Early systolic lengthening may identify minimal myocardial damage in patients with non-ST-elevation acute coronary syndrome

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Received 17 December 2013; accepted after revision 29 April 2014; online publish-ahead-of-print 27 May 2014

Aims
Ischaemic myocardial segments tend to stretch as the intraventricular pressure rises steeply during the isovolemic contraction phase, before they contract during ejection. We hypothesized that the time they remain stretched, called duration of early systolic lengthening (DESL), correlates with final infarct size as defined by contrast enhanced magnetic resonance imaging (CE-MRI). We also assessed whether DESL could identify patients with acute coronary occlusion, and compared it with traditional measures for myocardial function.

Methods and results
In this retrospective study, 150 consecutive patients with Non-ST-elevation acute coronary syndrome (NSTE-ACS) referred for coronary angiography were included. Speckle tracking echocardiography was performed prior to angiography to determine DESL. The final infarct size was quantified at follow-up 9 ± 3 months after initial admission in 61 patients and echocardiography performed in 143 patients. DESL showed good correlation with the final infarct size (r = 0.67, P < 0.001). Thirteen patients had no visible sign of infarct on CE-MRI (minimal myocardial damage), and DESL was significantly shorter in these patients than in patients with signs of infarct (27 ± 19 vs. 84 ± 41 ms, P < 0.001). Compared with left ventricular ejection fraction, wall motion score index, and global longitudinal strain, DESL showed the best accuracy in detecting patients with minimal myocardial damage, with an area under the receiver operating characteristic curve of 0.92 (0.82 to 0.99, P < 0.001). DESL was more prolonged in patients with coronary occlusions, compared with those without occlusions (86 ± 45 vs. 63 ± 31 ms, P < 0.01). DESL was significantly shorter at follow-up, compared with baseline (P = 0.04).

Conclusions
DESL could identify patients with minimal myocardial damage, differentiate between occlusion and non-occlusion, and may be helpful in the risk stratification of patients with NSTE-ACS.

Keywords
myocardial infarction • echocardiography • magnetic resonance imaging

Introduction
Non-ST-elevation acute coronary syndrome (NSTE-ACS) patients comprise a heterogeneous group, containing both stenotic and occluded coronary arteries1,2 and varying infarct sizes.3 Many studies have shown that the extent of damage correlates with clinical outcomes.4–7 Some NSTE-ACS patients probably share many of the pathophysiological features of ST-elevation myocardial infarction (STEMI),8 suffer large infarcts, but are rarely treated with urgent reperfusion due to the sub-optimal sensitivity of the electrocardiogram (ECG).9–11 On the other hand, many NSTE-ACS patients have minimal myocardial damage and may not warrant immediate coronary intervention. Identifying these patients can be important for decision-making when prioritizing patients to revascularization therapy.

An experienced cardiologist can easily identify large myocardial infarcts by visual analysis of echocardiograms, but identification of small infarcts might be challenging. Significant changes in left ventricle ejection fraction (LVEF) and wall motion score index (WMSI) require decreased function in several LV segments, which might not be present in patients with relatively limited myocardial scar. Both
these indices have a weak ability to identify patients with minimal myocardial damage.12

Recent studies have shown that ischaemic myocardium tends to lengthen before the onset of systolic shortening, probably due to its reduced ability to generate adequate active force as the LV pressure rises steeply during the isovolumic contraction phase (IVC).13,14 The duration of early systolic lengthening (DESL) has been shown to be proportional to the infarct size in STEMI patients.15

In this study we hypothesized that the DESL is proportional to the final infarct size in NSTE-ACS patients, and may identify individuals with minimal myocardial damage. The diagnostic performance of DESL was compared with other indices of LV function, such as LVEF, WMSI, and global longitudinal strain (GLS).

Methods
In this retrospective study, patients with an NSTE-ACS diagnosis, referred for coronary angiography according to current guidelines,16 were included. A total of 899 patients from referring hospitals were screened for inclusion, of whom 150 were selected for inclusion (Figure 1). All patients were considered clinically and haemodynamically stable during index admission. The study was approved by the regional ethics committee, and all patients gave written informed consent.

Twenty-nine of these had unstable angina pectoris. The patients received standard medical therapy (dual anti-platelet treatment, ß-blockers, low-molecular-weight heparin, and statins) if tolerable, according to guidelines.16 Patient data, angiography results, echocardiography films, and contrast enhanced magnetic resonance imaging (CE-MRI) results were acquired from the medical records. The NSTE-ACS diagnosis was made according to guidelines.16

Echocardiography
All patients were examined immediately before angiography (on average 2.3 ± 0.9 days after the initial admittance for NSTE-ACS). Echocardiography was performed with Vivid 7 machines (General Electrics, Horten, Norway).

Longitudinal strain was assessed by speckle tracking echocardiography (STE) in a 16-segment model.17 A region of interest was drawn manually, and motion tracking was done automatically by the software (EchoPac, General Electrics Vingmed, Norway) using default temporal and spatial smoothing settings. Frame rate was 72 ± 15 frames per second. For each segment, peak negative systolic strain (which represents the maximum segmental systolic shortening) and DESL were recorded. DESL was defined as the time period in which the corresponding strain curve stayed positive from onset of a Q-wave (or R-wave if Q was absent) (Figure 2). As a measure of global systolic function, peak negative strain values of all segments were averaged to obtain GLS. The DESL in all 16 segments were averaged to obtain an average DESL value per patient. Post-systolic shortening (PSS) is a marker of viable myocardium,18 and was also assessed. It was defined as peak negative strain in diastole minus peak negative strain in systole, and a value was calculated for each segment.19 The segmental values were averaged to obtain a PSS value per patient. End-systole was defined by aortic valve closure in the apical long-axis view.

In accordance with a standardized model for myocardial perfusion areas,19 regional strain and DESL were calculated as the average values of segments belonging to the perfusion areas of the left descending, left circumflex and right coronary artery, respectively. In each patient, we calculated the average strain and DESL values of the segments corresponding to the artery defined as the culprit, and the values of the remote segments.

WMSI was calculated from a 16-segment model.17 Each segment was analysed individually and scored on the basis of its motion and systolic thickening. Each segment’s function was confirmed in multiple views. Segments were scored as: normal or hyperkinetic = 1, hypokinetic = 2, akinetic = 3, and dyskinetic (or aneurysmatic) = 4. WMSI was derived as the sum of all scores divided by the number of segments visualized. LVEF was calculated ad modum Simpson.20

Follow-up echocardiography was performed in 143 patients (95%) 9 ± 3 months after inclusion.

Coronary angiography
Coronary angiography was performed by standard technique with digital image acquisition and storage. Significant stenosis was defined as a coronary stenosis >50%. Chronic coronary occlusions were differentiated from acute occlusion on the basis of visual angiographic characteristics.

Magnetic resonance imaging
Among the 121 patients with confirmed NSTEMI, 61 patients (29 with acute coronary occlusion at index admission) were examined with magnetic resonance imaging (MRI) 9 ± 3 months after inclusion to determine the final infarct size. A 1.5-T unit (Magnetom Sonata, Siemens) was used on 29 patients and a 3-T unit (Philips Medical Systems) on 32 patients. Late-enhancement images were acquired 10–20 min after intravenous injection of 0.1–0.2 mmol/kg gadopentetate dimeglumine (Magnevist, Schering) in short-axis slices covering the entire LV. Image parameters...
were slice thickness: 8 mm, gap: 2 mm and inversion time: 270 ms. Total myocardial area and area of infarcted myocardium were manually drawn (PACS, Sectra, Sweden) on each short-axis image. Areas with pixel intensities > 2 SDs above the mean pixel intensity of normal myocardium of the same slice were considered infarcted.\(^{12}\) Infarct size was calculated as infarct volume as a percentage of total myocardial volume.

For segmental analyses, the LV was manually divided into 16 segments, corresponding to those for WMSI- and strain-models. A segment was classified as infarcted if any infarcted myocardium was visible in that particular segment. Segmental DESL- and strain values were estimated. Between revascularization and MRI at follow-up, one patient had re-infarction with minimal enzyme release (troponin T, 0.18 \(\mu\)g/L) in the same vessel as was initially treated.

Minimal myocardial damage was defined as the absence of late enhancement on MRI images (infarct size = 0\%). The MRI cohort was therefore dichotomized by infarct size, using 0\% as cut-off. MRI was performed depending on laboratory availability on the day of follow-up, and there was no bias in giving priority to MRI referral based on age, symptoms or hemodynamic status. However, since the MRI group (containing only NSTEMI patients) differed from the non-MRI group (containing both NSTEMI and UAP patients), no comparative assessments were made between the two groups.

**Testing of the indices**
We investigated the relation between infarct size as quantified by CE-MRI vs. the different echocardiographic variables (DESL, GLS, WMSI, and LVEF) by bivariate correlations. Furthermore, we performed receiver operating characteristics (ROC) analyses to test the ability of the echocardiographic variables to differentiate between: visible and no visible infarct on CE-MRI, and coronary occlusions and non-occlusions.

**Statistical analysis**
Continuous variables were presented as means ± standard deviation (SD). Group differences were analysed with the Student’s t-test. Categorical variables were presented as numbers (%) and differences between groups were analysed with the \(\chi^2\) test. Linear correlations were presented with Pearson coefficients. The diagnostic accuracy of

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**Figure 2:** Examples of longitudinal strains by STE (from the apical 4-chamber view). (A) Strain traces from a patient with no visible late enhancement on CE-MRI, and there is no early systolic lengthening. (B) Strain traces from a patient with a large infarct, and early systolic lengthening can be seen. The white bracket indicates the duration of early systolic lengthening of the red segment.
the different variables was tested with ROC analyses. The optimal cut-offs were defined as the values of the ROC curves that were closest to the upper left corner. The reliability of the optimal cut-off values was validated using bootstrap resampling (1000 iterations), and 95% confidence intervals (CIs) based on bootstrap percentiles were presented.21 Area under the curve (AUC) was presented with 95% CI. All statistical analyses were performed with PASW version 18 (IBM Corporation), except for bootstrapping and differences between ROC curves, which were analysed in MedCalc (MedCalc Software).

**Results**

Patient characteristics, medication, and risk factors are listed in Table 1. The angiographic characteristics are shown in Table 2. The different echocardiographic parameters are summarized in Table 3.

**Feasibility**

LVEF was assessable in 149 patients (99%). Longitudinal strain values could be obtained in 2363 (98.4%) and WMS in 2395 (99.8%) LV segments. Revascularization was attempted in all patients with significant stenosis according to current clinical indications [24 coronary artery bypass graft (CABG), 86 percutaneous coronary intervention (PCI)], and was successful in 110 (96%). Reproducibility analyses were performed in 15 patients (randomly selected by PASW). Intra-class correlation coefficients for inter-observer and intra-observer variability of DESL were 0.90 and 0.92, of GLS 0.94 and 0.96, of LVEF 0.81 and 0.84, and of WMSI 0.92 and 0.98, respectively, P < 0.001 for all.

**Infarct size**

In the 61 patients investigated with CE-MRI, the median infarct size was 5.4% (inter-quartile range 1.7–11.4) of total LV myocardial volume. Forty-eight of these patients had visible scar on CE-MRI, while 13 patients had no visible scarring. Of 976 analysed segments, evidence of infarction by late enhancement was seen in 249 (26%). Of these, 199 (80%) demonstrated sub-endocardial and 50 (20%) transmural infarction. LVEF showed moderate correlation (r = 0.53), while GLS, DESL, and WMSI showed good correlation (r = 0.64, 0.67, and 0.74, respectively, P < 0.001 for all) with infarct size (Table 3). DESL and WMSI were significantly lower, and GLS was significantly more negative (i.e. better shortening) in patients with no visible scar (infarct size = 0%) than in those with a infarct size > 0% (Table 2). Scatterplots between infarct size and DESL and GLS, respectively, are shown in Figure 3. On a segmental level, the mean DESL was significantly longer, and strain significantly less negative in infarcted segments than in non-infarcted segments (110 ± 77 vs. 61 ± 57 ms, and 18.7 ± 4.4 vs. 14.5 ± 5.2%, P < 0.001 for both).

**Table 1** Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-occlusion (117)</th>
<th>Occlusion (n = 33)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.7 ± 9</td>
<td>58.1 ± 8</td>
<td>0.84</td>
</tr>
<tr>
<td>BMI</td>
<td>26.8 ± 4</td>
<td>28.3 ± 3</td>
<td>0.11</td>
</tr>
<tr>
<td>Heart rate (b.p.m.)</td>
<td>62 ± 10</td>
<td>64 ± 8</td>
<td>0.19</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>81 (69%)</td>
<td>29 (88%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Current smoker</td>
<td>41 (35%)</td>
<td>14 (42%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>27 (23%)</td>
<td>12 (36%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hypertension</td>
<td>47 (40%)</td>
<td>13 (39%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8 (7%)</td>
<td>4 (12%)</td>
<td>0.47</td>
</tr>
<tr>
<td>History of CAD</td>
<td>7 (6%)</td>
<td>1 (3%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Medication prior to angiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>116 (99%)</td>
<td>33 (100%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>113 (97%)</td>
<td>33 (100%)</td>
<td>0.58</td>
</tr>
<tr>
<td>LMWH</td>
<td>111 (95%)</td>
<td>33 (100%)</td>
<td>0.34</td>
</tr>
<tr>
<td>β-blocker</td>
<td>100 (85%)</td>
<td>20 (67%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Statin</td>
<td>106 (91%)</td>
<td>30 (91%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td>0.22</td>
</tr>
<tr>
<td>ACE-I or ARB</td>
<td>32 (27%)</td>
<td>8 (24%)</td>
<td>0.72</td>
</tr>
<tr>
<td>GpIIbIIIa inhibitor</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). BMI, body mass index; b.p.m., beats per minute; CAD, coronary artery disease; LMWH, low-molecular-weight heparin; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; GpIIbIIIa, glycoprotein IIbIIIa.

**Table 2** Angiographic characteristics of 150 patients with NSTE-ACS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant stenosis (n (%))</td>
<td>115 (77%)</td>
</tr>
<tr>
<td>Acute coronary occlusions</td>
<td>33 (22%)</td>
</tr>
<tr>
<td>Zero-vessel disease</td>
<td>35 (23%)</td>
</tr>
<tr>
<td>Single-vessel disease</td>
<td>46 (31%), 12 patients with occlusion</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>49 (33%), 14 patients with occlusion</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>20 (13%), 7 patients with occlusion</td>
</tr>
</tbody>
</table>

NSTE-ACS, non-ST-elevation acute coronary syndrome; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.
ROC analyses for the identification of patients with visible vs. no visible infarct revealed that DESL could accurately distinguish between these patients. DESL had the largest AUC (0.92), and it was significantly better than GLS, WMSI, and LVEF (P-values 0.016, 0.008, and 0.001, respectively). A cut-off value of 50 ms could identify patients with minimal myocardial damage with a sensitivity of 77% and a specificity of 92% (Figure 4, Table 4).

**Coronary occlusion**

Thirty-three of 150 patients (22%) had acute coronary occlusions. DESL and WMSI were significantly higher, and GLS and LVEF significantly worse in patients with coronary occlusion than in those without (Table 3). ROC analyses showed that the accuracy was moderate in identifying patients with acute coronary occlusions (Figure 5, Table 5). DESL had an AUC of 0.65, and a cut-off value of 100 ms could identify a coronary occlusion with a sensitivity level of 33% and a specificity level of 92%. WMSI had the largest AUC of 0.73, but the differences to the AUCs of the other variables were not statistically significant.

Myocardial strain was significantly lower in the segments corresponding to the culprit artery than in remote segments (17.2 ± 4.1 vs. 18.8 ± 2.7%, \( P = 0.001 \)). Regional DESL tended to be longer in the segments corresponding to the culprit artery, but did not reach statistical significance (77 ± 58 vs. 67 ± 34 ms, \( P = 0.16 \)).

**Follow-up echocardiography**

One hundred and forty-three patients were examined with echocardiography at follow-up. DESL was significantly shorter at follow-up than at baseline (before revascularization); 61 ± 34 vs. 68 ± 36 ms, \( P = 0.04 \). Furthermore, DESL at follow-up was significantly shorter than at baseline (before revascularization); 61 ± 34 vs. 68 ± 36 ms, \( P = 0.04 \). Furthermore, DESL at follow-up was significantly shorter than at baseline (before revascularization); 61 ± 34 vs. 68 ± 36 ms, \( P = 0.04 \).

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**Table 3** Differences in clinical variables in patients with NSTE-ACS

<table>
<thead>
<tr>
<th></th>
<th>No visible enhancement on CE-MRI (n = 13)</th>
<th>Visible late enhancement on CE-MRI (n = 48)</th>
<th>P-value</th>
<th>Correlation with infarct size by MRI, r-value</th>
<th>Non-occlusion (n = 117)</th>
<th>Coronary occlusion (n = 33)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESL (ms)</td>
<td>27 ± 19</td>
<td>84 ± 41</td>
<td>&lt;0.001</td>
<td>0.67*</td>
<td>63 ± 31</td>
<td>86 ± 45</td>
<td>0.001</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>−19.6 ± 2.6</td>
<td>−17.2 ± 2.7</td>
<td>0.007</td>
<td>0.64*</td>
<td>−19.0 ± 2.5</td>
<td>−16.9 ± 2.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.07 ± 0.11</td>
<td>1.20 ± 0.18</td>
<td>0.004</td>
<td>0.74*</td>
<td>1.08 ± 0.13</td>
<td>1.20 ± 0.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>59 ± 7</td>
<td>55 ± 9</td>
<td>0.08</td>
<td>−0.53*</td>
<td>59 ± 7</td>
<td>55 ± 9</td>
<td>0.009</td>
</tr>
<tr>
<td>PSS (%)</td>
<td>−0.4 ± 0.2</td>
<td>−1.1 ± 0.6</td>
<td>&lt;0.001</td>
<td>−0.24**</td>
<td>−0.8 ± 0.6</td>
<td>−1.0 ± 0.7</td>
<td>0.07</td>
</tr>
<tr>
<td>Heart rate (b.p.m.)</td>
<td>65 ± 10</td>
<td>64 ± 10</td>
<td>0.81</td>
<td>0.07</td>
<td>62 ± 10</td>
<td>64 ± 8</td>
<td>0.21</td>
</tr>
<tr>
<td>Trop T (µg/L)</td>
<td>0.9 ± 1.3</td>
<td>1.0 ± 1.3</td>
<td>0.80</td>
<td>0.64*</td>
<td>0.3 ± 0.7</td>
<td>1.0 ± 1.1</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

CE-MRI performed in 61 patients. Abbreviations are explained in the text.

\*\( P < 0.001 \).
**\( P = 0.02 \).**
\‡\( P = \text{n.s.} \).

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**Figure 3**: Scatter plots showing correlation between duration of early systolic lengthening (DESL) and infarct size (A), and between GLS and infarct size (B) in 61 patients.
in patients with no myocardial scar (44 ± 20 ms) than in patients who had visible scar on MRI (71 ± 41 ms, \(P = 0.002\)).

**Discussion**

The present study showed that DESL demonstrated good correlation with the final infarct size, and a short DESL could accurately identify patients with minimal myocardial damage, as defined by no visible signs of myocardial infarction on CE-MRI, in patients with NSTE-MI. The ability of DESL to identify patients with coronary occlusion was moderate, and the accuracy in doing so was not significantly different from that of GLS, WMSI, and LVEF. The results imply that very short, or lack of, DESL is associated with minimal myocardial damage, while prolonged DESL is associated with larger infarcts and occluded arteries, and hence higher risk in patients with NSTE-ACS.

The rationale for our proposed assessment of stretch during early systole is that during IVC, when the mitral valve has moved to its final closing position and LV volume is constrained, there is a substantial ‘tug-of-war’ effect between the different LV segments.22 This effect is enforced as the volume has to remain fixed, i.e. if one segment shortens, another has to lengthen, which is not a necessity when volume can change during ejection. Therefore, during IVC, the non-ischaemic segments with a preserved contractile force will cause ischaemic segments to lengthen as the ischaemic segments are incapable of increasing contractile force at a similar rate as the non-ischaemic segments.23 During ejection the constant LV volume constraint is no longer in play, the rate of pressure rise (\(dP/dt\)) decreases and partly ischaemic segments are able to shorten, but the magnitude of the shortening is dependent on the degree of myocardial damage. Therefore, our hypothesis was that the patients with the smallest infarcts would have a shorter DESL, and those with the largest infarcts would have a more prolonged DESL.

Patients with NSTE-ACS represent a heterogeneous group with both single-vessel disease and multi-vessel disease,24 coronary occlusions, and non-occlusions,25 and infarct sizes ranging from large, small to none.26,27 Despite the heterogeneous nature of the syndrome, most patients are treated equally according to the same guidelines.16 This warrants a need for better risk stratification of patients with the NSTE-ACS, and tailoring of the timing of the treatment.

**Prediction of final infarct size**

The final infarct size is a powerful predictor for cardiovascular outcomes and mortality.28 The gold standard for the quantification of the infarct size is contrast enhanced MRI.29 This modality is however expensive, time and resource consuming, and not easily accessible for all patients. GLS by 2D-STE and WMSI are excellent in predicting final infarct size,3 and in our study DESL was comparable with them concerning correlation with infarct size by CE-MRI. However, DESL was superior to GLS and WMSI in identifying patients with a minimal infarct size. A closer scrutiny of the scatter plots may offer an explanation to why DESL performs better than GLS. Most patients with no visible myocardial scarring had a DESL of less than the proposed cut-off value of 50 ms. GLS, on the other hand, was reduced in several patients even in the event of no visible scarring on CE-MRI.

**Table 4** ROC analyses in 61 patients with NSTE-ACS, for the identification of patients with minimal myocardial damage (no visible scar on CE-MRI)

<table>
<thead>
<tr>
<th></th>
<th>AUC(^a)</th>
<th>(P)-value</th>
<th>Cut-off(^{a,b})</th>
<th>Sensitivity(^a)</th>
<th>Specificity(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESL</td>
<td>0.92 (0.82–0.97)</td>
<td>&lt;0.0001</td>
<td>&gt;50 ms (10–50)</td>
<td>77% (63–88)</td>
<td>92% (64–100)</td>
</tr>
<tr>
<td>GLS</td>
<td>0.72 (0.60–0.83)</td>
<td>0.007</td>
<td>&gt;−18.6% (−22.6–−17.2)</td>
<td>71% (56–83)</td>
<td>69% (39–91)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.67 (0.52–0.77)</td>
<td>0.05</td>
<td>&lt;55% (47–66)</td>
<td>54% (39–67)</td>
<td>77% (46–95)</td>
</tr>
<tr>
<td>WMSI</td>
<td>0.71 (0.58–0.82)</td>
<td>0.003</td>
<td>&gt;1.06 (1.00–1.13)</td>
<td>69% (54–81)</td>
<td>69% (39–91)</td>
</tr>
</tbody>
</table>

Abbreviations are explained in the text.

\(^{a}\)Presented with 95% confidence intervals.

\(^{b}\)95% confidence interval calculated by bootstrap analysis (1000 iterations).
scar, resulting in a considerable number of false positives. This may be partly explained by the afterload dependency of GLS:30 reduced shortening in patients with no visible scar could be due to loading factors such as hypertension, rather than ischemia. In contrast, DESL may potentially be less dependent on afterload, as it takes place during IVC. This means that the DESL could be highly useful in identifying patients with minimal myocardial damage. Identifying these patients is important from a patient’s perspective as it offers comfort to know that the damage is limited. But it may also be important from a clinical view, as these patients may be suffering from sub-total or unstable lesions. They could therefore benefit greatly from PCI, as future infarction would be prevented. This may have implications for the priority of patients with NSTE MI anticipating angiography.

However, it must be noted that echocardiography was performed 1–3 days after the index admission and before mechanical revascularization. During this time patients may have myocardial segments with reduced contractility both due to stunning and hibernation, which can affect DESL and other measures of myocardial function. But after revascularization, not all ischaemic segments become scars. DESL may therefore over-estimate the magnitude, when predicting the final scarring.

### Identification of coronary occlusion

Patients with STEMI are treated urgently with acute reperfusion, either mechanically (PCI) or pharmacologically (thrombolysis), as they are believed to have acute coronary occlusion. Mortality increases if such treatment is delayed.32 Studies have shown that many patients with NSTE MI actually have acute coronary occlusions,3 challenging the traditional views that NSTE MI is caused by transiently or partially occluded arteries, and that the lack of ST elevation rules out transmural infarction. Many NSTE MI patients with coronary occlusions are not selected for urgent PCI because the occlusion is not detected by the ECG. Early identification and treatment of occluded arteries will undoubtedly reduce myocardial damage.

As stated above, ischaemic myocardium with reduced contractile force may display early systolic lengthening of the segments. Occluded arteries result in larger LV damage, and should theoretically lead to a comparatively longer duration of the lengthening of the ischaemic segments than non-occluded arteries. Our study showed that the changes in myocardial function caused by coronary occlusion in NSTE-ACS patients were detectable by DESL, GLS, and WMSI. There were, however, no statistically significant differences between these methods for detecting acute coronary occlusion.

There are several potential explanations to why DESL did not perform better in predicting occlusions. Several of the patients without coronary occlusions still had significant stenosis that could lead to prolonged DESL. Furthermore, both echocardiography and angiography were performed a couple of days after the onset of NSTE-ACS. During this period, patients received anti-coagulation therapy that could have resolved the occlusions before they could be detected on angiography, but still have existed long enough to cause myocardial damage or stunning, and increased DESL. Both these factors could have resulted in false positives with regard to patients with occlusions. In addition, several patients had short DESL despite of having coronary occlusions. The reason could be that some patients had patent collaterals that could continue to

![Figure 5: ROC curves, based on values from 150 NSTE-ACS patients, for the identification of coronary occlusion. The corresponding AUCs and cut-off values are displayed in Table 5.](image)

### Table 5: ROC analyses in 150 patients with NSTE-ACS for the differentiation of patients with coronary occlusion and non-occlusion

<table>
<thead>
<tr>
<th></th>
<th>AUC*</th>
<th>P-value</th>
<th>Cut-off*</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESL</td>
<td>0.65 (0.57–0.73)</td>
<td>0.009</td>
<td>&gt;100 ms (50–120)</td>
<td>33% (18–52)</td>
<td>91% (85–96)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.64 (0.55–0.71)</td>
<td>0.02</td>
<td>&lt;52% (44–52)</td>
<td>48% (31–67)</td>
<td>82% (74–88)</td>
</tr>
<tr>
<td>GLS</td>
<td>0.71 (0.64–0.79)</td>
<td>&lt;0.0001</td>
<td>&gt;17.2% (19.3–16.6)</td>
<td>64% (45–80)</td>
<td>77% (63–88)</td>
</tr>
<tr>
<td>WMSI</td>
<td>0.73 (0.65–0.80)</td>
<td>&lt;0.0001</td>
<td>&gt;1.06 (1.00–1.09)</td>
<td>73% (55–87)</td>
<td>68% (58–76)</td>
</tr>
</tbody>
</table>

Abbreviations are explained in the text.

*Presented with 95% confidence intervals.

*95% confidence interval calculated by bootstrap analysis (1000 iterations).
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perfuse the regional myocardium corresponding to the infarct related artery, resulting in lesser myocardial damage. Furthermore, one-third of the patients with occlusions had only single-vessel disease, also resulting in lesser overall myocardial damage. These factors would lead to relatively shorter DESL, and hence false negatives.

Segmental analyses

Our study showed that infarcted myocardial segments had significantly worse strain, and longer DESL, than non-infarcted segments. Furthermore, it also showed that segments belonging to the culprit arteries had worse strain, and a tendency towards longer DESL, than did remote segments. These findings support the results at the patient level, but were less robust. The reason might be that by performing segmental analyses, a higher level of uncertainty is introduced: MRI images can be challenging to assess, and the segments on MRI and echocardiography probably do not correspond fully. As for the assessment of culprit artery, there is tremendous variability in the coronary artery blood supply to the myocardial segments. Segments assigned to a certain artery might indeed be supplied by a totally different one, and in addition to the existence of patent collaterals, this may further weaken the predictive analyses.

Follow-up echocardiography

There was a significant reduction in DESL at follow-up, demonstrating the benefits of revascularization. The reduction was however small, perhaps showing that the ischaemic myocardium undergoes permanent structural remodelling, causing persistent early systolic lengthening. It may also indicate that perhaps revascularization should be performed even earlier in selected NSTE-ACS patients in order to salvage threatened myocardium. In addition, many of the patients who underwent revascularization of the culprit lesion also had non-significant coronary stenoses in other arteries, implying remaining atherosclerotic disease even after the intervention. This might cause changes in myocardial function other than the perfusion area of the culprit artery. Still, revascularization might provide long-term benefits even in the absence of full contractile recovery by preventing further ischaemic insults, progressive LV failure, and sudden cardiac death.

Limitations

Although the patients were enrolled in a prospective fashion, the design in this particular study was retrospective. Echocardiography and angiography were not performed immediately after the onset of symptoms, but generally a couple of days later. Medical therapy could have dissolved some of the thrombotic occlusions, and therefore we might have underestimated the true rate of acute coronary occlusions. Acute coronary occlusion is accompanied by very rapid alterations, and in fact expansion and oedema development during the first hours may affect systolic function. Therefore, this method requires prospective validation in the emergency room. Like all echocardiographic methods, 2D-speckle tracking relies on good image quality. In our study, all efforts were made to obtain the best possible image quality; however, this may not always be the case in a normal clinical setting. Since prior myocardial infarction and atrial fibrillation were exclusion criteria in this study, the methods may not be valid applied for patients with pre-existing systolic dysfunction or arrhythmia. Time measurements are critically dependent on temporal resolution of the images on which measurements are performed. A frame rate of 72 ± 15 frames per second makes it challenging to measure DESL accurately. The end of DESL is defined by the point at which the strain curve crosses the time axis and can be determined with fairly high precision by interpolating information from the two frames on either side of the crossing. The starting point of DESL is however more challenging to determine with high precision as the software (Echopac) allows it to be set only in one particular frame. Therefore, DESL is somewhat affected by where the user sets the starting point of systole. Tissue Doppler imaging (TDI) has much higher temporal resolution, and strain rate by TDI could potentially measure DESL more accurately. These data were however not fully available in this patient population. On the other hand, the angle dependency of TDI would make it much more difficult to assess the segments where early systolic lengthening does not occur parallel to the ultrasound beam.

Conclusion

Absent of, or a short, DESL could accurately identify patients with non-STEMI without visible scar on CE-MRI, and was superior to GLS and WMSI. DESL showed good correlation with infarct size, could also differentiate between patients with coronary occlusions and non-occlusions, and can be a useful tool for the risk stratification of NSTE-ACS patients.

Acknowledgements

We would like to thank biostatistician Are Hugo Prip (Department of Biostatistics, epidemiology and health economy, Oslo University Hospital) for valuable support in performing statistical analyses.

Conflicts of interest: none declared.

Funding

The study was funded by the South-Eastern Norway Regional Health Authority (W.Z.).

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