Assessment of left ventricular function with magnetic resonance imaging vs. echocardiography, contrast echocardiography, and single-photon emission computed tomography in patients with recent ST-elevation myocardial infarction

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Aims
Magnetic resonance imaging (MRI) is often considered to be the gold standard in measuring left ventricular function and volumes. The aim of this study was to assess the agreements between standard echocardiography (standard echo), contrast echocardiography (contrast echo), single-photon emission computed tomography (SPECT), and MRI in the determination of left ventricular ejection fraction (EF) and end-diastolic volumes (EDV) in patients treated for acute ST-elevation myocardial infarction (STEMI).

Methods and results
Standard echo, contrast echo, SPECT and MRI were performed on the same day, 3 months after STEMI in 150 patients participating in the NORwegian Study on District Treatment of ST-Elevation Myocardial Infarction (NOR-DISTEMI). Bland–Altman analysis of EF measured by all four imaging modalities showed generally low mean differences but wide limits of agreement. The mean EDV difference, however, was consistently higher when MRI was compared with standard echo (54.9 mL), contrast echo (41.7 mL) and SPECT (54.6 mL), and the limits of agreement were wider. The mean EDV differences between contrast echo vs. standard echo, SPECT vs. standard echo and contrast echo vs. SPECT were small.

Conclusion
Our data suggest that all four imaging modalities measured EF closely similar after STEMI as demonstrated by a very small bias. The limits of agreement were however wide. EDV measured by MRI was consistently higher when compared with the other methods which may be caused by different tracing-methods and imaging principles. As echocardiography is preferable from a cost-benefit point of view, further analysis would be needed to clarify the nature of such differences.

Keywords
Ejection fraction • Coronary disease • Left ventricular function

Introduction
Assessment of left ventricular function is important in the risk stratification of patients with ST-elevation myocardial infarction (STEMI).¹ Magnetic resonance imaging (MRI) with its high spatial resolution² is often considered the gold standard in measuring left ventricular volumes and ejection fraction (EF). MRI is, however, contraindicated in some patients, may not be available at all hospitals and is a rather expensive examination. Myocardial perfusion single-photon emission computed tomography
(SPECT) has been validated against both echocardiography and MRI in several studies with good accuracy, but SPECT has the disadvantage that it exposes the patients to a high radiation dose and that a regular cardiac rhythm is required.\(^5\) Transthoracic standard echocardiography (standard echo) is a widely available method; it is non-invasive and can be performed bedside. From a cost-benefit point of view, standard echo is the preferred method for evaluating left ventricular function. However, an echocardiographic examination is highly dependent on the examiner’s experience and has limitations in patients with obesity, obstructive pulmonary disorders or a poor acoustic window for other reasons.\(^5, 6\) The administration of contrast intravenously may improve the definitions of endocardial borders in patients with poor acoustic window.\(^7,8\) It is less expensive and more available method than MRI, but tracing the basal parts of the left ventricle with contrast echocardiography (contrast echo) can still be a challenge due to loss of ultrasound energy through the contrast and therefore difficulty in distinguishing the contrast material and the myocardium.

Studies comparing left ventricular EF and volumes measured with different imaging modalities have been performed previously, but with few patients included and with diverging results.\(^9-12\) The aim of our study was to assess the agreements between standard echo, contrast echo, MRI, and SPECT, in determination of EF, end-diastolic volumes (EDV), and end-systolic volumes (ESV) in patients recently treated for ST-elevation myocardial infarction (STEMI). All examinations were carried out individually on the same day, at one site 3 months following acute myocardial infarction.

### Methods

#### Study population

The patients in this study were participants in the NORwegian Study on District treatment of ST-Elevation Myocardial Infarction (NORDISTEMI-study), an open, prospective, randomized controlled trial, including 266 patients with STEMI treated with thrombolysis (tenecteplase) and randomized to either immediate transport to percutaneous coronary intervention (PCI) or a conservative, ischaemia-driven strategy.\(^13, 14\)

After PCI-treatment at Oslo University Hospital, Ullevaal, the patients were transferred back to their local hospitals. Three months after STEMI, a follow-up with standard and contrast echo, SPECT and MRI was performed to assess left ventricular EF, EDV, and ESV. The follow-up was performed at Oslo University Hospital to obtain uniform and standard examinations. The study was approved by the Regional Committee for Ethics and complies with the Declaration of Helsinki. The patients were enrolled after written consent had been obtained.

#### Standard echocardiography and contrast echocardiography

An experienced physician performed the echocardiography with a Vivid 7 scanner in second harmonic mode (GE Vingmed, Horten, Norway). An introductory standard echo test including measurements of the dimensions, Doppler of blood flow over the valves and tissue Doppler were first performed. Volumes and EF were calculated using Simpson’s biplane method. Contrast echocardiography was recorded in three consecutive cycles of apical four chamber and apical two chamber after given 0.5–1 mL Sonovue intravenously. The intraobserver variation coefficients for EF and EDV measured with contrast echo were 9.6 and 8.9%, respectively. Intraobserver variation coefficients for EF and EDV measured with standard echo were 9.5 and 6.5%, respectively. Interobserver variation coefficients for EF and EDV measured with standard echo were 10 and 12%, respectively.

#### Cardiac magnetic resonance imaging

Cardiac MRI was performed as previously described\(^15\) on a 1.5 T whole body scanner (Philips Interia, Best, the Netherlands), using five element synergy-cardiac coil and vector-based ECG. The left ventricle was scanned in two and four chamber long-axis view using balanced fast field echo sequences for functional analysis. Short-axis images were acquired for complete left ventricular volume analysis. The scanning parameters were set to slice thickness 8 mm, slice gap 0 and 25 mm heart phases.

MRI analysis was performed on View Forum workstation (Philips Medical Systems). Ejection fraction was calculated by assessment of the volumes of the endocardial contours in diastole and systole of the short-axis images. The included slice closest to mitral valve plane had myocardium in at least two-third of the circumference of the left ventricle. Papillary muscles were excluded from the volume calculations. The intraobserver variation coefficients for EF and EDV measured with MRI were 3.8 and 2.5%, respectively.

#### Myocardial perfusion tomography (single-photon emission computed tomography)

After injection of \(99m\)Tc-tetrofosmin (Myoview\(^\text{TM}\), GE Healthcare, UK), perfusion imaging was performed as a standard SPECT to obtain infarct size, supplemented with ECG gated SPECT. The injected dose was 400–500 MBq. Processing was achieved by the use of an interfaced, dedicated computer system (Siemens e.soft, Erlangen, Germany) equipped with the 4D-MSPECT Cardiac Package (University of Michigan, Ann Arbor, MI, USA) to produce short-axis, vertical, and horizontal long-axis tomographic slices as well as bull’s eye plot of the left ventricle. Left ventricular cavity volumes were obtained from the gated SPECT perfusion data throughout the cardiac cycles. The largest cavity volume was defined as EDV and the smallest cavity volume was defined as ESV. These measurements are geometry independent. The intraobserver variation coefficients for EDV and EF were 7 and 5%, respectively, and the interobserver variation coefficients were 6 and 5%, respectively.

#### Statistical analyses

Data were expressed as medians with inter-quartile range (IQR), mean with standard deviation (SD), or frequencies. Limits of agreement between imaging methods were estimated as mean difference (bias) \(\pm 2SD\) of the differences, as described by Bland and Altman.\(^16\) Intraobserver and interobserver variability were expressed as percentage. The difference between MRI, SPECT, standard echo, and contrast echo measurements of EF and EDV were tested for significance using Wilcoxon test and a two-tailed P-value of <0.05 was considered statistically significant. The statistical program GraphPad software, San Diego, CA, USA was used.

#### Results

Standard echo, contrast echo, SPECT, and MRI were performed individually on the same site and day \(\sim 3\) months after STEMI. As EF values in both treatment groups were essentially the
same,\textsuperscript{17} we considered the 266 patients as one group, and extracted the patients who had a complete data set of all four methods for further analysis of the left ventricular function. A total of 150 patients were thus included in this analysis (flowchart, Figure 1). Patient characteristics and risk factors at time of myocardial infarction are described in Table 1.

**Ejection fraction values**

The median values of left ventricular EF and volumes measured with all four methods are presented in Table 2. The median EF values measured with standard echo, contrast echo, and MRI were almost identical. Median EF measured with SPECT, however, was significantly higher than EF measured with the other methods including EF measured by MRI ($P < 0.01$).

Bland–Altman analyses of EF measured by all four imaging modalities are shown in Figure 2. When using MRI as standard, the limits of agreement were closest for MRI vs. contrast echo (Figure 2B) ($-17.2$ to $17\%$) and widest for MRI vs. standard echo (Figure 2A) ($-18.4$ to $18.3\%$). The mean differences (bias) in EF measured with the four imaging methods were generally small; almost negligible between MRI and the echocardiographic methods and $-4.5\%$ between MRI and SPECT (Figure 2C).

Comparison in EF between the echocardiographic methods and SPECT are shown in Figure 2D, E, and F.

**Diastolic volumes**

Median EDV was significantly larger measured with MRI ($P < 0.01$) than with the other methods. The median EDV values (Table 2)
were almost identical measured with standard echo and SPECT, but was significantly larger when measured with contrast echo.

Bland–Altman analysis of EDV using MRI as standard (Figure 3) showed that the volumes measured with MRI were consistently higher compared with the other imaging modalities with the largest difference measured between MRI and standard echo (54.9 mL) and the smallest mean difference between MRI and contrast echo (41.7 mL). The limits of agreement, however, were wider with contrast echo than with standard echo (Figure 3A and B).

**Table 1** Patient characteristics at the time of ST-elevation myocardial infarction (n = 150)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59 (53–66)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>121 (81)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80 (74–90)</td>
</tr>
<tr>
<td>Current and previous smokers, n (%)</td>
<td>113 (75)</td>
</tr>
<tr>
<td>Blood pressure before treatment</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>131 (119–150)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80 (70–92)</td>
</tr>
<tr>
<td>Heart rate</td>
<td>65 (58–75)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>38 (25)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Previous myocardial infarction, n (%)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.3 (4.6–6.1)</td>
</tr>
<tr>
<td>Infarct location on ECG, n (%)</td>
<td></td>
</tr>
<tr>
<td>Anterior infarction</td>
<td>70 (47)</td>
</tr>
<tr>
<td>New left bundle branch block</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Non-anterior infarction</td>
<td>71 (47)</td>
</tr>
<tr>
<td>Time intervals, min</td>
<td></td>
</tr>
<tr>
<td>Symptom onset to thrombolysis</td>
<td>110 (75–179)</td>
</tr>
<tr>
<td>Medication at discharge, n (%)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>148 (99)</td>
</tr>
<tr>
<td>Statins</td>
<td>149 (99)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>142 (95)</td>
</tr>
<tr>
<td>ACE-inhibitors or ARBs</td>
<td>79 (53)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>14 (9)</td>
</tr>
</tbody>
</table>

Values are given as medians with 25th and 75th percentiles or numbers (percentages). ECG, electrocardiography; ARBs, angiotensin II receptor blockers.

**Table 2** Left ventricular ejection fraction and volumes measured by standard echocardiography, contrast echocardiography, single-photon emission computed tomography, and magnetic resonance imaging (n = 150)

<table>
<thead>
<tr>
<th></th>
<th>Standard echo</th>
<th>Contrast echo</th>
<th>SPECT</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>56 (50–64)</td>
<td>57 (49–64)</td>
<td>64 (54–70)**</td>
<td>57 (50–63)</td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>104 (86–135)</td>
<td>129 (102–145)</td>
<td>102 (83–128)</td>
<td>162 (133–193)**</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>48 (34–62)</td>
<td>51 (38–70)</td>
<td>36 (25–57)</td>
<td>66 (50–92)</td>
</tr>
</tbody>
</table>

Values are given as medians (25th, 75th percentiles). EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; echo, echocardiography; SPECT, single-photon emission computed tomography; MRI, magnetic resonance imaging.

**Systolic volumes**

Median ESV measured with SPECT was lower than the other imaging modalities (Table 2). Bland–Altman analysis of ESV using MRI as standard showed that the limits of agreement were closest when comparing MRI and SPECT whereas the mean difference was smallest between MRI and contrast echo (Figure 4).

**Discussion**

In this relatively large clinical study, we found that EF was measured rather similar with all four imaging methods in patients 3 months after STEMI, as demonstrated with small mean differences in the Bland–Altman analyses. However, in individual patients the measurements varied considerably, as shown by rather wide limits of agreement. Importantly, the well-known underestimation of EF measured with standard echo compared with MRI, was improved when adding contrast to the echocardiography resulting in more optimal limits of agreement. The mean EDV measured with MRI was significantly higher when compared with mean EDV by the other methods. The mean EDV values measured with SPECT and standard echo, however, were almost identical, even though the measuring principles are very different.

The assessment of left ventricular function following STEMI is important for further risk stratification and medical therapy. The diagnostic alternatives for assessing EF and left ventricular function are many, and the choice often falls on the availability at the local hospitals; hence it is important to know whether these imaging modalities can be used interchangeably. The CHRISTMAS study compared left ventricular function and volumes in 52 heart failure patients by echocardiography, radionuclide ventriculography, SPECT, magnetic resonance imaging.

The mean EDV differences in-between standard echo, contrast echo, and SPECT were low as shown in Figure 3D, E, and F.

When revising the echo- and MRI-images in the individuals with the greatest discrepancies, we found that the images in the echo-recordings were of standard quality and were thus not the reason for the discrepancies.

In order to exclude calibration as a cause for the discrepancies in the EDV measurements we performed standard echo and MRI examinations on the same day in nine new patients. The aorta-diameter was measured at the same distance from the aortic valve with both MRI and standard echo, and was found to be 1.3% larger with MRI than with standard echo (P = 0.46).
and MRI and suggested that EF measured with these different techniques was not interchangeable. They suggested that MRI should be the preferred imaging modality for assessment of volumes and EF.9

Another similar study that compared gated SPECT, echocardiography, and MRI, in 21 patients with suspected coronary artery disease, showed overall good correlation between left ventricular volumes and EF and therefore suggested that these methods can be used interchangeably when measuring EF, but recommend care when comparing the volumes.10

Malm et al.8 evaluated the accuracy and reproducibility of contrast echo and MRI in 110 patients with known or suspected heart disease. Their study showed that EF and left ventricular volumes measured with standard echo was more accurate and reproducible when adding intravenous contrast material.

In our study, with a larger number of patients than in the studies mentioned above, the median EF measured with SPECT was significantly higher than with other methods, which is probably caused by different imaging methods where SPECT produces a generally lower ESV. When using Bland–Altman analysis, however, our findings in patients with STEMI suggest that standard echo, contrast echo, SPECT, and MRI are interchangeable when assessing EF as a group. The individual measurements, however, varied considerably. A patient with low EF measured with standard echo did not necessarily have low EF measured with any of the other methods. This is of clinical importance, e.g. when assessing the implantation of ICD on basis of a low EF or assessing the need of heart transplantation. When re-examining the individuals with the greatest discrepancies, we were not able to explain the difference by poor echo-image quality or distorted ventricles.

When assessing EDV, MRI measures higher volumes compared with the other methods. Contrast echo, in comparison to standard echo, seems to resemble more to MRI in tracing the left ventricular border closer to the endocardium, and the addition of contrast

Figure 2 Bland–Altman diagram of ejection fraction (%) demonstrating mean difference (solid line) and the limits of agreement (dashed lines). \( \Delta = \) Difference.
material results in the lowest mean difference when compared with MRI. SPECT and standard echo give practically the same EDV with a bias of 0.35 mL. The reason for higher EDV measured by MRI may be caused by different tracing-methods and imaging principles. With MRI summation of three-dimensional stacks in short-axis cines is used to determine volumes, whereas in echocardiography the volumes are calculated using Simpson’s biplane method. The ventricular dimensions with standard echo are calculated from the known ultrasound velocity in the tissue and poor quality of the image and varying gain settings may miscalculate the dimensions. The volume estimated by SPECT is based on measuring the amount of radioactivity within a region of interest, correcting for the density of radioactivity in the blood.

In order to exclude differences in calibration as a cause for the discrepancies in EDV between MRI and standard echo, we measured the aorta-diameter in nine new patients. We found a negligible difference between these measurements and hence we reasonably well excluded a difference in calibration as a reason for the discrepancies in EDV measurements. Second harmonic echo-imaging has been regarded to overestimate wall thickness at the expense of the cavity size. The latter experiment, however, excluded this explanation in this study.

Our study was a relatively large clinical study compared with previous and similar studies. The patients included were not preselected and only very few examinations were excluded due to technical inadequacy. The fact that 25% of patients were not included...
because of reduced capacity of echocardiography in a busy clinical department was a strict administrative issue unrelated to the patients' medical status and the population was thus importantly representative for regular clinical practice.

Limitations
The patients included in this study received early treatment with thrombolysis resulting in a STEMI population with a relatively well preserved EF. The inclusion of patients with longer time delays to treatment might have lead to larger variations in EF and EDV values measured with the different methods.

MRI may overestimate volume measurements due to difficulties in the selection of correct mitral plane which could have been corrected by long-axis view. However, short-axis view lately has been the most common method used for assessing left ventricular volumes and was therefore the only method used in our study.

Conclusion
Our data suggest that all four imaging modalities measured EF closely similar after STEMI as demonstrated by a very small bias. However, the limits of agreement were wide. EDV and ESV measured by MRI were consistently higher when compared with the other methods which may be caused by different tracing-methods and imaging principles. As echocardiography is preferable from a cost-benefit point of view, further studies are required to elucidate the discrepancy in volume measurements between MRI and the other methods. Beating heart phantoms might be

Figure 4 Bland–Altman diagram of end-systolic volumes, (mL) demonstrating mean difference (solid line) and the limits of agreement (dashed lines). $\Delta = \text{Difference}$. 

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helpful, but we are not aware of any such phantoms that could be measured by all of these techniques.

**Supplementary data**

Supplementary data are available at European Journal of Echocardiography online.

**Conflict of interest:** none declared.

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