95%) of the segments (κ = 0.86): DE was present in 90 (25%), absent in 269 (73%), and not possible to assess in 7 (2%) of the segments. Wall motion analysis by CMR was possible in 81 (90%) of the segments with infarction by DE-CMR. According to the pre-specified criteria 64 segments with either non-transmural or transmural infarction were identified. Wall motion was normokinetic in all of the 262 (98%) segments without infarction available for wall motion analysis. Wall motion analysis was impossible in one patient with ventricular extrasystole during CMR registration.

Strain-mapping scores and quantitative strain values

Of a total of 416 segments, 333 (80%) had sufficient image quality for strain-mapping analysis. Strain-mapping was possible in 134 basal (86%), 129 mid (83%), and 70 apical (67%) segments. End-systolic strain values could be measured in 331 (99%) of the segments analysed by strain-mapping. There was substantial inter-observer agreement for strain-mapping scores: the coefficient of agreement ‘kappa’ was 0.63 between two observers.

The strain values increased with increasing strain-mapping scores with minor overlapping between any of the four groups (Figure 2A). Global strain-mapping and strain scores were calculated in each patient by averaging strain-mapping scores and quantitative strain values, respectively, of all the left ventricular segments. There was a significant correlation between these global scores (Figure 2B).

Assessment of the extent of infarction by strain-mapping

Strain-mapping scores increased with increasing segmental extent of DE. Correspondingly, the quantitative strain values and the WMS were worse in the segments with greater transmurality of the infarction (Table 2). Strain-mapping scores and absolute strain values were significantly different (P < 0.006) in the segments with transmural infarction in comparison with the segments with non-transmural or no infarction (Figure 3). However, there was not a statistically significant difference between the segments without infarction and the segments with non-transmural infarction with either method. Conversely, the extent of DE increased with increasing strain-mapping scores and was significantly higher (P < 0.001) in segments with strain-mapping scores 3 and 4 than in segments with strain-mapping scores 1 and 2. Accordingly, quantitative strain values deteriorated with increasing strain-mapping scores in parallel with worsening WMS assessed by B-mode echocardiography and CMR imaging (Table 3).

The average global infarction percentage was 14 ± 11%. There was a significant correlation between the global

![Figure 2](image-url) Comparison of strain-mapping scores and quantitative strain analysis. (A) Quantitative strain values (mean ± SD) in 331 segments according to the strain-mapping scores 1–4 (score 1: n = 210; score 2: n = 76; score 3: n = 18; score 4: n = 27). (B) The correlation between global strain-mapping and global quantitative strain scores in 26 patients.

<table>
<thead>
<tr>
<th>Extent of DE (%)</th>
<th>n</th>
<th>Strain-mapping score</th>
<th>Strain value (%)</th>
<th>B-mode WMS</th>
<th>CMR WMS</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>262</td>
<td>1.3 ± 0.6</td>
<td>−13.6 ± 9.2</td>
<td>1.1 ± 0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>1–25</td>
<td>11</td>
<td>1.6 ± 1.0</td>
<td>−14.6 ± 8.7</td>
<td>1.5 ± 0.8*</td>
<td>1.3 ± 0.5*</td>
</tr>
<tr>
<td>26–50</td>
<td>21</td>
<td>1.8 ± 1.1</td>
<td>−12.4 ± 10.0</td>
<td>1.5 ± 0.7*</td>
<td>1.6 ± 0.5*</td>
</tr>
<tr>
<td>51–75</td>
<td>13</td>
<td>2.3 ± 1.2*</td>
<td>−7.1 ± 10.2*</td>
<td>1.9 ± 0.9*</td>
<td>2.3 ± 0.5*</td>
</tr>
<tr>
<td>76–100</td>
<td>19</td>
<td>3.1 ± 1.0*</td>
<td>−4.3 ± 6.3*</td>
<td>2.6 ± 1.0*</td>
<td>2.7 ± 0.5*</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. Values that differ significantly (P < 0.036) from the values in segments without DE are marked with an asterisk. CMR, cardiac magnetic resonance; DE, delayed contrast enhancement; WMS, wall motion score.
infarction percentages assessed by DE-CMR and the global strain-mapping scores \((r = 0.758)\) as well as the global strain scores \((r = 0.738)\) (Figure 4).

**Detection of transmural infarctions**

Strain-mapping was feasible in 258 (79%) and B-mode wall motion analysis in 285 (87%) of the 326 segments in which the transmurality of infarction could be defined.

**Sensitivity and specificity**

In order to assess the sensitivity of strain-mapping in discriminating segments with transmural infarction, we regarded strain-mapping scores 3 and 4 as positive test results, as these strain-mapping scores represent strain-values \(> -6\)% considered severely abnormal. Of the segments with transmural infarction, 60% had strain-mapping scores \(> 3\). In comparison, the sensitivity was 50% of B-mode WMS \(> 3\) in detecting transmural infarctions. Of all the segments with a transmural extent of infarction \(> 75\)%, 61% had strain-mapping score 4 and 11% WMS 4 indicating dyskinesia.

For the purpose of determining specificity, the strain-mapping scores 1 and 2 were regarded as negative test results, including segments with strain values \(< -6\)% indicating remaining contractile function. Of the segments without transmural infarction, 95% had strain-mapping score 1 or 2. The specificity was 96% for B-mode WMS \(\leq 2\).
Positive and negative predictive values
Segments with strain-mapping score 3 or 4, corresponding to strain values \(-6\%\) to \(-12\%\), were thought to be severely damaged. Of these segments, 71\% were infarcted and 54\% had transmural infarctions. The positive predictive value was 64\% for B-mode WMS \(\geq 3\) in detecting transmural infarction. Of the segments with strain-mapping score 4 vs. WMS 4 indicating dyskinesia 58\% vs. 50\% had a transmural extent of infarction \(>75\%\).

Segments with strain-mapping score 1 or 2, corresponding to strain values \(-6\%\) to \(-12\%\), were considered to have normal or slightly impaired myocardial contractile function. Of these segments, 96\% did not have transmural infarction. The negative predictive value was 94\% for B-mode WMS \(\leq 2\). Of the segments with strain-mapping score 1 or 2, a great majority had either no infarctions (88 and 81\%, respectively) or non-transmural infarctions (9 and 11\%, respectively).

Discussion
Main findings
In spite of the advantages of quantitative strain and strain rate measurements in the assessment of regional myocardial function, the use of these methods in clinical practice has been hampered by the long time needed to analyse individual segments. In the present study, we validated strain-mapping as a new technique for the assessment of regional myocardial function, possessing the advantages of strain analysis as well as providing the clinician with a quick overview of the areas with abnormal systolic function in the left ventricle. We found that strain-mapping can equally well with quantitative strain values distinguish segments with transmural infarction from segments with non-transmural or no infarction and provide an estimate of the size of the infarction. Strain-mapping scores were in agreement with quantitative strain values and the feasibility and inter-observer variability of strain-mapping was reasonably good. The strain-mapping analysis was most difficult to perform in the apical segments with a feasibility of 67\%. This may affect the identification of infarctions caused by peripheral occlusions in the coronary arteries.

Assessment of the infarction scar
It has earlier been demonstrated that radial strain values correlate with the histologically confirmed transmural extent of the infarct scar in pigs.\(^8\) Supporting these data, we found a progressive increase in strain-mapping scores with increasing segmental extent of infarction transmurality. Strain-mapping scores were significantly higher in segments with transmural infarction than in segments with non-transmural or no infarction suggesting that strain-mapping can differentiate viable from non-viable myocardial segments. We also calculated global strain-mapping scores that increased progressively with increasing global infarction percentage, providing a fair estimate of the size of infarction. In our study, strain-mapping performed as well as quantitative strain analysis in the assessment of the segmental transmurality and the global size of the infarction. Our results are in agreement with two recent clinical studies showing that quantitative longitudinal strain measurements are able to differentiate myocardial segments with variable transmural extent of infarction and are useful in assessing the global size of the infarction.\(^11,12\)

Assessment of left ventricular regional systolic function by standard B-mode wall motion analysis from two-dimensional grey-scale images has been found somewhat inaccurate. The reduction in wall motion was not proportional to the percentage of necrosis in an animal study.\(^18\) and in a clinical study, the WMS index was not related to infarct transmurality as defined by DE-CMR.\(^19\) In our study, we found that strain-mapping could demonstrate remaining contractile function with excellent specificity (95\%) and was superior to B-mode analysis in the detection of transmural infarctions; the sensitivities were 60 and 50\%, respectively. Our findings suggest that strain-mapping is especially useful in detecting dyskinesia, as strain-mapping found dyskinesia in 61\% of the segments with transmural extent of infarction \(>75\%\) and wall motion analysis in only 11\%. Previously, it has been shown that also visual assessment of strain rates by curved M-mode analysis was better than B-mode wall motion analysis for detecting myocardial infarction segments using nuclear imaging as reference.\(^20\)

Implementation of strain-mapping in clinical practice
We found that strain-mapping scores 1 and 2 (corresponding to strain values \(-6\%\) to \(-12\%\)) indicate that the segment is viable. A majority of these segments (96\%) did not have any infarctions at all.

Most of the myocardial segments with strain-mapping score 2 did not have any infarctions, although corresponding strain values \(-6\%\) to \(-12\%\) should be abnormal, as mean strain values in healthy subjects have varied between \(-15\%\) and \(-23\%).\(^5,9,11,15,16\) However, a proportion of the segments might be within normal variation, as strain values have been reported to range between \(-9\%\) and \(-30\%\) in normal healthy subjects.\(^5\) An abnormal strain value in segments without infarction could also be explained by other reasons causing impairment of myocardial function. Our study population represented typical patients admitted to the coronary care unit for acute coronary syndrome, many of the patients had hypertension and some of the patients were obese, factors that have been shown to be associated with impaired strain values.\(^21,22\)

Strain-mapping scores \(\geq 3\) (corresponding to strain values \(-6\%\) to \(-12\%\)) indicate that the segment is infarcted, and a transmural infarction is more probable than a non-transmural infarction. A strain-mapping score of 4 (corresponding to positive strain values) suggests that the segment is dyskinetic and not viable.

Limitations
In this study, we used DE-CMR as a standard, which has been shown to be an accurate method for detection of infarction scars.\(^1-3\) Radiologists analysed radial slices of the CMR images and strain imaging was performed in longitudinal myocardial segments, as has been done in other studies as well.\(^11,12,19\) This might affect the results, as the findings in radial slices by DE-CMR only correspond to an intersection at one level of the longitudinal segments assessed by strain imaging. We wanted to make our CMR-standard more solid by combining the WMS with the extent of DE when defining the transmurality of infarction. Only
segments that were concordant regarding wall motion and the extent of DE were included in comparisons with echocardiography. Because of our strict criteria concerning the CMR-standard only 64 (71%) segments with infarction were included in further analysis which is a limitation to our study and might affect the assessment of sensitivities and specificities in particular.

Conclusion

Strain-mapping is a semi-quantitative and objective method for the assessment of the size and transmurality of the myocardial infarction and may be useful in the evaluation of myocardial function in post-myocardial infarction patients.

Acknowledgement

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Conflict of interest: none declared.

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