Severe regional myocardial dysfunction by stress echocardiography does not predict the presence of transmural scarring in chronic coronary artery disease

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Received 28 January 2015; accepted after revision 25 March 2015; online publish-ahead-of-print 28 April 2015

Aims
Detection and correct localization of transmural lesions can be important for optimal treatment of patients with chronic coronary artery disease (CAD). The aim of the study was to investigate the ability of peak longitudinal ejection strain (PLS) to detect the presence and extent of scar-tissue in CAD patients with normal or near normal ejection fraction, in comparison to cardiac magnetic resonance (CMR).

Methods and results
Before coronary artery bypass grafting, 57 patients underwent late gadolinium enhancement (LGE) CMR and echocardiography at rest and dobutamine stress (DS). According to the degree of LGE, segments were allocated to groups of none, subendocardial (1–50%), subtotal (51–75%), and total transmural scars (>75%). Dysfunctional segments were identified by PLS or wall motion scores (WMS). The finding of normal/near normal resting WMS and PLS, excellently identified segments without transmural LGE (AUC 94.0 CI 90.6–97.3 and AUC 85.7 CI 79.0–92.3, respectively). However, the finding of akinesia did not necessarily indicate transmural scarring. The negative predictive value was high (99%, CI 98–100%) while the positive predictive value was low. Detection-rates for subendocardial LGE were low.

Conclusion
Normo- and slightly hypokinetic myocardium by resting WMS or strain detects the absence of transmural scars. However, the finding of severe hypo- and akinesia does not reliably predict transmural scarring, with no improvement by the addition of DS. Detection of predominant akinesia with less than two normo- or hypokinetic segments in the territory of a high-grade coronary stenosis or occlusion, warrants further examination by LGE-CMR.

Keywords
Strain-echocardiography • Dobutamine-stress echocardiography • Coronary artery disease • Detection of scar-tissue

Introduction
To evaluate the potential benefit of revascularization in chronic coronary artery disease (CAD), especially in the presence of chronic total occlusions (CTO), the need for correct identification and localization of transmural scar-tissue is mandatory.1 There is a broad consensus in favour of treating even complicated CTO lesions in these patients, if viability in downstream myocardium can be demonstrated.2,3 However, in clinical practice, the majority of patients with stable angina, including those with CTO, have normal or nearly normal EF.4 Previous studies on myocardial viability have mainly focused on chronic CAD patients with heart failure and ejection fraction (EF) < 35–45%, and the potential of functional improvement.5 Accordingly, present guidelines on revascularization of viable vs. non-viable myocardium do not include patients with nearly normal and normal EF.

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With late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR), transmural and subendocardial infarcts can be detected with high accuracy. However, availability of CMR is limited. Dobutamine stress echocardiography (DSE) is therefore routinely used in heart failure patients for viability assessments, and both wall motion scores (WMS) and longitudinal strain measurements are easily acquired. In the present patient population with normal or nearly normal EF, undergoing coronary artery bypass grafting (CABG), we have previously published data focusing on myocardial function before and after revascularization. We found that resting peak longitudinal ejection strain (PLS) after CABG does not improve in the majority of preoperatively dysfunctional segments. In the present study, the focus is shifted from assessing improvement after revascularization to evaluating the diagnostic accuracy of different resting and stress echocardiographic parameters for the detection of subendocardial or transmural LGE positive segments pre-CABG.

Methods

Patients

In a prospective study, 67 patients with CAD scheduled for CABG were consecutively included. They underwent resting echocardiography, DSE, and LGE-CMR 1–7 days before and 8–10 months after CABG, and a coronary angiogram 1–2 months before CABG. CMR was generally performed 1 day before or after the resting echocardiography, and the DS test at a maximum of 8 days delay between both studies. Detection of scar-tissue was analysed on preoperative data, while cut-off values were derived from postoperative data. Twenty patients had a history of previous myocardial infarction. Exclusion criteria were valvular heart disease, chronic obstructive lung disease or asthma, atrial fibrillation, unstable angina, myocardial infarction within 3 months prior to CABG, left bundle branch block, or any contraindications to CMR such as claustrophobia, pacemaker implants, or significantly reduced renal function as assessed by glomerular filtration rate.

All patients gave written informed consent, and the study was approved by the Regional Ethical Committee of Northern Norway (REK/NORD34/2005).

Cardiac magnetic resonance imaging

LGE-CMR was acquired using a 1.5-T scanner (Philips Intera release 2.1, Best, the Netherlands). T1 weighted LGE-images were obtained 15 min after infusion of 0.1 mmol/kg gadoversetamide (Optismark, Mallinckrodt, St Louis, MO, USA). Slice thickness was 8 mm with an interslice gap of 2 mm, cine-CMR frame rates were 30–35 Hz. Images were analysed according to the standard 16-myocardial-segment model as used for echocardiography. One reader (D.A.) measured the end-diastolic and end-systolic myocardial wall diameters in 16 segments in SAX-views. Quantification of the extent of myocardial scar-tissue was performed by visual assessment of LGE short- and long-axis images, as a consensus reading by two observers (D.A., A.R.). LGE readers were blinded to echocardiographic results. The extent of segmental myocardial scar-tissue was divided into four categories: LGE = 0, LGE = 1–50%, LGE = 51–75%, and LGE = 76–100%.

Echocardiography

Data acquisition

Echocardiographic studies were performed using an iE33-scanner (55-1 probe, Philips Medical Systems, Andover, MA, USA) with a 1–5 MHz transducer in the left lateral decubital position. Conventional 2D grey scale images for the assessment of WMS and longitudinal tissue velocity imaging (TVI) data for strain-measurements in separate walls, were obtained in the apical two-, three-, and four-chamber views at a frame rate of 120–180 Hz. DSE was performed using infusion rates of 2.5, 5, 10, and 20 µg kg\(^{-1}\) min\(^{-1}\).

Image analysis

All 2D and TVI data were analysed by a single observer (A.R.), blinded to CMR results, using commercially available software (QLAB, Philips Medical Systems, Andover, MA, USA). Global LV function was assessed by calculating end-systolic and end-diastolic volumes and EF by biplane Simpson. Regional LV function was evaluated in a 16-segment model. Wall motion score was defined as normal (score = 1), slightly hypokinetic (1.5), highly hypokinetic (2), akinetic (3), or dyskinetic (4). End-diastolic wall-thickness was measured in 16 segments in apical views. In a cine-loop of five cardiac cycles, the first cycle was analysed, except in the case of extra-systoles or insufficient quality of the first beat. Then, the second or following cycles were analysed.

The beginning of the cardiac cycle was set at peak R, which is most likely to coincide with the time point of mitral valve closure at the presence of normal QRS width. Ejection-time (ET) strain was chosen in order to measure systolic strains with exclusion of post-systolic strains. PLS was defined as the highest peak negative or positive value between aortic valve opening and closing. The ET-period was determined by Doppler detection of the aortic valve opening and closing clicks. Post-systolic strain (PSS) was defined as the difference between PLS during ET and peak strain during the cardiac cycle. For strain-analysis, each segment was tracked manually by positioning a region of interest (ROI), with a length between 1.0 and 1.8 cm and a width of 0.25 cm, in the centre of the myocardial wall throughout five cardiac cycles. Measurements were discarded in segments with aliasing, missing Doppler data for more than 50% of the cardiac cycle, large reverberations, and angle deviation above 25°, when velocity and SR curves lacked E-waves, and when curve shape and peak values changed more than 20% from beat to beat. SR was expressed as the mean of all SR values during ET.

During DS at doses from 2.5, 5, 10, and 20 µg kg/min, the lowest WMS and the highest (peak negative) PLS were registered. For viability assessment, the highest absolute values from all dobutamine stages were extracted. Hypokinesia was defined by cutoff values derived from data of our previously published study, including a cohort of normal individuals. The 97.5% percentile for segments from normal individuals indicated a cutoff for strain of < −10%.

Statistical analyses

If not stated otherwise, all data are expressed as means ± standard deviations (SD). Probability values <0.05 were considered statistically significant.

Differences between echocardiographic parameters in different LGE groups were tested by one-way ANOVA with Bonferroni post-hoc analysis. Detection of different degrees of LGE was evaluated by receiver operating characteristic (ROC)-curves. The results are expressed as area under the curve (AUC) and 95% confidence-interval (CI). A lower AUC-CI value above 50% was regarded as significant. AUC-values of one parameter outlying the CI of another test parameter, were regarded as a significant difference between AUC’s. Cutoff values for sensitivity and specificity of the preoperative test parameters, were derived from ROC curve analyses of data from post-CABG CMR, resting, and DS echocardiography. These cutoff values were derived from the highest sum of sensitivity and specificity values. CIs for sensitivity and specificity were calculated by ‘VassarStats’ clinical calculator (http://vassarstats.net).
All other statistics were performed in SPSS version 21.0 (IBM, New York, USA).

For estimation of intra- and interobserver variability, two independent readers reassessed 15 randomly selected patients at rest and in 12 patients at highest DS dose. Variability between readers (A.R., S.M.) was expressed as intra-class correlation (ICC) for strain and WMS measurements as well as Pearson’s R and Kappa for WMS assessments.

**Results**

**Patient characteristics and distribution of LGE**

Table 1 lists patient characteristics.7 Of the 67 included patients, 57 completed both CMR and DSE, pre- and post CABG. Twenty patients had previously suffered a myocardial infarction, and 17 had earlier been treated with percutaneous coronary intervention. Mean EF was 52 ± 10% before and 50 ± 9% after CABG, respectively. As shown in Table 1, 90% of patients presented with angina. Seven percent had ECG changes during the treadmill test without angina, while 3% of patients had neither angina nor a positive treadmill test, and the indication for revascularization was heart failure, only. Four patients had a perioperative myocardial infarction with CKMB at 130, 101, 87, and 59 U/L, respectively, but none of these showed ST-elevations in the ECG. The total amount of LGE/myocardial mass was unaltered in these four patients, as well as in the total study population (from 3.6 to 4.4% (P = 0.557)).

Segments with 51–100% scar-tissue were found in 10 patients, with EF ranging between 27 and 61% with a mean EF of 44.6%. More than two segments with scars >75% were found in three patients with EF at 27, 30, and 50%. Of 57 patients, 35 had at least one chronic occluded vessel, and 228 segments were defined as downstream an occluded vessel. Twelve patients had one occlusion, 13 two, and 10 patients had three occluded vessels in different main vascular areas. Territories downstream occluded vessels per patient with CTO, had the average size of 3.9 ± 3.2 segments (range 1–12), and per occluded vessel 3.2 ± 1.4 (range 1–6) segments. Eight (4%) segments out of 11 with LGE 76–100% LGE, 7 (3%) segments out of 12 with LGE 51–75%, 31 (14%) segments out of 56 with LGE 1–50%, and 182 (79%) of segments without LGE, were found downstream occluded vessels. There was a higher number of segments included for strain-analysis compared with WMS. The discrepancy was caused by higher numbers of 2D segments excluded from WM analysis compared with TV segments excluded from strain-analysis.

**Reproducibility**

Figure 1 depicts an example of strain curves. The ICC for the intra- and interobserver variability of PLS was 95.8 and 95.0%, respectively. ICC for segments varied between 86 and 98%, with the highest correlations for basal anteroseptal and basal inferolateral as well as all apical segments. Lower correlations (ICC < 90%) were observed for the mid and basal inferior walls and the basal anterolateral wall. For WMS, Pearson’s R (and Kappa) for intra- and interobserver variability was 0.56 (0.44) and 0.42 (0.37), respectively. The ICC for WMS was 71% for intra- and 59% for inter-observer variability. Segmental PLS and WMS correlated significantly (P < 0.0001) with Pearson’s R of 0.350.

**Myocardial functional parameters compared with the presence of LGE**

Table 1 demonstrates the number of pre-CABG akinetic and hypokinetic segments defined by WMS and PLS at rest. Figure 2 displays the distribution of myocardial segments in different LGE groups vs. functional echo parameters. The majority of segments demonstrate normal function and no sign of scar, as expected. However, 30% of all segments were dysfunctional but proved to be unscarred, while 8% were dysfunctional and displayed some degree of LGE, and only 1% of all segments was dysfunctional and displayed transmural scars. Table 2 displays the distribution of segments and segmental echo parameters in the four LGE groups.
Figure 3 displays comparative ROC curve analyses of the preoperative echocardiographic parameters on myocardial function. The outcome was the presence of LGE 76–100%. The sensitivities and specificities, negative and positive predictive values on both at segmental and patient level are displayed in Table 3. With a PLS cutoff value of greater than $2\%$, sensitivity for the detection of transmural LGE was $>90\%$. Using strain rate did not improve test results, and neither post-systolic shortening nor end-diastolic wall-thickness by echo could significantly detect or exclude the presence of transmural LGE (data not shown).

In Table 4, we present the results of ROC curve analyses for the detection of subtotal transmural and subendocardial scars on a segmental level. The detection-rate for subendocardial scars was rather low, while subtotal transmural scars were detected with moderate-to-good accuracy by WMS and DS PLS. However, AUC for the detection of subtotal myocardial scars by resting PLS was not significant. For the detection of transmural scar-tissue by CMR EDWT (cutoff <5.5 mm), CMR ESWT (cutoff <7 mm), and by echocardiography EDWT (cutoff <6 mm), sensitivities and specificities were 81 and 85%, 90 and 96%, and 63 and 67%, respectively. The number of thin-walled segments were 10 out of 849 (1.1%) for CMR EDWT, 32 out of 890 (3.5%) for CMR ESWT, and 143 out of 749 (19.0%) for echocardiographic EDWT. Table 5 displays the AUC for detection of different degrees of myocardial scar-tissue by echocardiographic and CMR wall-thickness.

**Discussion**

**Major findings**

In patients with chronic CAD with nearly normal EF, the finding of normal/near normal resting segmental WMS and PLS could accurately exclude transmural LGE. However, there was a substantial number of dysfunctional as well as thin-walled segments with no scarring, i.e. a clinically significant number of false positives when using echo for detection of non-viability.

**Detection of transmural LGE**

In ischaemic heart failure, echocardiography at rest using WMS and strain has been used to predict the presence of myocardial viability. Previous studies have shown that akinessia by WMS and longitudinal or circumferential strain at rest and during DS is highly indicative on the presence of transmural scar-tissue in chronic CAD and shortly after acute myocardial infarctions.

In the present study, the finding of normo- or slight hypokinesia by WMS or PLS had an excellent negative predictive value for the absence of transmural scars, and thus the presence of viability.

The low-positive predictive values for the detection of transmural scars by PLS and WMS in the present study can be explained by the lower prevalence of transmurally scarred segments, combined with the higher percentage of dysfunctional, unscarred segments. In previous studies, 35–40% of segments were dysfunctional with scars, and only 10–15% of segments were dysfunctional without scars. In comparison, we found that only 8% of dysfunctional segments had scars and 30% were without scars. Transmural lesions were present in only 12–15% of akinetic segments at rest and in 20% of akinesia during DS.

Furthermore, we found a distinct difference between segmental PLS in the >75% LGE group and the LGE ≤ 75%, contributing to the good exclusion rates for transmural scars. By using TVI strain, our transmural scars (LGE > 75%) presented with a mean strain of $-2\%$, significantly less negative values compared with scars of 51–75%. Studies defining transmural scars as 51–100% LGE, may thus not recognize segmental PLS as indicator on
Table 2  Segmental preoperative functional parameters in graded groups of myocardial scarring

<table>
<thead>
<tr>
<th></th>
<th>LGE 0%</th>
<th></th>
<th>LGE 1–50%</th>
<th></th>
<th>LGE 51–75%</th>
<th></th>
<th>LGE 76–100%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
</tr>
<tr>
<td>WMS</td>
<td>715</td>
<td>1.5</td>
<td>0.7</td>
<td>52</td>
<td>1.9</td>
<td>0.8</td>
<td>11</td>
<td>2.0</td>
</tr>
<tr>
<td>DS: WMS</td>
<td>786</td>
<td>1.2</td>
<td>0.4</td>
<td>56</td>
<td>1.4</td>
<td>0.7</td>
<td>12</td>
<td>2.0</td>
</tr>
<tr>
<td>PLS (%)</td>
<td>748</td>
<td>-14</td>
<td>10</td>
<td>53</td>
<td>-10</td>
<td>9</td>
<td>11</td>
<td>-11</td>
</tr>
<tr>
<td>DS: PLS (%)</td>
<td>808</td>
<td>-21</td>
<td>11</td>
<td>56</td>
<td>-18</td>
<td>9</td>
<td>12</td>
<td>-15</td>
</tr>
</tbody>
</table>

From ANOVA analyses; significant difference (*P < 0.05) compared with †LGE 0; ‡LGE 1–50; §LGE 51–75.
WMS, wall motion score; PLS, peak longitudinal ejection strain; DS, dobutamine stress; LGE, late gadolinium enhancement.

Figure 2  Histograms showing the distribution of segments from different LGE groups over myocardial functional parameters; in the left column segments both, with and without scarring, in the right column segments with different degrees of scarring (LGE group 1–3), only. (A) The relation of wall motion score (WMS) and the amount of scar-tissue, while (C) demonstrates the relation of systolic peak longitudinal ejection strain (PLS) and scar-tissue. In order to illustrate the distribution of different degrees of LGE transmurality (B and D) show extracted and enlarged LGE positive segments from (A and C), respectively.
transmurality. In addition, segment-to-segment analyses by TVI may be more sensitive to inter-segmental differences compared with 2D-strain software with higher inter-segmental smoothing.

It has to be emphasized that WMS was not inferior to PLS. On the contrary, WMS displayed higher AUC compared with PLS in detecting the absence of transmural scars, and was significantly different between three of the four LGE groups. However, lower ICC for segmental WMS compared with strain could reflect difficulties in reproducible segmental localization of dysfunctional segments.

Our CMR data show low EDWT and ESWT as strong indicators for the presence of transmural scars in accordance to previous viability studies. As in the study of Shah et al., we found that some thin wall segments still contain a low percentage of viable tissue. However, EDWT by echocardiography was less sensitive and specific for the detection of transmural than CMR. As for functional parameters, noise, artefacts, and low lateral resolution might be a challenge for accurate echocardiographic EDWT measurements. Compared with functional parameters, EDWT by echocardiography had even lower accuracy for the identification of transmural scarring in this specific patient population. In our study, the use of DS did not increase the positive predictive value of echo parameters. The reason for this could be that ischaemic segments before revascularization may be akinetic with no positive DS-response, even at the absence of scar-tissue. Previously, we have demonstrated that DS could activate dysfunctional non-scarred segments in a much higher percentage after revascularization.

Detection of subendocardial scars

The prognostic value of detecting scar-tissue of a lesser extent, expand the indication from revealing scars in heart-failure patients to hearts with nearly normal EF. In the context of defining total scar load, the detection of subendocardial scar-tissue may have clinical importance in the chronic CAD patient population. However, our data suggest that in hearts with nearly normal EF, subendocardial scar-tissue cannot be reliably detected by echo. The high number of dysfunctional but unscarred segments substantially lowers the detection-rates. As shown in Figure 1, the distribution of LGE groups compared with myocardial function was similar comparing resting strain with WMS. Both methods showed that the numbers of unscarred dysfunctional segments were relatively high.

![Figure 3](image_url) ROC curve analysis of indicators of segmental presence of transmural scar defined as late gadolinium enhancement (LGE) > 75%. The cutoff values used were derived from the same population after revascularization: wall motion score (WMS):2.75; dobutamine-stress (DS) WMS:2.25; peak longitudinal ejection strain (PLS): −10%; DS PLS: −15%.

Table 3  Sensitivity, specificity, positive and negative predictive values for the detection of transmural late gadolinium enhancement

<table>
<thead>
<tr>
<th>Segments</th>
<th>LGE &gt; 75% present</th>
<th>LGE &gt; 75% absent</th>
<th>Cutoff</th>
<th>Sensitivity% (CI)</th>
<th>Specificity% (CI)</th>
<th>PPV% (CI)</th>
<th>NPV% (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WMS</td>
<td>10</td>
<td>734</td>
<td>2.75</td>
<td>80 (48–97)</td>
<td>94 (92–95)</td>
<td>15 (7–27)</td>
<td>99 (98–100)</td>
</tr>
<tr>
<td>DS:WMS</td>
<td>11</td>
<td>854</td>
<td>2.25</td>
<td>82 (48–97)</td>
<td>91 (89–93)</td>
<td>10 (5–20)</td>
<td>99 (99–100)</td>
</tr>
<tr>
<td>PLS</td>
<td>9</td>
<td>812</td>
<td>−5%</td>
<td>56 (23–84)</td>
<td>84 (82–87)</td>
<td>4 (1–9)</td>
<td>99 (98–100)</td>
</tr>
<tr>
<td>DS:PLS</td>
<td>11</td>
<td>876</td>
<td>−15%</td>
<td>73 (39–92)</td>
<td>72 (68–74)</td>
<td>3 (1–6)</td>
<td>99 (99–100)</td>
</tr>
<tr>
<td>Patients</td>
<td>LGE &gt; 75% in ≥ 2 segments</td>
<td>LGE &gt; 75% in 0–1 segments</td>
<td>Cutoff</td>
<td>Sensitivity% (CI)</td>
<td>Specificity% (CI)</td>
<td>PPV% (CI)</td>
<td>NPV% (CI)</td>
</tr>
<tr>
<td>WMS</td>
<td>3</td>
<td>53</td>
<td>2.75</td>
<td>100 (31–100)</td>
<td>83 (70–92)</td>
<td>25 (6–57)</td>
<td>100 (90–100)</td>
</tr>
<tr>
<td>DS:WMS</td>
<td>3</td>
<td>53</td>
<td>2.25</td>
<td>100 (31–100)</td>
<td>74 (60–84)</td>
<td>17 (4–44)</td>
<td>100 (89–100)</td>
</tr>
<tr>
<td>PLS</td>
<td>3</td>
<td>54</td>
<td>−5%</td>
<td>100 (31–100)</td>
<td>93 (81–98)</td>
<td>43 (12–80)</td>
<td>100 (91–100)</td>
</tr>
<tr>
<td>DS:PLS</td>
<td>3</td>
<td>54</td>
<td>−15%</td>
<td>67 (13–98)</td>
<td>91 (79–97)</td>
<td>29 (5–70)</td>
<td>98 (88–100)</td>
</tr>
</tbody>
</table>

Parameters from dobutamine stress and resting echocardiography

WMS, wall motion score; PLS, peak longitudinal ejection strain; DS, dobutamine stress; CI, confidence-interval; PPV, positive predictive value; NPV, negative predictive value; LGE, late gadolinium enhancement.
In chronic CAD with and without reduced EF, strain values vary from low normokinetic to akinetic, both in subendocardial scars as well as in unscarred myocardium. Strain reduction in unscarred segments may have several explanations, like hibernation (with postoperative improvement), long-term ischaemic stunning, or microscars of different degrees. To date, these ischaemic substrates can neither be sufficiently differentiated by functional assessment nor by direct visualization of scar-tissue or by cellular-functional imaging modalities.

In order to investigate a representative detection-rate of subendocardial scars, we excluded transmural scars from the ROC-curve analysis for subendocardial scars. In contrary, when comparing segments without LGE with segments with any amount of LGE, the AUC increased in our patient population. This may be a reason for higher AUCs in other studies on patients with chronic CAD. Higher detection-rates of subendocardial lesions are generally reported in patients with acute myocardial infarctions. However, lower strains are reported for acutely ischaemic subendocardial segments compared with dysfunctional unscarred segments. In the majority of acute myocardial lesions, ischaemic substrates may not include long-term stunning of chronic ischaemic areas, reducing the number of dysfunctional segments to the acutely infarcted territory.

The high overlap of PLS values from subendocardially scarred and unscarred tissue may be the main reason for the low detection-rates of subendocardial scars in chronic CAD patients, both with reduced and normal EF. Even though the detection-rate of subendocardial scars seems to be limited, global peak longitudinal strain (GPLS) has been shown to be closely related to the scar-load in hypertrophic hearts and after acute myocardial infarctions. Thus, GPLS may be an independent prognosticator for major adverse cardiac events also in chronic CAD, without localizing the segments with subendocardial LGE. This has to be further investigated.

**Limitations**

The number of LGE positive segments and patients with transmural scars was low, creating wide CIs for sensitivities and low PPVs on patient and segment basis. However, due to high specificities, NPVs and AUC displayed narrow CI reflecting reliable negative test-results in the average CAD population. Cutoff values for ROC curves were derived from postoperative tests. We assume that DS may activate postoperatively stunned myocardium, while hibernating myocardium before revascularization was not activated due to low blood supply. However, adjusting cutoff values for preoperative DS tests did not lead to significant changes in AUCs.

TVI strain analysis is time consuming and difficult to interpret, and have thus not yet reached broad clinical use. On the contrary, 2D-strain is being implemented in more user friendly systems. However, in the setting of stress tests with high heart rates and deterioration of 2D image quality, it was already in 2007 shown that TVI strain is equal and in some segments superior to 2D-strain. Since then, 2D-strain software and image quality have improved, but the problem

**Table 4  AUC for the detection of subendocardial and subtotal transmural infarctions**

<table>
<thead>
<tr>
<th>LGE 1–50%</th>
<th>LGE 51–75%</th>
</tr>
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<tbody>
<tr>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>WMS</td>
<td>713</td>
</tr>
<tr>
<td>DS: WMS</td>
<td>713</td>
</tr>
<tr>
<td>PLS (%)</td>
<td>713</td>
</tr>
<tr>
<td>DS: PLS (%)</td>
<td>713</td>
</tr>
</tbody>
</table>

**Table 5  AUC for end-diastolic and end-systolic wall-thickness by echocardiography and CMR predicting the segmental degree of ischaemic scars**

<table>
<thead>
<tr>
<th>All segments n = 749</th>
<th>LGE 1–50% (n = 23)</th>
<th>LGE 51–75% (n = 12)</th>
<th>LGE 76–100% (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n pos = 54</td>
<td>n pos = 12</td>
<td>n pos = 11</td>
</tr>
<tr>
<td>Cutoff (mm)</td>
<td>AUC (95%CI)</td>
<td>Cutoff (mm)</td>
<td>AUC (95%CI)</td>
</tr>
<tr>
<td></td>
<td>Cutoff (mm)</td>
<td>AUC (95%CI)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echo EDWT</td>
<td>9.0</td>
<td>60 (53–68)</td>
<td>8.0</td>
</tr>
<tr>
<td>CMR EDWT</td>
<td>7.5</td>
<td>59 (51–66)</td>
<td>7.5</td>
</tr>
<tr>
<td>CMR ESWT</td>
<td>11.5</td>
<td>69 (61–77)</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Segments with higher LGE value were taken out of the analysis of LGE 1–50% and LGE 51–75%.

AUC, area under the curve; CI, confidence-interval; EDWT, end-diastolic wall-thickness; ESWT, end-systolic wall-thickness; GPLS, global peak longitudinal strain; LGE, late gadolinium enhancement; PLS, peak longitudinal ejection strain; WMS, wall motion score; sys systolic; PLS, peak longitudinal ejection strain; DS, dobutamine stress; LGE, late gadolinium enhancement.
with high heart rates and limited frame rates in 2D-imaging is still not completely solved. Measuring strain at the endocardial border might render a more sensitive measure for segmental pathology. In the present study, only mid-myocardial strain could be measured due to the limited lateral resolution of TVI.

CMR EF was not performed due to time constraint. However, according to previous studies, the mean estimates of echocardiographic EF are with high probability consistent with CMR EF.26

Clinical implication and conclusion

If more than 10–12.5% of the LV-myocardium can be identified to be at risk, percutaneous treatment of CTO shows a clear survival benefit. The reopening of a CTO in the presence of viability in patients with less than two normo- or hypokinetic segments in the territory of an occlusion or high-grade stenosis, will indicate the significant presence of viable tissue at risk. In the presence of predominantly akinesia in the CTO region, especially when longitudinal function is generally reduced like with increased afterload in LV hypertrophy or dilated cardiomyopathy, the viability of viable segments in akinetic regions may be high, thus leaving echocardiography inconclusive, both by functional and EDWT assessments.

In unselected chronic CAD patients, with normal or near normal EF, echo WMS and PLS at rest excellently identify the absence of transmural scar-tissue. Dobutamine stress has no significant increase in EF, echo WMS and PLS at rest excellently identify the absence of global two-dimensional strain as a surrogate parameter of myocardial fibrosis and scar detection. Detection of predominant akinesia with less than two normo- or hypokinetic segments in the territory of high-grade coronary stenosis or occlusion warrants further examination by LGE-CMR.

Conflict of interest: none declared.

References